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The Indirect Costs of Depression on the Portuguese Population in 2014 and 2019

Mestrado em Gestão da Saúde

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This path was hard, and attitude was the key to drive me through motivation, hard times and fears. It lit the perseverance to go beyond the knowledgeable path and make it to success. This was certainly my driver, and I am glad I have reached my goal.

Might this work support the awareness and improvement of mental health care services.

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This dissertation is dedicated to my family, friends, and colleagues, so that they might all know that there is always a light at end of the tunnel, even when there only seems to be darkness around. May them all find that light in the darkest periods and might that light be anyone and any connection around ready to let them know how good and how valued they are.

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Abstract

Depression is a highly prevalent and very disabling disease. Different factors may contribute to its development and, even in mild cases, depression causes loss of productivity and generates high indirect costs to the society. Literature on the Portuguese context is scarce and not up to date. This study intended to provide additional and updated information on the indirect costs of depression due to absenteeism and on disease prevalence in the years of 2014 and 2019 for the adult population.

The study used data from the population-based National Health Surveys of 2014 and 2019 to study the prevalence, risk factors and association of depression to work absence. The indirect costs were estimated based on these data and on the average monthly earnings in Portugal from the Instituto Nacional de Estatística.

The prevalence of depression in the adult Portuguese inhabitants increased from 2014 to 2019 both in the general (13.7 vs 15.1%) and working populations (7.8 vs 9.2%). Having depression represented an additional work absence of 10.3 to 33.0 days in 2014 and between 15.2 to 41.0 days in 2019. The mean individual excess cost related to depression varied between 535.12 and 1,716.09 EUR in 2014 and between 852.45 and 2,291.11 EUR in 2019. These values may represent 163-524 million EUR in 2014 and 294-790 million EUR in 2019 when considering the Portuguese work force. These results demonstrate the importance of an intervention to improve the mental health care to the Portuguese society and implement cost-effective measures.

Key words: Absenteeism; Depressive Disorder/economics; Depressive Disorder/epidemiology; Adult; Portugal

Resumo

A depressão é uma doença altamente prevalente e incapacitante. Diferentes fatores poderão contribuir para o seu desenvolvimento e, mesmo em casos ligeiros, causa perdas de produtividade e origina altos custos indiretos para a sociedade. A literatura sobre o contexto português é escassa e não está atualizada. Este estudo pretendeu fornecer informação adicional e atualizada sobre os custos indiretos da depressão devida ao absentismo e a sua prevalência nos anos 2014 e 2019 nos adultos.

O estudo usou dados dos Inquéritos Nacionais de Saúde, de base populacional, de 2014 e 2019 para estudar a prevalência, fatores de risco e a associação de depressão à ausência ao trabalho. Os custos indiretos foram estimados com base nestes dados e no ganho médio mensal em Portugal de acordo com o Instituto Nacional de Estatística.

A prevalência de depressão nos residentes portugueses adultos aumentou de 2014 para 2019 na população geral (13.7 vs 15.1%) e na empregada (7.8 vs 9.2%). Ter depressão representou uma ausência ao trabalho adicional de 10.3 a 33.0 dias em 2014 e de 15.2 a 41.0 dias em 2019. O custo adicional médio individual da depressão variou entre 535.12 e 1,716.09 EUR em 2014 e entre 852.45 e 2,291.11 EUR em 2019. Considerando a força de trabalho portuguesa, estes valores podem representar 163-524 milhões EUR em 2014 e 294- 790 milhões EUR em 2019. Estes resultados demonstram a importância de uma intervenção para melhorar os cuidados de saúde mental à sociedade portuguesa e implementar medidas que sejam custo-efetivas.

Palavras-chave: Absentismo; Doença depressiva/economia; Doença depressiva/epidemiologia; Adultos; Portugal

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Abbreviations

95%CI - 95% Confidence Interval

aOR - Adjusted Odds Ratio

AUD - Australian Dollar

BDI - Beck Depression Inventory

BMI - Body Mass Index

CAPI - Computer-assisted Personal Interviewing

CAWI - Computer-assisted Web Interviewing

CES-D - Center of Epidemiological Scales

DALYs - Disability-adjust Years

DSM-IV - Diagnostic and Statistical Manual IV

EU - European Union

EUR - Euro

GBP - Great Britain Pound

GDP - Gross Domestic Product

HRSD - Hamilton Rating Scale for Depression

IHME - Institute for Health Metrics and Evaluation

ICD-10 - International Classification of Diseases, 10th revision

INE - Instituto Nacional de Estatística

ISCED - International Standard Classification of Education

MDD - Major Depressive Disorder

NHS - Portuguese National Health Survey

NUTS - Nomenclature of Territorial Units for Statistics

OR - Odds Ratio

OECD - Organization for Economic Co-operation and Development

PHQ - Patient Health Questionnaire

PHQ-8 - Patient Health Questionnaire of 8 items

PHQ-9 - Patient Health Questionnaire of 9 items

USA - United States of America

USD - United States Dollar

WHO – World Health Organization

WMHS – World Mental Health Survey

1. Introduction

Characterized by a sad mood and loss of interest in almost all activities, individuals with depression have a sense of lowered self-worth and self-confidence. Individuals tend to have reduced ability to concentrate and to think, fatigue, weight change, sleep disturbance and suicidal ideation. In severe cases, depressed patients may show symptoms of hopelessness and worthlessness. Depressive states impair ones social and occupational functioning (1) and will change the patient's perceived quality of life (2).

According to the World Health Organization (WHO), depression was the third cause of burden of disease worldwide in 2004 and was estimated to be the leading cause by 2030(3). The onset is usually gradual, but it can also occur abruptly. Throughout lifetime, individuals can experience several depressive episodes varying in number, duration and pattern and thus being unpredictable (4). The number of incident cases of depression has increased nearly 50% globally from 1990 to 2017 (5). Major depressive disorder (MDD) is the most common type of depression, corresponding to 97.3% of the patients with depression in 2017 (5), and has an overall 12-month prevalence of 6% (4). In Portugal, the prevalence of MDD was estimated to be 6.8% and of depressive disorders of 7.9% (6).

In addition to its high prevalence and to being highly disabling, depression is associated with high morbidity and mortality (7) leading to reduced productivity (8–12) and increased costs to society (13–15).

Even in mild cases, depression highly impacts the loss of productivity of patients, resulting in a significant incremental indirect cost due to the disease (16). Lower employment and lower productivity due to mental ill-health, were responsible to estimated indirect costs equivalent to 1.6% of gross domestic product (GDP) across European Union (EU) countries in 2015. Between direct and indirect costs and social security programs, the Organization for Economic Co-operation and Development (OECD) estimated that it can exceed 4% of GDP in total (17).

Upon a literature search for country-specific studies regarding the economic cost of depression to the Portuguese population, it was identified that there is a lack of studies on this subject. Regarding the Portuguese context, only an article was found referring to the estimated costs of depression in 1992 for the Portuguese society. Thus, the aim of this observational cross-sectional study is to assess the indirect costs associated to depression for the adult population in the years of 2014 and 2019, estimated by the work absence. Moreover, this study intends to provide a comparison of the prevalence of

depressive disorders in the adult Portuguese population in the years of 2014 and 2019 and a characterization of the groups of population with and without reported depression and the differences from 2014 to 2019 based on some demographic, economic and health-related variables that might be related to higher prevalence of depression.

With this work, the author expects to provide important updated information on the characteristics and the economic burden of depression in the Portuguese society that could support decision-makers on the implementation of more effective and preventive measures to improve population's mental health and to build health and social plans capable of providing the needed support to this population, particularly in times of need such as economic hardship periods.

This work is organized as follows. After this brief introduction to the theme in Chapter 1, Chapter 2 presents an overview of the theoretical framework on the prevalence and incidence of mental health disorders and depression, the risk factors of depression, its adverse effects in the labour market and indirect costs. Chapter 3 describes the methods, identifying the databases and study variables used, as well as the statistical analysis performed. Chapter 4 is dedicated to the results on the main goals of this study, general adult and employed Portuguese population characterization and indirect costs estimations for the years 2014 and 2019. In Chapter 5, the study results will be reviewed and compared with the information available in literature. The main conclusions and outcomes coming from the study will be addressed in Chapter 6. References used in the study are listed in Chapter 7 and in Chapter 8 (Appendix) additional information complementary to the one provided in the previous chapters will be available

2. Theoretical Framework

a. Mental Health and Depression

In 2016, around 16% of the global population was affected by mental and addictive disorders, with particular emphasis on the population of high-income countries (18). Only as few as 17% of the population does not experience a mental disorder through adolescence and adulthood (age 38) (19). According to data from the Institute for Health Metrics and Evaluation (IHME), in 1990 the prevalence of mental disorders was 12.7% worldwide and 19.4% in Portugal. The prevalence has been mostly stable ever since. At a global level, it has increased to 13.2% in 2004, then decreased to 13.0% in 2014, reaching a steady state with a similar value until 2019. In Portugal, the prevalence has increased throughout the years, reaching 20.0% in the year 2000, then decreasing to 19.0% in 2015 and increasing again to 19.3% in 2019. Between 2008 and 2009, the first and only general population survey of psychiatric morbidity was conducted, using a country representative sample of the Portuguese population. The survey revealed similar results as the ones reported previously, with 22.9% of the Portuguese population inquired presenting with a mental disorder in the 12-months period preceding the interview and the estimated lifetime prevalence being of 42.7% (6).

In terms of incidence rate of mental disorders, in 1990 it was 8,093/100,000 in Portugal and 4,502/100,000 worldwide. Worldwide, the incidence rate showed a very slight variation with an increase to 4,866/100,000 in 2005, followed by a decrease to 4,652/100,00 by 2010 and then initiating a slight increase and being at 4,801/100,000 in 2019. The incidence rate followed a similar trend of prevalence in Portugal. It raised to 9,091/100,000 in 2000, decreased to 7,439/100,00 in 2015 and had a slight increase to 7,813/100,000 in 2019 (20).

Depression is one of the most common mental disorders (21) and has a higher prevalence in high-income countries (22) . A meta-analysis estimated that from 1994 to 2014 the aggregate point prevalence, one-year prevalence and lifetime prevalence were 12.9%, 7.2% and 10.8%, respectively. Additionally, it was found that the aggregate point prevalence was significantly higher in the studies from 2004 to 2014 (15.4%) than in those published from 1994 to 2003 (9.8%). (23) When analysing the global number of incident cases of depression, the increase observed from 1990 to 2017 was nearly 50%, from 172 to 258 million incident cases. (5).

According to the IHME's data, in 1990 the prevalence of depressive disorders was 3.3% worldwide and 5.8% in Portugal. At a global level, the prevalence has been roughly stable with only some slight variations, reaching its highest value of 3.8% in 2019. In

Portugal the prevalence has increased until the year 2000, reaching a maximum of 6.7%, and then a decreasing trend was observed with the value being fixed at 5.9% in 2019. The country representative survey done between 2008 and 2009 in the Portuguese population indicated a prevalence of 7.9% (6). Furthermore, when considering, MDD, the most common type of depression, corresponding to 97.3% of the patients with depression in 2017 (5), the prevalence in the Portuguese population was estimated to be 6.8% (6).

The incidence rate of depressive disorders in 1990 was 6,597/100,000 in Portugal and 3,405/100,000 worldwide. At a global level the incidence rate has had mild variations reaching a maximum value of 3,797/100,000 in 2005 and initiating a new increasing trend in 2011 and being at 3,750/100,00 in 2019. In Portugal, the incidence rate has reached a peak at 7,688/100,00 in 2000, followed by another peak at 6,978/100,00 in 2010 and being currently in an increasing trend since 2016 and a with a value of 6,569/100,000 in 2019.(20).

Despite the prevalence of depressive disorders being higher among managers, tradespersons are those with higher work impairment (24). Working populations usually have milder forms of depression and whose symptom severity is increased later in the day and possibly due to fatigue exacerbation and reduction in cognitive abilities (25). Employed people are less affected by mental disorders than unemployed people. In 2013, 22.3% of the unemployed adults in the United States of America (USA) had at least one mental disorder where, on the other hand, full-time employed adults had a frequency of 15.4%. The frequency of any mental disorder was also higher among adults with lower income, ranging from 26.1% in those with a family income below the Federal poverty level, to 16.0% among those with income at 200% or more of the Federal poverty level (26). In the German population, it was concluded that unemployed individuals receiving means-tested benefits had almost twice the risk of depression when compared with the employed population. The frequency of depression in the unemployed receiving means-tested benefits was 21.2% compared to 5.7% in the employed individuals. In the unemployed population receiving entitlement-based benefits, the frequency of depression was 11.3% (27). In Finland, a population-based study in 2000 identified a prevalence of depressive disorders in the unemployed population (11.9%) greater than in the economically inactive population (7.9%) and in the employed population (6.4%) (28). Another Finish study identified that individuals pertaining to groups with higher risk of permanent exit out of paid employment have higher incidence of sickness absence due to mental disorders than those with permanent job (29).

The population's mental health can be studied based on indicators such as suicide rates, hospitalization rates, healthcare resources utilization rates or using self-reported data, for instance from national surveys, regarding mental disorders and health services (30). There are several screening instruments used in the measure of self-reported diagnostic depressive disorder being the most frequently used the Beck Depression Inventory (BDI), the Hamilton Rating Scale for Depression (HRSD), the Center of Epidemiological Scales (CES-D) (31,32) and more recently the Patient Health Questionnaire (PHQ) of 9 items (PHQ-9) (33). With exception for the HRSD that is for clinician administration only, the other scales are composed by a set of items considering Diagnostic and Statistical Manual IV (DSM-IV) criteria for the diagnosis of depression and can be self-administered (34–37). Although the scales are used interchangeably, there is a low overlap among them, which challenges the replicability and generalizability of depression research (31,32). Different screening methods produce different estimates (38,39). To surpass the wide variability of prevalence estimates across studies, the WHO organized cross-national community epidemiological studies, the World Mental Health Survey Initiative (WMHS). All the participating countries had trained lay interviewers using the WHO Composite International Diagnostic Interview (CIDI) screening scales to generate diagnoses of DSM-IV disorders (7,40). In addition to generating diagnoses based on DSM-IV criteria, the CIDI also permits diagnoses to be based on the International Classification of Diseases, 10th revision (ICD-10) criteria(41). Besides the diagnosis based on scales, it can also be done by physicians using the criteria established by the DSM-IV or ICD-10 or any other version of the documents implemented by the time of the diagnosis(14,15,42,43).

For those with mental disorders, and particularly those with depression, it means an increased risk of morbidity and mortality. These patients are at a higher risk of attempted suicide and of committing suicide (7,44,45) and depression is also significantly associated with several chronic physical disorders, being either the consequence and cause of subsequent onset and worsening of disorders such as hypertension, diabetes, arthritis, cancer, asthma and other chronic respiratory disorders, chronic pain conditions and particularly cardiovascular disease (7,46,47). As a coping mechanism, people with depression are more likely to engage in hazardous alcohol use (48). Despite the increased risk of premature death associated to depression (7), the associated mortality is not directly attributed to mental disorders but rather to the cause-specific mortality that does not consider the underlying disorders (49,50). Therefore, the excess deaths associated to mental disorders are not accurately represented and are underestimated in the commonly used mortality indicators (49,50). The elevated risk of mortality is not

only associated with major depression but also in subclinical forms, being a life-threatening disorder in some cases (51). Depressive disorder is responsible for a 70% increase in the risk of all-cause mortality (52). Even though, mental disorders are not particularly fatal when compared with other diseases, in example, cancers, cardiovascular and chronic respiratory diseases and diabetes, they are however associated with high disability rates. It is then important to consider the years of life lived with disability in addition to the years of life lost due to premature mortality, meaning assessing the disability-adjusted life years (DALYs). The DALYs can provide a more complete picture of the impact of mental disorders (18). Disability in patients with depression is relatively chronic and stable and increases during depressive symptomatology, returning to premorbid levels after symptomatic recovery. Those with a longer duration of recovery have their functioning in daily activities and at work improved (53). In the Portuguese population, 21.6% of the individuals with a mood disorder reported disability during the WMHS taken place between 2008 and 2009(54). Whilst a decrease on age-standardized rates of DALYs and deaths were observed between 1990 and 2016 for all diseases, an increase was observed for mental disorders until 1995 for deaths and until 2005 for DALYs and has been more or less stable since then (18). In Portugal, however, the number of deaths reduced until 2000 while DALYs increased. After 2000, a continuous reduction in DALYs was observed with the rate being similar to that observed by 1990. The burden of disease due to depressive disorders in 2019 was 577.75 DALYs per 100,000 population in the world and 787.15 DALYs per 100,000 population in Portugal (20).

Furthermore, individuals with depressive disorders are affected in other domains of their lives. Depression is associated with higher risk of educational failure and lower personal earnings and household income. In terms of marital functioning, these patients have higher marital dissatisfaction and discord, lower probability of marrying and higher risk of divorce. Depression seems to be associated as well with negative parenting behaviour. Work disability, greater risk of unemployment and higher number of days out of role are other adverse consequences of depressive disorders (7).

b. Risk Factors

A variety of factors were identified to be associated with depression. Among the sociodemographic factors, gender is known to play a significant role, with females being at an increased risk compared to males (7,22,55–57). Depression is typically negatively associated with age. Although the prevalence of depression is higher among younger

population and lower among the elderly in high-income countries, the opposite is observed in several middle and low-income countries (22,40,55,57,58). Marital status is associated with depression as well. Individuals that are divorced, separated or widowed are at an increased risk of depression compared to the married ones (22,40,55,57,59). However, this seems to be only applicable to males and the odds ratio decline with age (59). The education level seems to be associated with the onset of depressive disorder, despite conflicting evidence was found in different regions. Overall, those with less education are at higher risk (22,55,57,58,60).

Concerning the economic factors, evidence was found in high-income countries that individuals in the lowest income groups have an increased risk of depression (22,40,55). In addition, employment status is also associated with depressive disorder and unemployment is both a risk factor (7,57,60–63) and a consequence of depression (40). Employed workers (either part-time or full-time) with perceived job insecurity have higher odds of MDD, particularly full-time men workers (1,64). Although the work environment may provide a protective effect against depression by providing social support, increasing self-esteem and sense of purpose and the like, it may as well be a risk factor for depression through the psychological demands of work, in example, faster, harder and excessive work, insufficient time to complete it and conflicting demands (1,65). Additionally, depressive symptoms may increase through time when there is lack of decision latitude, job strain and bullying at work (65,66). Cultural and organizational characteristics of the workplace seem to play role in productivity though the influence they might have in the employees' experience and consequences of depression. Support and openness of managers and flexible working hours help offering the supportive environment these patients need to feel comfortable to disclose their condition (67). Overtime workers (working more than 40 hours per week) are exposed to an increased risk of depressive disorders with findings suggesting a dose-response relationship with work hours (56,65,68,69). Working less than 20 hours per week seems to be associated with a higher prevalence of depression as well (69). Other negative features in the work environment such as unfavourable social climate, conflicts with co-workers, low support, effort reward imbalance, lack of procedural and relational justice, limited skill discretion and job insecurity may contribute to increase the risk of depression (65).

The neighbourhood environment in which the individuals are inserted plays an important part in the development of depressive disorders. The neighbourhood socioeconomic conditions seem to be associated with depression, although evidence is inconsistent and might be impacted to specific neighbourhood conditions and evolution through time of individual characteristics (70). Living in areas with lower median neighbourhood income

(60), adverse living environment (poor housing quality and non-functioning, lack of green spaces, noise and air pollution) (71), higher unemployment rates and higher proportions of visible minorities and more cultural community centres or community organisations (55), and conflict affected areas (72) are associated with an increased risk of depressive symptoms. Family history of mental health disorders was similarly found to be positively associated with depression (55).

The social environment of modern societies is characterized by lower social support, increased individual competitiveness and greater inequalities. This in turn may expose individuals to more frequent and/or intense stressful events and thus making them more susceptible to depression (73). Modern societies lower exposure to bright light and insomnia lead to circadian dysregulation and are a cause of depressive disorders (73) with insomnia doubling the risk of developing depression (74).

In what concerns the effect of diet in depression, evidence was found that tea, coffee and caffeine consumption are associated with a lower risk (75) and overweight, particularly obesity, (73,76,77), occasional alcohol consumption (55,76,78,79) and smoking habits (76) are associated with a greater risk. On the other hand regular physical activity was found to be a protective factor for depressive disorder (73,76,80,81). As referred before, depression is associated with other physical disorders being either a consequence or the cause of those. Multimorbidity, and in particular cardiovascular disease, diabetes and arthritis, is associated with elevated risk of depression (82).

The childhood environment is also an important factor in the risk of depression during adulthood. Childhood poverty and lower childhood physical health and cognitive ability are associated with risk of mental disorder during adulthood. Further to this, children that are less exposed to emotional difficulties and social isolation and higher self-control tend to have enduring mental health (19).

It is important to mention that some factors may increase the risk of depression recurrence, although the demographic variables as sex, socioeconomic status and marital status are not risk factors. The risk of recurrence is increased by factors such as age at onset and number of prior episodes, severity of the first/index episode, family history, comorbid psychopathology and psychological and psychosocial variables (poor social support, negative cognitions, high neuroticism and stressful life events) (83).

c. Adverse Events in Labour Market

Mental disorders, and particularly depression, are highly disabling (84) and, even in mild cases, depression is associated with loss of productivity and represents a significant increment in indirect costs(16). Loss of productivity may come from absence to work

(absenteeism) and/or reduced functioning at work (presenteeism). Having depression represents an additional risk of absenteeism and presenteeism (8,9,24,85–87). Psychological distress may result in a net productivity loss of 6.7% by increasing absenteeism by 1.7% and decreasing in 6.1% the work performance (88). Lower levels of absenteeism are observed within those with higher income, higher levels of education and individuals of middle age (compared to young age). Higher levels of education are also associated with lower levels of presenteeism. Those who did not disclose depression to the employer due to fear of losing their job had lower levels of presenteeism due to depression. On the opposite side, individuals in countries with higher prevalence of the disease had higher levels of presenteeism as well as individuals with higher incomes (12).

At a global level, per year, a patient with depression is out of role 34.4 days in mean, representing 9 additional days when compared with those without the disorder and ranging from 4.1 additional days in higher income countries (in which Portugal is included) to 13.1 days in lower income countries and 14.7 days in medium ones (85). Other studies obtained different results. In the Dutch population, a study conducted between 2007 and 2009 associated 19.8 days additional days out of role to major depression (86). In the USA, between 2001 and 2003, MDD was associated to 8.7 workdays of work absence (89), while another study from 2002 associated 0.6 hours additional hours per week of work absence with depression (69). In Portugal, data collected between 2008 and 2009 associated depression to additional 0.2 days per month of work absence, representing 1.9% of the total work absence days in the population (90). The results may differ due to lack of standardized reporting methods, and, according to Lerner and Henke, values may vary between 0.3 and 3.8 missed workdays per month(8). In the USA population, patients with depression had 2.37 times the odds of spending in bed at least 10 of the missed work days comparing to individuals with no mood disorder (91).

Patients with depression have significantly higher odds of physical (2.46), social (2.85), cognitive (3.97), work (3.19) and household (2.71) limitations that may affect their productivity at work (91). In addition to work absence, a patient with depressive disorder experiences both quantitative and qualitative reduced functioning. Qualitative functioning is reduced in 10.0 days annually and, between absenteeism and presenteeism, an individual with MDD may have a productivity loss of 25.6 additional days in a year. When looking at population-level in the Netherlands, depression represents 4.5% of total work loss days (86). In the USA, MDD was associated to 18.2 days of presenteeism in 12 months (89). Another study from 2002 in the USA population identified that workers with

depression had a significantly higher loss of productive time than those without the condition. Those patients had a mean of 4.1 additional hours per week of loss of productivity, being 3.5 due to presenteeism. This loss was even greater within patients with major depression, 8.4 hours per week, followed by those in partial remission, 5.3 hours, being those with dysthymia the ones less affected by productivity losses (3.3 hours per week) (69). In the South Korean population in 2005, workers with depression had a mean of 2.0 work loss days per month (92).

Beyond productivity losses, depression is a cause of functional limitation, either full or partial disability (considered as either reduced quantity or quality or extreme effort in daily work). Data from WMHS of 26 countries associated depression with an increase in 1.65 days of partial disability per month (93). For Spain, data from the WMHS found that depression was associated to 24.5 additional days of full role limitation and 44.0 of partial role limitation in 12 months (94). In the Portuguese population, those with MDD had 3.49 higher chances of disability after adjusting for age, gender, education, presence of any physical disorder and any other mental disorder (54).

Job performance deficits come from different domains such on mental-interpersonal tasks, time management, output tasks and physical tasks and is decreased by 20% (8,9,25). Also, the task focus is decreased (25). The greater the depression severity and its symptoms duration, the higher the work disability and the impact on the job performance. Further to this, although individuals may improve job performance with clinical improvement, they do not fully recover it (8,10,16,95,96). Patients in remission showed less days of work disability compared to those without remission (31.0 vs 38.5) (2). The fact that full-time workers have a greater productivity loss than those working part-time might be explained by less schedule flexibility, the need to use sick leave days and the higher exposure to depression symptoms while working full-time (16). Men and younger workers presented lower task focus and productivity (25), although employees older than 35 years old had more recurrent episodes of work disability than those aged between 21 and 34 years old. Episodes of work disability were less frequent among workers with higher education and aged 50 or less years (69,97). As it would be expected, the impact in work productivity is enhanced by the presence of other mental or physical comorbidities (86).

According to data from the 2002 World Health Survey of the World Health Organization, 8.4% of the European population was estimated to not be working because of depression (without any other comorbidity) (98). Impaired job performance, among other factors, may partially explain the higher rates of unemployment in patients with depression. Patients with depressive disorders experience significantly more job loss (8–10).

Individuals diagnosed with depressive disorders experienced an additional 6 days per year unemployment compared to others without the disease (99) and the proportion of employed patients decreased by 20% during a follow-up at 5 years (10).

In addition to the direct disabling effect of the mental disorder, the high unemployment rates can be further justified by how mentally ill individuals perceive themselves and how they are perceived by either employers and colleagues (87). Stigma plays as well an important role influencing access to jobs, social networks, and self-confidence (100). Although there is a correct general awareness about mental health, people with depression still face social stigmatization (101–103) and there might also exist a cultural reluctance in disclosing depression (12). Stigma leads to discrimination when hiring people with mental disorders regarding their competence and particularly to work with vulnerable groups such as children and occupying positions of authority or power (87,104,105). High levels of stigmatization are further observed regarding potential for self-directed violence, intimate settings as becoming part of family and apprehension on how to interact with individuals with depression (104). Working through exclusion and rejection, stigma puts people with mental illness at risk of losing important protective factors such as social and psychological resources and exposing them to stress and increasing the risk of prolongation or recurrence of mental illness (100). Further to increase the risk of unemployment, poorer mental health increases the odds of subsequent unemployment. Something that seems cyclical as unemployment itself aggravates the individual's mental health (10,106–108).

Depressed individuals that experienced job turnover had also higher probability of accepting a lower paying job due to health reasons and have lower chances of increasing their income (9). Furthermore, workers above 50 years are less likely to return to work after a disability episode (97). On average, depressed individuals retire 1.5 years younger than those non-depressed (109). Schofield et al. found that workers aged 45 to 64 years who retired early due to depression had a 73% lower income comparing to those without comorbidities working full time (11).

In addition to the reduced income generated by loss of productivity and unemployment of the population with depression, history of adolescent depression, specifically persistent depressive disorder, mediated by recurrent depression in early adulthood results in reduced adult earnings of 15% for females and 24% for males. The difference between depressed and non-depressed population is more marked in the lower percentiles of the earnings distribution and gradually increases through age as the general earnings increase (110). When compared to non-depressed full time employed individuals, those that retired earlier due to depression at ages between 45 and 64 years

had a 73% lower income (11). Leaving labour force earlier also leads to financial difficulties as people who retire due to depression have significantly less accumulated savings by the retirement age of 65 (111).

d. Indirect Costs

Depression is a highly incapacitating disorder that, in 2015, represented 7.5% of all years lost to disability and was the single leading cause of global disability(21). In addition, depressive disorders are strong contributors of all-cause mortality and particularly of suicide(50,112). The high prevalence(22) and its impact on functioning are the main causes of high costs associated to depressive disorders(13). It is however of notice that the association with mortality decreases after remission(113) which emphasizes the importance of early diagnosis and appropriate treatment of the depressive episodes. Although the awareness of this need has increased, depression still requires attention from health providers and politicians considering that, in example, only as few as 1 in 5 people with MDD received minimally adequate treatment in high-income countries, in which group Portugal is included(114). Patients with depression also tend to utilize significantly more health care resources (exams, in- and outpatient visits, hospitalization and medication) leading to higher direct costs(2,115,116). Cost of Illness studies can also take into consideration other non-medical direct costs such as transport ad social services(15). According to recent meta-analysis, direct costs of depressed individuals were 158% higher than those without the disease and excess costs ranged between 124 and 18,174 United States Dollar (USD)(14). Hospitalization costs represented 43 to 75% of the direct costs(15).

This burden increases particularly during periods of economic crisis during which the prevalence of mental health problems increases due to a strengthen in risk factors such as unemployment, job insecurity, indebtedness, and financial deprivation(117,118). To deal with the financial distress, individuals might increase alcohol consumption, smoking and illicit substance usage habits as coping mechanisms(117). Furthermore, the demand for care at general care level, use of prescription drugs and hospital admissions for mental disorder are also increased in patients facing depression(119). The need to actively treat patients with mental disorders is further justified as these patients are at higher risk of experiencing financial hardship and decreasing their socioeconomic status during economic recession then those without any mental disorder(120).

Societal costs related to depression may come from its treatment and the time spent under treatment, other healthcare resources utilization, premature death due to suicide,

productivity costs with absenteeism, presenteeism and unemployment, and the eventually affected educational attainment may lower the earning potential. From these costs' domains, the greater economic burden is related to indirect costs resulting from absenteeism and presenteeism that represent more than 60% of the total costs(13). The indirect costs are significantly higher in cases of treatment resistant depression and can be twice as high(121,122). Presenteeism costs tended to be 4 to 10 times greater than those with absenteeism (12,69).

According to the OECD, the indirect costs of mental ill-health, based on lower employment and lower productivity, are estimated to be equivalent to 1.6% of GDP across EU countries in 2015. These costs added to social security programs (1.2%) and direct spending on health system (1.6%) can exceed 4% of GDP in total (17).

Upon a literature search for country-specific studies regarding the economic cost of depression to the Portuguese population, it was identified that there is a lack of studies on this subject. None of them presented a review of the costs of depression in Portugal. From the reading of additional literature on this field of interest, only an article was found referring to the estimated costs of depression in 1992 for the Portuguese society. According to that study, the total costs represented the equivalent to 1,230 million euros (EUR), assuming a mean prevalence of depression in 17.5% of the population. From the total costs, the direct costs (health care resources use) only represent 17% of the amount and the costs related to suicide 3% (123).

In Europe, indirect costs of mood disorders (MDD and bipolar disorder) represent more than 60% of the total costs. The indirect cost per patient in Europe in 2010 was estimated as 2,161 EUR and the total cost 3,406 EUR(124). Another study, considering the European Union (EU) plus Iceland, Norway, and Switzerland, in 2010, estimated major depression to be responsible for an indirect cost per patient of 1,782 EUR and a total of 53,996 million EUR (around 60% of the total costs incurred)(125) .

The indirect costs associated to productivity losses due to MDD in Spain were estimated to be 1,809.6 EUR in 2006, representing 67.1% of the total costs. These values differed from patients in remission (1,631.5 EUR) and not in remission (2,024.2 EUR)(2). In the Catalonia population in 2006, the cost of productivity loss due to sick leave was close to 200 million EUR, or 6,013 EUR per individual, and accounted for 27.1% of the total costs. Indirect costs represented 78.8% of the total costs and permanent disability represented 60.9% of the indirect costs, sick leave 34.4 and premature death 4.6%(126).

A study in the Dutch population between 2007 and 2009 associated major depression with a 12-month prevalence of 4.2%, to a cost of 1.1 million days and 242.4 million EUR

to the Dutch society in terms of total annual work loss per million workers(86). Another study in the Netherlands with data from 2003 estimated the indirect costs (considering productivity losses at work due to absence and at the domestic sphere) per capita of minor depression 2,101 USD (an excess cost of 1,093 USD) and of major depression 2,535 USD (an excess cost of 1,527 USD), representing 98.1% and 76.5% of the total costs, respectively(127).

In England, for an estimated depression prevalence of 7.0% in females and 2.9% in males, total lost earnings due sick leave in 2000 were estimated to be over 8.1 billion Great Britain Pounds (GBP) (and 3,052.1 GBP per individual) and represented 89.7% of the total costs(128).

When considering total USA civilian labour force yield, the loss of productivity per year associated to major depression, between 2001 and 2003, was estimated on 225.0 million workdays and 36.6 billion USD in terms of salary, considering an identified 12-month prevalence of 6.4%(89). Another study from 2002 in the USA population estimated a 2-week prevalence of depressive disorder of 9.4% and its associated cost of loss of productivity on 30.94 billion USD per year to the employer, with 18.9% of the value (4.37 billion USD) coming from costs due to absence to work. Furthermore, major depression accounted for 48.5% of that total amount(69).

In the South Korean population in 2005, despite the lower prevalence (2.5%), MDD represented a total cost 3.0 billion USD with loss of productivity representing 73.1% of the costs (1.1 billion USD due to absenteeism and 1.8 billion USD due to presenteeism at workplace)(92).

Chisholm et al. performed a multinational study between 1998 and 1999 and the estimated costs of work absence per person were 515 USD in Seattle (USA), 279.2 USD in Be'er Sheva (Israel), 276.4 USD in Melbourne (Australia), 256.2 USD in Barcelona (Spain), 58.8 USD in Porto Alegre (Brazil), and 9.3 USD in St. Petersburg (Russia)(129). A study from 2013 reported annual productivity costs per person associated with absenteeism due to depression of 1,567 USD for Canada, 1,361 USD for Brazil, 928 USD for Mexico, 894 USD for South Africa, 390 USD for USA, and 136 USD China. On the other hand, presenteeism due to depression was responsible for the following productivity annual costs per person: 6,066 USD for South Africa, 5,788 USD for Brazil, 5,524 USD for USA, 4,270 USD for Canada, 3,801 for Japan, 2,918 USD for Mexico, 2,114 for Korea, and 547 USD China. (12)

In the Australian population, 40% of the employed population took days off from work due to depression and an average of 35 working days of work absence. This represented a cost of 43 million Australian Dollar (AUD) due to productivity losses (130).

In addition to work absence and reduced productivity at work, additional indirect costs may come from premature mortality. Costs due to premature mortality accounted for 384,708 EUR per individual and close to 27 million EUR in total (considering that 45% of the completed suicides are due to depression) in the Catalonia's population(126). In South Korea, this value represented 921.6 million USD in 2005, considering a rate of 60% of suicides due to depression(92). In 2000, the estimated cost to the English society resulting from premature death represented a loss of 562 million GBP (and 214,971.7 GBP per individual), with 70% of suicide cases being attributed to depression(128).

The other domain of the indirect costs is unemployment. In Australia, 39% of the population with depression was unemployed, generating a productivity loss costing 822 million AUD(130). Early retirement due to depression between those aged 45 to 64 years old represented an annual income loss of 1 billion AUD (0.55 billion GBP) to Australia in 2009(11). In Catalonia, permanent disability led to an estimated loss of productivity costs equivalent to 353 million EUR or 20,420 EUR per individual(126).

According to a recent meta-analysis, indirect costs (due to absenteeism and presenteeism) of depressed individuals were 128% higher than those without the disease and excess costs ranged between 153 and 12,374 USD(14). According to a literature review from 2007, mortality costs ranged from 200 to 400 USD(15).

Discrepancies between studies may be due to different approaches utilized in the estimations. It may come from depression estimation, if used prevalence or incidence data. Most of the studies are based on prevalence data and may differ on the time frames used for quantification as well as on the approaches for identification. Depression cases can be identified using those already diagnosed by a physician/psychiatrist and identified in the health system or through structured interviews or depression scales part of a study protocol. Another point of difference is the type of samples used. Individuals might be selected using population-based, primary care or specialized care samples and this might have an additional impact in terms of the disease severity of the individuals being selected. Costs' estimations may also differ between studies. These can be done per capita or national cost studies and through two methodological approaches: bottom-up, based on the individual resource's consumption, or top-down, using national health statistics and combining prevalence rates and relative risks from and costs of inpatient and outpatient services and number and cost of prescriptions. Data can be obtained from

different sources, such as databases of health care providers, physician's electronic medical records or using cost diaries. Another source of heterogeneity is the fact that the studies are being conducted in different countries and regions with different health and social systems and the multiplication of the appropriate values by the number of services will lead to differences in the monetary valuing of direct and indirect costs. The costs will depend on the market prices, fees or costs on the basis of the accounting system and the earnings in the region/country of the population sample. Studies might do a comparison between disease and non-disease populations whose differences between costs provide the disease-specific costs or excess costs(14,15).

Indirect costs are usually calculated using the Human Capital method. This approach measures the loss of production for society in terms of loss wages that can be either based on the average earnings in a region, considering the patient's occupation, age and gender salary level, or it can be the real earnings of the employee. Studies may also include estimations on unpaid work. Indirect costs' estimations might include costs on loss of productivity due to morbidity or to mortality. Morbidity costs may refer to loss of productivity due to work absence or reduced productivity at work. Early retirement from work can also be included in the estimations of loss of productivity. Mortality costs are based on assumed suicide rates due to depression(15).

e. Research Question and Objetives

At the start of this study, the main question posed to conduct the analysis was how work absence due to depression resulted in higher indirect costs. The main objective of the study is to quantify the excess costs of work absence in people suffering from depression in two moments, 2014 and 2019, in the Portuguese population. Knowing these costs might help raising awareness of this health problem and the potential gains with its treatment.

As a secondary objective, this study pretended to characterize the groups of individuals with self-reported depression in the general adult and employed Portuguese population in the years of 2014 and 2019. The characterization was done based on the analysis of the following variables: gender, age, education, marital status, employment status, salary range, work absence, overweight, tobacco and alcohol consumption, physical activity, number of comorbidities and healthcare utilization. This information might help identify convergent areas of action that can further support the improvement of mental health in the Portuguese population.

3. Methods

a. Study Design

In order to estimate the indirect costs of depression resulting from work absence in the adult Portuguese population, data from cross-sectional observational studies, the Portuguese National Health Survey (NHS) from 2014 and 2019, was used. The same data was used to determine depression prevalence and days of work absence, as well as other information for the population characterization. Being population-based studies, the NHSs provide a country's representative sample and enable a more accurate estimate of disease prevalence in Portugal. Data from 2014 and 2019 will enable us to understand how the disease prevalence and its costs evolved during a time of economic growth and decrease of unemployment rates after an economic crisis in 2008 and prior to a new one due the COVID-19 pandemics in 2020(63). To calculate the work absence costs, the average monthly earnings in Portugal were obtained from the ecological data published by the from Instituto Nacional de Estatística (INE)(131).

b. Databases

The data collected during the NHS from 2014 and 2019 was used in order to study the prevalence of depression and the sociodemographic and health related characteristics of the adult Portuguese population.

The NHSs are population-based surveys containing questions on three main domains: health status, health care and health determinants related to lifestyle. They are administered to individuals aged 15 years or older and residing in the Portuguese territory within a reference period. Based on accommodation units that were defined by the data from the 2011 Population and Housing Census, the sampling method followed a multistage, stratified and cluster sampling per region and sub-region NUTS (Nomenclature of Territorial Units for Statistics) Level 2. The households were randomly selected and only one individual per household completed the questionnaire (method of the last birthday prior to the survey). The sample size took in account a homogenous distribution of the participants in order to be representative at the regional level. The surveys were administered using either computer-assisted personal interviewing (CAPI) or computer-assisted web interviewing (CAWI) (132,133).

On 2014, 22 538 households were contacted for the NHS between September 10th and December 15th, with an overall response rate of 80,8% corresponding to 18,204 valid answers(132,134). On 2019, 22 191 households were contacted and for the NHS

between September 16th and December 20th, with an overall response rate of 65,9% corresponding to 14 617 valid answers(133,135).

To estimate the indirect costs with depression in 2014 and 2019, data from INE on the average monthly earnings in Portugal (131) was used for the referred years. As data on the average monthly earnings for 2019 was not yet available by the time of the analysis, this was calculated based on the value from 2018 and applying the inflation rate for 2019. The calculation was done using the INE's tool to estimate the value update between two periods based on the rates of change of the consumer price index (136).

c. Study variables

The variable of interest in this study was the presence of depression, based on data available in the NHS from 2014 and 2019.

As a main variable, depression was assessed using the self-reported occurrence of depression on the last 12 months prior to the completion of the NHS.

As an alternative method, the occurrence of depression was assessed using the answers in the mental health section of the NHS based someone certain symptoms and feelings in the 2 weeks prior to the completion of the NHS. The items in this section were transposed to the PHQ of 8 items (PHQ-8) and its score used to estimate the presence of depression. The PHQ is a self-administered instrument used for diagnosis of depressive and other mental disorders based on criteria from the DSM-IV, whose 9 item version (PHQ-9) has been confirmed as a reliable and valid diagnostic algorithm and a tool for the measurement of depression severity ((37,137). The validity of PHQ-9 was also confirmed in the Portuguese population (138). The PHQ-8 is a depression scale like the PHQ-9 with exception for the ninth item on self-harm and death thoughts that is omitted. The deletion of this question has a minor effect on scoring, as suicidal ideation responses are rare in the general population. The PHQ-8 scale has good sensitivity and specificity, and has comparable operating characteristics to the PHQ-9 in terms of diagnosing depressive disorders, being particularly useful in epidemiological studies (37,139). Current depression could be defined in two ways: 1) based on a PHQ-8 algorithm diagnosis of major or other depression; 2) a PHQ-8 score of ≥10. For epidemiological studies, the cut-point approach is sufficient and a score of ≥10 in the PHQ-8 represents a clinically significant depression, with 88% sensitivity and 88% specificity(139). To assess the prevalence of depression, the score method was used. Additionally, depression severity was assessed and presented using the follow thresholds of the PHQ-8 score: 0-4 (None-minimal); 5-9 (Mild); 10-14 (Moderate); 15-19

(Moderately Severe) and 20-24 (Severe) (37,137,139). For the purpose of the bivariate analysis and odds ratio (OR) calculation for the general adult and employed populations characterizations, self-reported depression was the dependent variable used.

In the characterization of the Portuguese adult population, a descriptive analysis was performed using data from the NHS from 2014 and 2019 for the following demographic, socioeconomic and health related variables:

Demographic variables:

- **Gender:** male; female
- **Age group:** data was recoded to obtain the following age groups: 18-24; 25-34;35-44; 45-54; 55-64 and more than 65 years.
- **Education:** as data from NHS 2014 regarding the highest level of education completed did not differentiate the tertiary education group according to the International Standard Classification of Education (ISCED) 2011, data from NHS 2019 was transformed so all 3 levels of tertiary education (Short-term Tertiary Education, Bachelor, Master and Doctoral Level) were grouped together in one group. Given this, the following categories were used: No Education Level; Primary Education (first and second cycle of basic education); Lower Secondary Education (third cycle of basic education); Upper Secondary Education; Post-Secondary Non-Tertiary Education and Tertiary Education (Short-term Tertiary Education, Bachelor, Master and Doctoral Level)
- **Marital Status:** single; married; widow; divorced.

Socioeconomic variables:

- **Employment Status**: the NHS' categories student, retired, permanently disabled, community and civic service, household tasks and other inactivity situation were grouped into one single group named Other Working Inactivity Type. Thus, the following groups were analysed: Employed; Unemployed and Other Working Inactivity Type.
- **Income Range**: data grouped in quintiles, 1 to 5, of net monthly income by equivalent adult.
- **Work Absence:** self-reported work absence due to health conditions in the 12 months preceding the NHS completion was assessed based on the following groups of complete days missed: no absence; 1-7; 8-14; 15-30; 31-180 and at least 181 days.

Health related variables:

- **Overweight:** using data reported by individuals for weight (in kg) and height (in cm), body mass index (BMI) was calculated according to the formula BMI= weight/(height)^2. Overweight was defined as BMI ≥ 25 kg/m^2.This includes both overweight and obese categories.
- **Consumption of Tobacco**: the following categories regarding smoking habits were used: Smoker (which includes daily and occasional consumers); Former Smoker and Non-smoker.
- **Consumption Alcohol**: using self-reported data on alcohol consumption in the 12 months prior to the NHS completion, individuals were grouped on high-risk and non-high-risk drinkers. High-risk drinking was defined as the consumption of alcohol over 40g of alcohol per day for women and 60g of alcohol per day for men, following the WHO guidelines (140). For the purpose of this study, 40g per day was used as the cut-off for high-risk drinking. The mean consumption per day was obtained by multiplying the number of days from Monday to Sunday of alcohol consumption by the reported mean number of units consumed on those days and by 10 g (equivalent dose of alcohol in each unit) and dividing by 7 days. The following formula was used: Alcohol Consumption (g/day) = ((Frequency of alcohol consumption from Monday to Thursday x Mean number of units consumed per day from Monday to Thursday) + (Frequency of alcohol consumption from Friday to Sunday x Mean number of units consumed per day from Friday to Sunday)x10g)/7days.

  Since, for a consumption higher than 3 units per day, the categories were grouped per a range of units (4 to 5; 6 to 9; 10 to 15 and 16 or more units), the calculation of the mean number of grams of alcohol per day was done considering the minimum number in each range.
- **Physical Activity**: defined as at least 10 straight minutes of exercise. Based on the reported number of days per normal week of physical activity, the following groups were identified: non-regular (0-1 day) and regular (at least 2 days of exercise)
- **Number of comorbidities** (other than depression): The occurrence of the following self-reported chronic physical conditions in the 12 months prior to the NHS completion were considered: asthma; chronic bronchitis, chronic obstructive pulmonary disease or emphysema; myocardial infarction; coronary heart disease or chest angina; arterial hypertension; cerebral vascular disease; arthrosis (excluding arthritis); lumbar pain and other back chronic pain; cervical pain or

other neck chronic pain; diabetes, allergy (excluding allergic asthma); hepatic cirrhosis; urinary incontinence or other bladder control problems and renal problems. The NHS from 2019 foresaw a question regarding the occurrence of high cholesterol or triglycerides, although this was not counted in the analysis since this information was not present in the NHS from 2014. Individuals were grouped in the following categories considering the number of comorbidities: 0; 1-2 and at least 3 comorbidities.

- **Healthcare resources utilization**: this variable was assessed summing the number of consultations to the general practitioner and to other specialities in the 4-week period prior to the NHS completions. Value presented as mean value.

In the estimation of the indirect costs associated to work absence, only employed individuals aged at least 18 years old were considered. Initially, an association study of the work absence with depression was performed, as well as with the other variables presented above except for the employment status. For the calculation of the indirect costs, the records of the respondents were weighted to be representative of the entire sample of the Portuguese population and to adjust for differential probability in the selection of the households.

The following variables were used in the calculation of the indirect costs:

- **Depression:** presence of depression was assessed according to the self-reported data already described above. The abovementioned depression diagnosis and severity variables obtained through the method of extrapolation to the PHQ-8 questionnaire were used to perform a sensitivity analysis. For the variable using severity levels, the “None/Minimal” group was considered the population without depression.
- **Average monthly earnings**: as the value for 2014 was only available for continental Portugal according to INE, the value used for 2019 was the average monthly earnings for continental Portugal. As previously stated, the 2019 value was calculated based on the value from 2018 and applying the inflation rate for 2019.
- **Work Absence:** In the initial study of the association of depression to work absence, a self-reported binary variable was used: no absence or at least 1 day of work absence due to health conditions in the 12 months preceding the NHS completion.
- **Indirect Cost per individual:** As it was not possible to obtain the exact days of absence per individual, the calculation of the indirect costs per individual was done using self-reported work absence due to health conditions in the 12 months

preceding the NHS completion. Work absence was assessed based on the following groups of complete days missed: 1-7; 8-14; 15-30; 31-180 and at least 181 days. This variable was recalculated twice, one using the minimum value of each group: 1; 8; 15; 31 and 181; and the other using the maximum values: 7; 14; 30; 180 and 365. The indirect cost per individual per year was calculated considering that a month has 21 working days and using the following formula:

Indirect cost (per individual per year) = (Average monthly earnings/ 21) x number of days of working absence

To calculate the indirect costs due to depression per individual per year, or excess cost due to depression, the following formula was used:

Excess Cost (per individual per year) = Mean indirect cost per individual in the depressed population - Mean indirect cost per individual in the non-depressed population.

Total excess costs per year in the Portuguese population, were calculated by multiplying the excess cost per individual by the total number of individuals in each depression group.

According to INE's data, the average monthly earnings in Portugal for 2014 was 1,093.20 EUR and for 2018 the value was 1,170.30 EUR(131). Using the INE's tool(136) to estimate the value update from 2018 to 2019, an actualization factor of 1.0034 was applied and the 2019's average monthly earnings was estimated to be 1,174.28 EUR.

A sensitive analysis of the costs was performed using the minimum and maximum possible values of work absence and using estimates of depression prevalence based on the self-reported data and data obtained through the method of extrapolation to the PHQ-8 questionnaire, using the defined thresholds explained above, and assuming the 2-week prevalence being the same in 12 months.

d. Statistical Analysis

In the characterization of the general adult and employed population study, descriptive statistics were done performing an initial univariate analysis to determine, for each categorical variable, the absolute frequencies and the relative frequencies of each category. For the numeric variable "healthcare resources utilization", it was determined the central localization (mean and median) and dispersion (standard deviation, interquartile amplitude, minimum and maximum values) measures. A bivariate analysis and chi-square test were performed to examine the relationship between the prevalence

of depression and the different categorical variables studied. A Mann-Whitney test was performed to examine the relationship with the numeric variable “healthcare resources utilization”, since the Kolmogorov-Smirnov test performed rejected the normality hypothesis. Unadjusted OR were calculated using a bivariate binary logistic regression model and the respective 95% confidence intervals (95%CI) are presented.

For the estimation of the indirect costs of depression, an initial association study between work absence and depression was done. A similar statistical analysis was used as for the population characterization. Univariate analysis results were only presented for work absence and the different depression variables. The other variables used were part of the employed population characterization results. Cross-tabulation was also used to study the relationship between work absence, depression, and the other categorical variables. Similarly, the Mann-Whitney test was performed for the numeric variable “healthcare resources utilization”. In the binary logistic regression applied, the model was optimized by only adding the variables that showed statistically significant association with work absence in the bivariate analysis and/or $p<0.20$. In addition to depression, the initial model included gender, age, marital status, overweight, tobacco consumption, alcohol consumption, physical activity, number of comorbidities, and healthcare resources utilization for the 2014’s NHS data; and gender, age, education level, marital status, overweight, tobacco consumption, alcohol consumption, physical activity, number of comorbidities, and healthcare resources utilization for the 2019’s NHS data. To optimize the model, those variables that were not statistically significantly associated with work absence ($p<0.05$) were removed, starting with those variables with higher p-value (alcohol consumption, physical activity, marital status and overweight for the 2014’s data and, physical activity, alcohol consumption, overweight and education level for the 2019’s data). The exceptions to these were gender in the 2014 data analysis and marital status in the 2019’s one. In the binary logistic regression model of 2014’s data, despite gender p-value being above 0.05, the variable was maintained in the regression as it is an important and extensively studied sociodemographic risk factor of depression (7,22,55–57). In the 2019’s binary logistic regression, marital status was initially included in the mode. However, in the different models using the different depression estimation variables, marital status had not a p-value constantly below 0.05 across the different models and was removed as well. P-value was only statistically significant for the model using depression variable of self-reported data. From the regression model, the applicable adjusted odds ratio (aOR) and 95%CI for work absence among patients with and without depression were obtained according to the different methods of depression assessment.

As the sample did not follow a normal distribution, a Mann-Whitney test was performed to examine if there was a statistically significant difference between the indirect costs (both minimum and maximum) means of depressed and non-depressed populations using the different methods of assessment as previously described.

The statistical analysis was performed using the IBM SPSS Statistics version 26 for Windows software. A 5% significance level was used for all statistical tests.

4. Results

a. Employed Population Characterization

A higher percentage of the adult employed individuals reported depression in 2019 (9.2%) than in 2014 (7.8%). The opposite occurred when using the PHQ-8 score for which in 2014 5.0% of the employed population presented depression symptoms whereas in 2019 only 4.2% had symptoms compatible with the diagnosis of depression. A minority of the working population, 1.7% in 2014 and 1.4% in 2019, had more severe symptoms of depression. (table 1). An analogous trend was observed in the general adult population, although with higher prevalence levels of depression (Appendix 1). Mild cases accounted for 14.0% of the employed population in 2014 and 13.8% in 2019. When these individuals were considered together with the persons with the more severe symptoms, this group would represent 19.0% of the workers in 2014 and 18% in 2019 (table 1).

***Table 1**- Employed adult population sample characteristics of NHS 2014 and 2019 on self-reported depression in the last 12 months and PHQ-8 depression prevalence and severity in the last 2 weeks.*

		Year	
		2014 (N=7,788)	**2019 (N=6,469)**
Variable		**n (%)**	**n (%)**
Self- reported Depression	**n**	n= 7,764	n= 6,403
	No	7,155 (92.1)	5,811 (90.8)
	Yes	609 (7.8) 95%CI= [7.3-8.4]	592 (9.2) 95%CI= [8.5-10.0]
Depression (PHQ-8)	**n**	n= 7709	n= 6254
	No	7,323 (95.0)	5,989 (95.8)
	Yes	386 (5.0) 95%CI= [4.5-5.5]	265 (4.2) 95%CI= [3.7-4.7]
Depression Severity (PHQ-8)	**n**	n= 7,709	n= 6,254
	None/Minimal	6,246 (81.0)	5,127 (82.0)
	Mild	1,077 (14.0)	862 (13.8)
	Moderate	252 (3.3)	176 (2.8)
	Moderately Severe	89 (1.2)	57 (0.9)
	Severe	45 (0.6)	32 (0.5)

In 2014 as well in 2019 the employed population sample presented a slightly higher number of females, and most of the individuals were married. Persons aged between 35 and 44 years represented the biggest group in the labour force in 2014 while in 2019 it was the group between 45 and 54 years (table 2). The education level of the employed population increased from 2014 to 2019. In 2014 48.3% of the employees had completed at least the upper secondary education while in 2019 the relative frequency was 53.3%

(table 2). Generally, the percentage of individuals with higher education level was greater among employed population than in the general population (Appendix 2).

Table 2- *Employed adult population sample demographic characteristics of NHS 2014 and 2019.*

		Year	
		2014 (N=7,788)	**2019 (N=6,469)**
Variable		**n (%)**	**n (%)**
Gender	**n**	n= 7788	n= 6469
	Female	3980 (51.1)	3387 (52.4)
	Male	3808 (48.9)	3082 (47.6)
Age group (years)	**n**	n= 7,788	n= 6,469
	18-24	260 (3.3)	268 (4.1)
	25-34	1,349 (17.3)	883 (13.6)
	35-44	2,554 (32.8)	1,717 (26.5)
	45-54	2,150 (27.6)	1,869 (28.9)
	55-64	1,279 (16.4)	1,497 (23.1)
	>=65	196 (2.5)	235 (3.6)
Education Level	**n**	n= 7,788	n= 6,469
	No Education Level	168 (2.2)	72 (1.1)
	Primary Education	2,299 (29.5)	1,683 (26.0)
	Lower Secondary Education	1,562 (20.1)	1,269 (19.6)
	Upper Secondary Education	1,715 (22.0)	1,569 (24.3)
	Post-Secondary Non-Tertiary Education	108 (1.4)	111 (1.7)
	Tertiary Education	1,936 (24.9)	1,765 (27.3)
Marital Status	**n**	n= 7,781	n= 6,442
	Single	2,087 (26.8)	2,060 (32.0)
	Married	4,477 (57.5)	3,349 (52.0)
	Widow	263 (3.4)	176 (2.7)
	Divorced	954 (12.3)	857 (13.3)

Both in 2014 and 2019 most of the population had a monthly net income at least in the range of the 4th quintile and had no work absence in 12 months (table 3).

As observed in the general population (Appendix 4), also the greater part of the employed population in each year were overweight, non-smokers, non-drinkers and did not practice physical activity regularly (table 4). More than half of the employees in 2014 had no chronic physical condition reported in contrast with 2019 when only 45.1% of the

individuals were in a similar position. In 2014 employed population had a mean of 0.42 medical consultations in a 4-week period whereas the mean in 2019 was 0.58. When considering the general adult population, the mean number of healthcare resources utilization was higher, 0.51 and 0.74, respectively (Appendix 4).

***Table 3**- Employed adult population sample economic characteristics of NHS 2014 and 2019.*

		Year	
		2014 (N=7,788)	**2019 (N=6,469)**
Variable		**n (%)**	**n (%)**
Income Range	**n**	n= 7,788	n= 6,469
	1st Quintile	826 (10.6)	856 (13.2)
	2nd Quintile	1,165 (15.0)	878 (13.6)
	3rd Quintile	1,666 (21.4)	1,262 (19.5)
	4th Quintile	1,992 (25.6)	1,764 (27.3)
	5th Quintile	2,139 (27.5)	1,709 (26.4)
Work Absence	**n**	n= 7,738	n= 6,324
	No Absence	5,779 (74.7)	4,636 (73.3)
	1-7 days	1,104 (14.3)	915 (15.1)
	8-14 days	188 (2.4)	151 (2.4)
	15-30 days	284 (3.7)	248 (3.9)
	31-180 days	296 (3.8)	248 (3.9)
	At least 181 days	87 (1.1)	86 (1.4)

***Table 4**- Employed adult population sample health-related characteristics of NHS 2014 and 2019*

		Year	
		2014 (N=7,788)	**2019 (N=6,469)**
Variable		**n (%)**	**n (%)**
Overweight	**n**	n= 7,788	n= 6,469
	No	3,716 (47.7)	3,020 (46.7%)
	Yes	4,072 (52.3)	3,449 (53.3%)
Tobacco Consumption	**n**	n= 17758	n= 6435
	Non-smoker	3,920 (50.4)	3,432 (53.3%)
	Smoker	2,094 (26.9)	1,517 (23.6%)
	Former Smoker	1,768 (22.7)	1,486 (23.1%)
Alcohol Consumption	**n**	n= 7,740	n= 6,442
	Non-drinkers	4,248 (54.5)	3,708 (57.6%)
	Non-high-risk drinkers	3,081 (39.8)	2,441 (37.9%)
	High-risk drinkers	411 (5.3)	293 (4.5%)

Variable		Year	
		2014 (N=7,788)	2019 (N=6,469)
		n (%)	n (%)
Physical Activity	n	n= 7764	n= 6351
	Non-regular	5,431 (70.0)	4,448 (70.0%)
	Regular	2,333 (30.0)	1,903 (30.0%)
Number of comorbidities (other than depression)	n	n= 7,735	n= 6,311
	0	3,990 (51.6)	2,849 (45.1%)
	1-2	2,429 (31.4)	2,178 (34.5%)
	3 or more	1,316 (17.0)	1,284 (20.3%)
Healthcare resources utilization	n	n= 7,774	n= 6,375
	Mean	0.42	0.58
	Median	0.0	0.0
	Standard Deviation	0.01	0.01
	Min	0.0	0.0
	Max	24.0	20.0
	Interquartile Amplitude	1.0	1.0

Table 5- *Frequencies of PHQ-8 depression severity in the last 2 weeks in the employed adult population with and without self-reported depression in the last 12 months in 2014 and 2019.*

Variável		Year			
		2014 (N=7,788)		2019 (N=6,469)	
		No Depression	Depression	No Depression	Depression
		n (%)	n (%)	n (%)	n (%)
Depression Severity	n	n= 7,690		n= 6,212	
	None/minimal	6,063 (85.5)	169 (28.3)	4,907 (86.9)	194 (34.3)
	Mild	848 (12.0)	227 (38.0)	630 (11.2)	222 (39.3)
	Moderate	142 (2.0)	107 (17.9)	89 (1.6)	82 (14.5)
	Moderately Severe	27 (0.4)	62(10.4)	18 (0.3)	38 (6.7)
	Severe	12 (0.2)	33 (5.5)	3 (0.1)	29 (5.1)

Overweight did not show association with depression in the employed population of 2014 per the chi-square independence test (p=0.072). For all the other variables, the chi-square independence test indicated a relation with depression in both years.

The odds of being depressed were lower among males and higher within the older employees compared with those aged between 18 and 24 years. Those within the range of 55 to 64 years had the highest odds both in 2014 and 2019. On both years the employees that had completed any kind of educational level did not have significantly

different odds of having depression when compared with those without any education level completed (table 6). Among the employed population in both years, those that were single had the lowest chances of being depressed while those that were widowed presented the higher odds when compared with those that were single.

In terms of economic variables (table 7), only the employees with a net monthly income in the fifth quintile presented significantly lower odds of depression than those in first quintile. Additionally, in 2014 those with earnings in the range of the fourth quintile also had lower chances however not as low as those in the fifth. A negative association was observed in the general population between income range and depression with those in the quintiles higher than the second having lower odds compared to the individuals with a monthly net income in first quintile (Appendix 7). Being absent from work due to a health condition was positively associated with depression in both years and the association was the strongest among those workers that had an absence of at least 181 days in 12 months (table 7).

Regarding the health-related characteristics (table 8), employed individuals had higher odds of depression when they had overweight and other comorbidities with a particularly strong association in those with at least 3 other medical conditions. Lower chances of depression were found employees that were alcohol drinkers and that practice regular physical activity when compared with non-alcohol drinkers and those that do not practice regular physical activity, respectively. Concerning tobacco consumption, employed population that were current and former smokers had lower odds of depression in 2014 however this difference was not observed in 2019. This potential protective effect was however observed in both years at the general population (Appendix 8). For both years, employed patients with reported depression had significantly higher chances of having more medical consultations in 4 weeks.

Table 6- *Frequencies in employed adult population with and without self-reported depression and associations of demographic characteristics with self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Gender	**n**	n= 7,764			n= 6,403		
	Female	3,485 (48.7)	482 (79.1)	ref.	2,898 (49.9)	451 (76.2)	ref.
	Male	3,670 (51.3)	127 (20.9)	0.250 [0.205- 0.306]	2,913 (50.1)	141 (23.8)	0.311 [0.256-0.378]
Age group (years)	**n**	n= 7764			n= 6403		
	18-24	257(3.6)	3 (0.5)	ref.	258 (4.4)	8 (1.4)	ref.
	25-34	1,291 (18.0)	54 (8.9)	3.583[1.112- 11.548]	827 (14.2)	45 (7.6)	1.755 [0.817-3.771]
	35-44	2,387 (33.4)	161 (26.4)	5.778 [1.831-18.236]	1,567 (27.0)	127 (21.5)	2.614 [1.264-5.405]
	45-54	1,926 (26.9)	216 (35.5)	9.607 [3.052-30.246]	1,653 (28.4)	194 (32.8)	3.785 [1.844-7.769]
	55-64	1,119(15.6)	155 (25.5)	11.866[3.755-37.495]	1,300 (22.4)	190 (32.1)	4.713 [2.295-9.682]
	>=65	175 (2.4)	20 (3.3)	9.790 [2.866-33.449]	206 (3.5)	28 (4.7)	4.383 [1.956-9.822]
Education Level	**n**	n= 7,764			n= 6,403		
	No Education Level	154 (2.2)	13 (2.1)	ref.	63 (1.1)	9 (1.5)	ref.
	Primary Education	2,026 (28.3)	271 (18.6)	1.585 [0.887-2.830]	1,478 (25.4)	198 (33.4)	0.938 [0.459-1.915]
	Lower Secondary Education	1,444(20.2)	113 (17.7)	0.927 [0.510-1.685]	1,123 (19.3)	136 (23.0)	0.848 [0.412-1.743]
	Upper Secondary Education	1,602 (22.4)	108 (16.1)	0.799 [0.439-1.453]	1,431 (24.6)	120 (20.3)	0.587 [0.285-1.209]
	Post-Secondary Non-Tertiary Education	101 (1.4)	7 (1.1)	0.821 [0.317-2.128]	98 (1.7)	10 (1.7)	0.714 [0.275-1.855]
	Tertiary Education	1,828 (25.5)	97 (15.9)	0.629 [0.344-1.147]	1,618 (27.8)	119 (20.1)	0.515 [0.250-1.061]

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Marital Status	n	n= 7,757			n= 6,382		
	Single	1,977 (27.7)	104 (17.1)	ref.	1,893 (32.7)	141 (23.9)	ref.
	Married	4,115 (57.6)	346 (56.8)	1.598 [1.276-2.003]	3,010 (52.0)	318 (53.9)	1.418 [1.154- 1.744]
	Widow	210 (2.9)	53 (8.7)	4.798 [3.347-6.877]	137 (2.4)	38 (6.4)	3.724 [2.501- 5.544]
	Divorced	846 (11.8)	106 (17.4)	2.382 [1.796-3.159]	752 (13.0)	93 (15.8)	1.660 [1.261- 2.186]

Legend: OR = unadjusted odds ratio.

Table 7- *Frequencies in employed adult population with and without self-reported depression and associations of economic characteristics with self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Income Range	n	n= 7,764			n= 6,403		
	1st Quintile	730 (10.2)	95 (15.6)	ref.	754 (13.0)	95 (16.0)	ref.
	2nd Quintile	1,055 (14.7)	109 (17.9)	0.794 [0.594-1.062]	779 (13.4)	93 (15.7)	0.948 [0.700-1.283]
	3rd Quintile	1,502(21.0)	157 (25.8)	0.803 [0.613-1.052]	1,119 (19.3)	134 (22.6)	0.950 [0.719-1.256]
	4th Quintile	1,838 (25.7)	149 (24.5)	0.623 [0.475-0.817]	1,590 (27.4)	153 (25.8)	0.764 [0.583-1.001]
	5th Quintile	2,030 (28.4)	99 (16.3)	0.375 [0.279-0.503]	1,569 (27.0)	117 (19.8)	0.592 [0.445-0.786]
Work Absence (days)	n	n= 7,717			n= 6,272		
	No Absence	5,474 (76.9)	291 (48.3)	ref.	4,326 (75.8)	272 (48.3)	ref.

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
	1-7	983 (13.8)	114 (18.9)	2.182 [1.739-2.737]	831 (14.6)	112 (19.9)	2.144 [1.699-2.704]
	8-14	154 (2.2)	34 (5.6)	4.153 [2.813-6.132]	120 (2.1)	29 (5.2)	3.844 [2.516-5.871]
	15-30	228 (3.2)	56 (.9.3)	4.620 [3.371-6.332]	199 (3.5)	49 (8.7)	3.916 [2.799-5.479]
	31-180	218 (3.1)	78 (12.9)	6.731 [5.065-8.943]	181 (3.2)	67 (11.9)	5.887 [4.336-7.994]
	At least 181	57 (0.8)	30 (5.0)	9.901[6.265-15.645]	52 (0.9)	34 (6.0)	10.399[6.635-16.298]

Legend: OR = unadjusted odds ratio.

Table 8- *Frequencies in employed adult population with and without self-reported depression and associations of health-related characteristics with self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Overweight	**n**	n= 7,764			n= 6,403		
	No	3,432 (48.0)	269 (44.2)	ref.	2,755 (47.4)	227 (38.3)	ref.
	Yes	3,723(52.0)	340 (55.8)	1.165 [0.986-1.376]	3,056 (52.6)	365 (61.7)	1.450 [1.219-1.724]
Tobacco Consumption	**n**	n= 7,759			n= 6,382		
	Non-smoker	3,544 (49.6)	360 (59.1)	ref.	3,091 (53.4)	313 (52.9)	ref.
	Smoker	1,944 (27.2)	147 (24.1)	0.744 [0.610-0.909]	1,366 (23.6)	139 (23.5)	1.005 [0.815-1.239]
	Former Smoker	1,662 (23.2)	102 (16.7)	0.604 [0.481-0.758]	1,333 (23.0)	140 (23.6)	1.037 [0.841-1.279]

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Alcohol Consumption	n	n= 7,717			n= 6,379		
	Non-drinkers	3,802 (53.5)	432 (71.2)	ref.	3,257 (56.3)	409 (69.2)	ref.
	Non-high-risk drinkers	2,918 (41.0)	154 (25.4)	0.464 [0.384-0.562]	2,248 (38.8)	173 (29.3)	0.613 [0.509-0.738]
	High-risk drinkers	390 (5.5)	21 (3.5)	0.474 [0.302-0.743]	283 (4.9)	9 (1.5)	0.253 [0.129-0.496]
Physical Activity	n	n= 7,742			n= 6,300		
	Non-regular	4,926 (69.1)	492 (80.8)	ref.	3,942 (69.0)	474 (81.0)	ref.
	Regular	2,207 (30.9)	117 (19.2)	0.531 [0.431-0.653]	1,773 (31.0)	111 (19.0)	0.521 [0.420-0.645]
Number of comorbidities (other than depression)	n	n= 7,723			n= 6,287		
	0	3,878 (9.0)	107 (17.7)	ref.	2,777 (48.6)	65 (11.4)	ref.
	1-2	2,229 (22.2)	196 (32.3)	3.187 [2.504-4.057]	1,953 (34.2)	215 (37.7)	4.703 [3.543-6.244]
	3 or more	1,010 (68.7)	303 (50.0)	10.873 [8.630-13.699]	986 (17.2)	291 (51.0)	12.609[9.544-16.659]
Healthcare resources utilization	n	n= 7,752			n= 6,315		
		7,146	606	1.503 [1.399-1.615]	5,735	580	1.297 [1.225-1.374]
	Mean	0.38	0.89		0.53	1.05	
	Median	0.0	0.0		0.0	1.0	
	Standard Deviation	0.01	0.07		0.01	0.06	
	Min	0.0	0.0		0.0	0.0	
	Max	10.0	24.0		20.0	15.0	
	Interquartile Amplitude	1.0	1.0		1.0	2.0	

Legend: OR = unadjusted odds ratio.

b. Indirect Costs Calculation

From 25.7% in 2014, the relative frequency of employed individuals that missed work for at least 1 day due to a health condition increased to 28.0% in 2019.

Table 9- *Absolute and relative frequencies of work absence in the last 12 months in the employed adult population sample of NHS 2014 and 2019.*

		Year	
		2014 (N=7,788)	**2019 (N=6,469)**
Variable		**n (%)**	**n (%)**
Work Absence	**n**	n= 7,780	n= 6,440
	No Absence	5,779 (74.3)	4,636 (72.0)
	At least 1 day	2,001 (25.7)	1,804 (28.0)

Depression showed association with absence to work consistently across the different methods of assessment and in both years even when adjusted for gender, age group, tobacco consumption, number of additional comorbidities and healthcare resources utilization (table 10 and Appendix 10-12). Workers with depression in 2014 had similar odds of work absence than those in 2019 when compared with employed population without depression. This association was stronger among workers with more severe forms of depression with exception for the workers with severe symptoms in 2019 for whom there was no significant higher odds of having work absence than those with no or minimal symptoms. Employees with severe depression in 2014 had more than 6 times the chances of having work absence than those without depression (Appendix 12).

The mean number of days a worker without depression was absent was similar in 2014 and 2019, around 3 and 11 days per year. Although patients with depression had significantly more days of work absence than workers without depression in both years, depressed employees in 2019 had a higher number of days off work than their counterparts in 2014 (table 11).

Similarly, the mean annual indirect costs due to work absence per depressed worker in 2019 were higher than in 2014 (table 12). In 2014 it varied between 696.58 and 2,264.21 EUR while it ranged from 1,026.82 to 2,913.34 EUR in 2019. Compared to the costs with non-depressed employees, this represented an increase in minimal and maximum costs of 331.4 and 313.1% in 2014 and 488.9 and 368.2% in 2019.

***Table 10**- Frequencies in employed adult population with at least 1 day and without any work absence due to a health condition and associations of self-reported depression in the last 12 months with work absence in the last 12 months in 2014 and 2019. Odds ratio adjusted (aOR) for gender, age group, tobacco consumption, number of comorbidities and healthcare resources utilization.*

Variable		Year					
		2014 (N=7,788)			2019 (N=6,469)		
		No Absence	At Least 1 day		No Absence	At Least 1 day	
		n (%)	n (%)	aOR [95%CI]	n (%)	n (%)	aOR [95%CI]
Depression (self-reported)	n	n= 7,758			n= 6,382		
	No	5,474 (76.6)	1,676 (23.4)	ref.	4,326 (74.7)	1,468 (25.3)	ref.
	Yes	291 (47.9)	317 (52.1)	2.283[1.898-2.746]	272 (46.3)	316 (53.7)	2.244[1.851-2.721]

***Table 11**-Minimal and maximum mean annual work absence days per employee according to self-reported depression in 2014 and 2019.*

		Year			
		2014		2019	
		Minimum Absence (days)	Maximum Absence (days)	Minimum Absence (days)	Maximum Absence (days)
Self-reported Depression	No	3.1	10.5	3.1	11.1
	Yes	13.4	43.5	18.4	52.1

***Table 12-** Minimal and maximum mean annual indirect cost due to work absence per employee with and without self-reported depression in 2014 and 2019.*

		Year					
		2014			2019		
		N	Minimum Cost (EUR)	Maximum Cost (EUR)	N	Minimum Cost (EUR)	Maximum Cost (EUR)
Self-reported Depression	No	3,829,899	161.46	548.12	4,160,083	174.37	622.23
	Yes	305,078	696.58	2,264.21	344,573	1,026.82	2,913.34

Table 13- *Minimal and maximum mean individual annual excess costs related to self-reported depression in 2014 and 2019. p<0.0005*

	Year			
	2014		2019	
	Minimum Excess Cost (EUR)	Maximum Excess Cost (EUR)	Minimum Excess Cost (EUR)	Maximum Excess Cost (EUR)
Self-reported Depression	535.12	1,716.09	852.45	2,291.11

c. Sensitivity Analysis

Work absence due to a health condition was consistently higher in 2019 than in 2014 among those with depression with those with more severe forms having a higher number of days off work (table 14). The exception was the population with moderately severe depression in 2019 that was the group with higher mean annual work absence days per employee, between 54.3 and 135.7 days.

The minimum mean individual cost observed in the depressed population in 2014 was 336.88EUR and in 2019 was 415.99 EUR. When considering the maximum value, the mean annual individual cost could reach 4,128.01 EUR in 2014 and 7,590.12 EUR in 2019 (table 15).

These costs translated into minimal indirect costs related to depression per individual ranging in 2014 from 200.56 EUR among mild depression patients to 1,131.19 EUR among moderately severe ones. For that year the maximum excess costs per individual ranged from 627.46EUR (those with mild depression) to 3,640.90 EUR (those with severe depression) (figure 1). In 2019, minimal excess costs varied from 272.17 EUR in patients with mild depression to 2,894.94 EUR in patients with moderately severe depression. On the other hand, maximum excess costs varied between 783.48 EUR (mild depression) and 7,042.53 EUR (moderately severe depression) (figure 2).

Table 14- *Minimal and maximum mean annual work absence days per employee according to PHQ-8 depression diagnosis and severity in 2014 and 2019.*

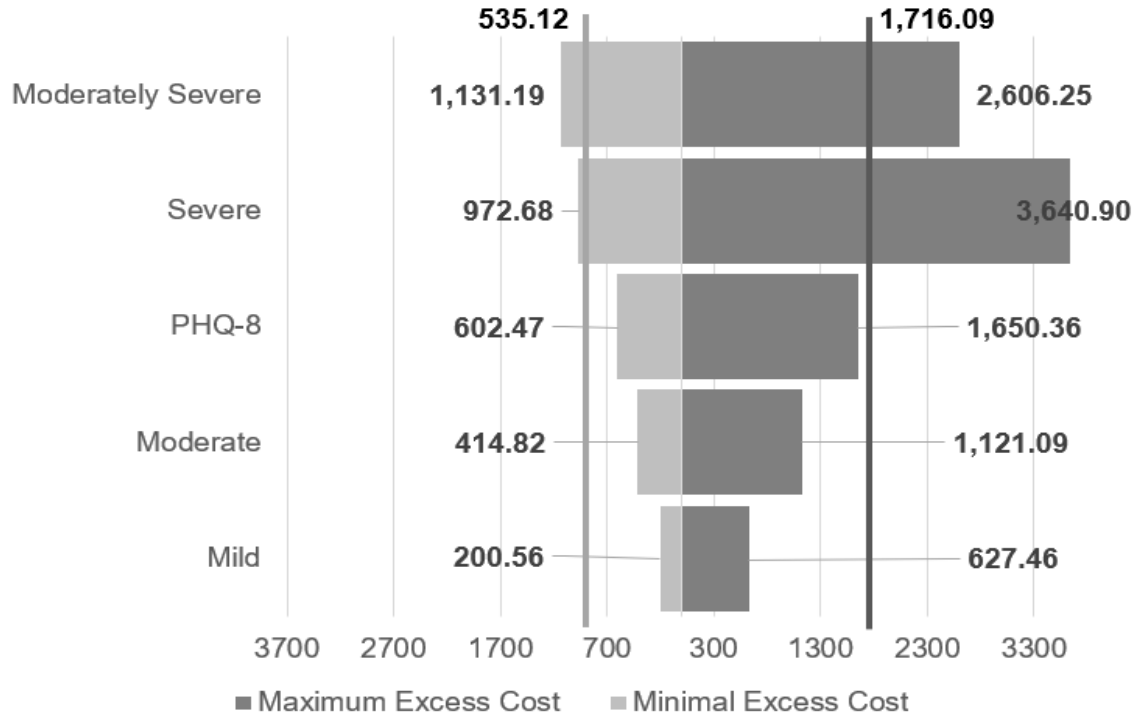
		Year			
		2014		2019	
		Minimum Absence (days)	Maximum Absence (days)	Minimum Absence (days)	Maximum Absence (days)
Depression (PHQ-8)	No	3.2	11.0	3.2	11.7
	Yes	14.7	42.7	27.3	69.8
Depression Severity (PHQ-8)	None/Minimal	2.6	9.4	2.6	9.8
	Mild	6.5	21.4	7.4	23.8
	Moderate	10.6	30.9	18.7	51.4
	Moderately Severe	24.3	59.4	54.3	135.7
	Severe	21.3	79.3	29.5	60.7

Table 15- *Minimal and maximum mean annual indirect cost due to work absence per employee according to PHQ-8 depression diagnosis and severity in 2014 and 2019.*

		Year					
		2014			2019		
		N	Minimum Cost (EUR)	Maximum Cost (EUR)	N	Minimum Cost (EUR)	Maximum Cost (EUR)
Depression (PHQ8)	No	3,884,092	164.15	574.18	4,217,291	180.85	654.20
	Yes	227,321	766.62	2,224.54	193,731	1,524.82	3,905.19
Depression Severity (PHQ-8)	None/Minimal	3,345,148	136.32	487.11	3,643,427	143.82	547.59
	Mild	538,944	336.88	1,114.57	573,864	415.99	1,331.07
	Moderate	152,687	551.14	1,608.20	131,372	1,044.68	2,875.80
	Moderately Severe	46,351	1,267.51	3,093.36	39,837	3,038.76	7,590.12
	Severe	28,283	1,109.00	4,128.01	22,522	1,647.65	3,391.78

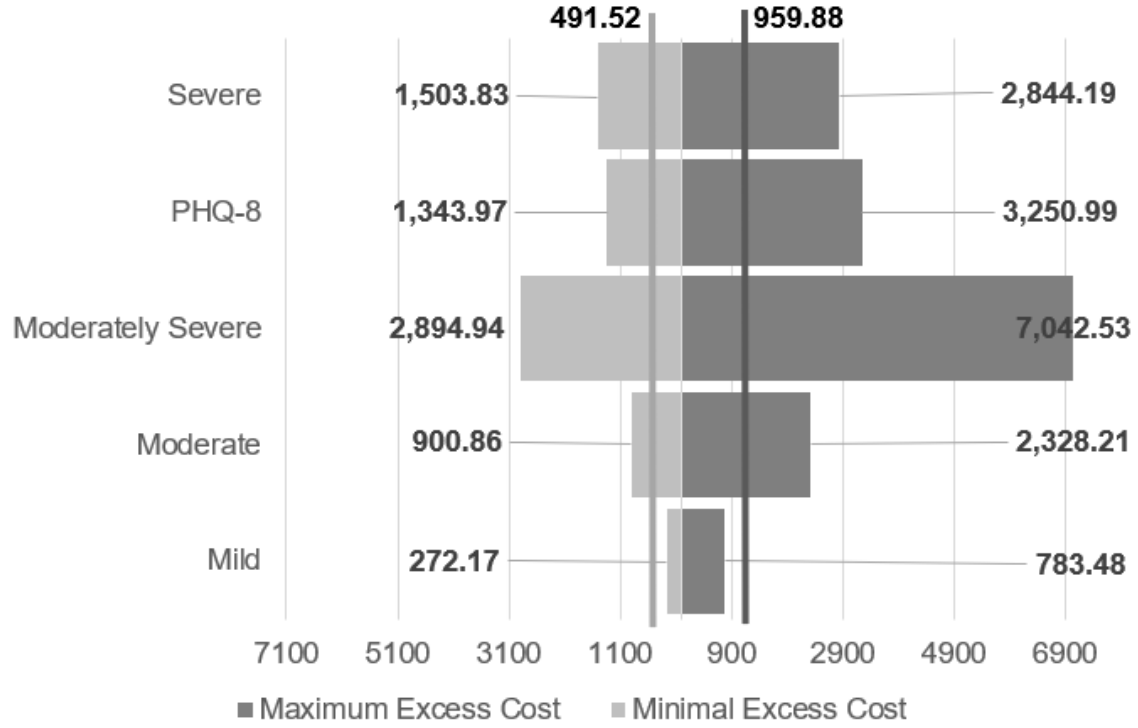
When considering the entire Portuguese workforce, total indirect costs of depression ranged between 27,510,153.59EUR (minimal excess cost from patients with severe depression) to 733,117,319.70EUR (maximum excess costs from patients with mild to severe depression) in 2014 and between 33,869,635.22EUR (minimal excess cost from patients with severe depression) to 1,100,081,650.28EUR (maximum excess costs from patients with mild to severe depression) in 2019.

Figure 1- *Minimal and maximum mean individual annual excess costs related to PHQ-8 depression diagnosis and severity in 2014. Vertical lines represent the values for self-reported depression (base case).*



Note: Differences between the mean costs in depressed and non-depressed population were tested and found significantly different (p<0.0005).

Figure 2- *Minimal and maximum mean individual annual excess costs related to PHQ-8 depression diagnosis and severity in 2019. Vertical lines represent the values for self-reported depression.*



Note: Differences between the mean costs in depressed and non-depressed population were tested and found significantly different (p<0.0005).

5. Discussion

The main goal of this work was to provide a more recent estimate of the indirect costs due to work absence related to depression in the Portuguese population. Furthermore, it sought to provide a broader characterization of the population under study and evaluate the prevalence of depression.

In the general population, being employed had a protective effect in both 2014 and 2019. The prevalence of depression has increased from 2014 to 2019, despite being always lower within the employed individuals. In 2014, 7.8% of the working individuals had depression compared to 13.7% of the general adult population and, in 2019, these values were 9.2 and 15.1%, respectively. It is of notice that, according to the PHQ-8 score, the prevalence of depression decreased from 2014 (5.0% among workers and 10.1% in the general population) to 2019 (4.2% and 8.8%, respectively), and so has the severity of the cases.

Generally, those individuals that were of the female gender, elderly, widowed or that had any other chronic physical condition were at higher odds of having depression. Healthcare resources utilization was also positively associated with depression. On the opposite side, a protective effect was observed within those in the highest quintiles of income, smoking, drinking, and having regular physical activity.

Workers with depression were associated with significantly higher work absence, possibly leading to higher indirect costs. The mean number of additional days off work increased from 2014 to 2019. In 2014 depressed workers were absent to work between 10.3 to 33.0 additional days compared to their non-depressed counterparts. The mean additional work absence ranged between 15.2 to 41.0 days in 2019. The additional work absence represented a mean individual excess cost related to depression between 535.12 and 1,716.09 EUR in 2014 and between 852.45 and 2,291.11 EUR in 2019. When considering the entire work force these costs translated into 163 million and 524 million EUR in 2014 and between 294 million and 790 million EUR in 2019 of productivity loss. Even for mild cases, the mean individual cost within those with depression would be more than twice the cost of those without depression.

When interpreting the findings of this study, it is important to have in mind its limitations. Starting with its cross-sectional nature, this study does not allow to establish a temporal relationship between the cause and the effect and thus establishing a causal relationship, in example, between depression and work absence, as other factors may have justified the absence depending on the logical temporal sequence in which they might have occurred. Further to this, the NHS is based on self-reported data which makes it

susceptible to recall bias particularly when considering higher time intervals such as the occurrence of depression and work absence in the last 12 months. Recall bias can lead to underestimations. Another limitation is that the occurrence of depression was not validated by a clinical assessment. Being self-reported, given the reluctance in disclosing depression(12), it would be more plausible that underreporting occurred. However, literature identified that self-reported instruments overestimate depression's prevalence due to overvaluation of the depressive symptoms while not qualifying as clinical depression(23). To explore this limitation, the author used another method for the assessment of depression's prevalence through the PHQ-8 score. Although it might not be as accurate as the clinical assessment, this tool is known to have good sensitivity and specificity (88%) for MDD (139). Nevertheless, it does not consider other types of depression (for instance, dysthymia) nor the individuals that have their depressive disorder controlled due to treatment. As the scale only refers to the symptoms experienced in the last two weeks prior to the NHS completion, it only reflects the point prevalence and not the year prevalence, which might result in lower prevalence estimates.

Another limitation in the study is the fact that individual data on earnings and work absence days were not available in the NHS due to confidentiality purposes. This data was provided in quintiles and ranges, respectively and, to overcome this, ecological data available for the average earnings of the Portuguese population was used. Since depression seems to affect more individuals with lower earnings(111), this might overestimate the cost of the productivity loss due to depression. For the estimation of work absence, the lowest and highest values according to the applicable individual range were considered in order to estimate the mean days of absence due to depression. Although it was not possible to obtain the exact individual mean absence days, results are presented in an interval considering the optimistic and the pessimist estimations. Still concerning the indirect costs of depression, the NHS did not contemplate data on work disability to assess the impact of depression on presenteeism, nor did the study consider associated morbidity and mortality costs. While not considering the economic impact of these variables, the study underestimates the total indirect costs.

Comparison between years is also limited given the cross-sectional nature of the surveys and their independence. It is not possible to infer about the incidence of depression from 2014 to 2019 as it is not known if the participants were the same and which was their depressive status in each year.

Despite the presented limitations, the study is able to provide a general overview of the identified trends and is representative of the Portuguese population.

Overall, the variables studied and identified to be associated with depression presented a similar pattern to what was identified in literature (7,22,40,55–63,73,76,77,80–82), As to explore their relationship with depression was not the main purpose of this study, the binary logistic regressions were not adjusted for possible confounding factors and so results need to be interpreted with care. An example of this is the protective effect identified in this study within those with smoking and drinking habits and that opposes what is described in literature (55,76,78,79). Having in mind that this was a cross-sectional study, and that the analysis was not adjusted for possible confounding factors, the results obtained are more probably related to those with depression recurring to smoking and drinking as a coping mechanism(117).

As stated at the beginning of this document, Portugal was going through a period of economic growth and decrease in the unemployment rates between 2014 and 2019(63) and, considering that mental health problems increase during periods of economic crisis and high unemployment rates(117,118), it would be expected a decrease in depression's prevalence from 2014 and 2019. Interestingly, study results found that self-reported depression prevalence increased, although a decreasing trend in the incidence rate was reported after 2013 and until 2014 for the Portuguese population(63). When looking to the study results on the prevalence of depression according to the PHQ-8 score, a decreasing trend was however observed. Information available for the general Portuguese population is conflicting. According to IHME'S data, incidence and prevalence have been relatively stable with a slight increase after 2015 (20). Also, the prevalence values are far below the observed in this study. In 2019, it was fixed at 5.88% for depressive disorders and 4.58% for MDD (20). In a country representative survey, Caldas de Almeida and Xavier found higher prevalence for depressive disorders (7.9%) and MDD (6.8%) (6) though still below what was found in this study. Caldas de Almeida and Xavier used a similar sampling selection method to the one used in the NHS but used a smaller sample of the Portuguese population. Despite this, instead of the self-reporting and the PHQ-8 questionnaire, the diagnosis was based on fully-structured interviews using the CIDI and done by trained interviewers(141). Notwithstanding the possible overestimation of the prevalence by the self-reported instruments (23), the differences encountered across studies might indicate 1) the prevalence of more persistent forms of depression that do not account for the incidence rate described by Coelho et al.(63); 2) the presence of non-diagnosed cases in the population, due to the diagnosis difficulty(142) or because the individuals do not seek consultation (141); 3) the presence of cases other than MDD or dysthymia, with subthreshold depressive symptoms or depressive phases of bipolar patients(4); and 4) a change in cultural stigma

surrounding mental health and the improvement of the mental health care support to the population (143,144), leading to the population being more aware of the depressive symptoms and possibly looking for treatment, thus having less episodes of major depressive symptoms and with less severe symptoms, as identified in this study. The observed increase in the number of work absence days from 2014 to 2019 may further corroborate this latter idea of higher awareness of the depressive symptoms.

Even though the reported cases of depression by the population might not truly represent cases of depressive disorders, it reveals a condition that needs to be addressed, since it may impact the individual's performance at work and thus generate an indirect cost to the society.

In terms of the additional days of work absence related to depression, the findings from the study are in line with what has been observed in other studies, for which values may vary between 3.6 and 45.6 missed workdays per year(8). The exception was for depression assessed by the PHQ-8, where in 2019 higher values of absence were obtained (27.3 to 69.8 days) among those with the disease. The values of work absence were nonetheless similar between those with self-reported and depression assessed by PHQ-8 in 2014. The results of this study were markedly higher when comparing with another study carried out in the Portuguese population between 2008 and 2009, that revealed as few as 0.2 additional days per month of work absence associated to depression. The differences might be partially explained by the fact that that study has been conducted in a smaller population, with a lower response rate, using a different method of depression assessment (CIDI) and the work absence being only considered in the month prior to the completion of the questionnaire and not giving an annual picture with possible periods of symptoms exacerbation and higher number of days out of the role (90). Ramos et al., using the method of the nominal group and data from NHS of 1987, estimated that depressed individuals under medical care had in mean 33.3 days of absolute incapacity for work whereas those not in follow-up had 45 days off work per episode of depression (123).

Despite the cases of depression having relatively less severe symptoms in 2019 than in 2014, the number of days of absenteeism were higher in 2019. The increase was particularly higher among those with moderately severe symptoms. This seems to go in agreement with the author's hypothesis that the Portuguese population is more aware of the depressive symptoms and how disabling the disease is. It is also important to mention that the mean number of consultations a depressed worker attended increased from 2014 to 2019. Despite this, the care patients are receiving may not be adequate to

reduce the disease burden (114) it would be otherwise expected a reduction in the number of absence days(145).

The observed work absence also directly led to substantial- and significantly higher costs within those with depression. The costs were especially higher in 2019 than in 2014 due not only to the increase in the mean earnings (there was an estimated salary inflation of 1.039 (136)), but also to the higher number of days of work leave. The mean individual costs of those with depression assessed by the PHQ-8 tended to be higher than the costs among those with self-reported depression. One hypothesis is that individuals with self-reported depression might have less severe symptoms and thus less impact on their productivity. The costs tended to be higher for patients with more severe symptoms of depression. The exception to this were the workers with severe symptoms that had lower indirect costs associated than their counterparts with moderately severe symptoms. The study sample may have not been great enough to capture accurately the work absence within this group of patients and particularly in 2019. In 2014, workers with severe symptoms of depression had the highest odds of missing work. The annual individual indirect costs associated to depression estimated in this work are comparable with what was found in other studies (2,125–128). Despite this, the estimated costs in this study only included the loss of productivity due to absenteeism which means that these costs would probably be higher than those find in literature if they also contemplated the costs with presenteeism. Given that presenteeism costs are 4 to 10 times greater than absenteeism (12,69), this means we would need to multiplicate the estimated absence costs by 5 to obtain the individual costs due to absolute and partial loss of productivity at work.

When considering the entire Portuguese workforce, the productivity loss due absenteeism associated to self-reported depression represented a cost of 163 to 524 million EUR in 2014 and 294 to 789 million EUR in 2019. If we considered only the workers with severe symptoms assessed by the PHQ-8, the absence costs related to depression would range between 27 and 103 million EUR in 2014 and between 34 and 64 million EUR in 2019. When considering the workers with mild to severe symptoms, the excess cost of depression varied between 251 and 733 million EUR in 2014 and 424 and 1,100 million EUR in 2019. The indirect costs due absence for 2014 and 2019 were generally lower than those estimated for 1992. Ramos et al. estimated these costs to be equivalent to 989 million EUR (123). The superior value is mainly explained by the higher estimate of the prevalence of depression (17.5%), since the average earnings were below the ones used for this study and the mean number of work absence days was similar or below the maximum mean values used in the present study.

If we consider the reported cases of depression in the present study and multiply its costs by 5 to obtain the costs of presenteeism and absenteeism of depression(12,69), the indirect costs would be between 816 and 2,618 million EUR in 2014 and around 1,469 and 3,947 million EUR in 2019. These values would be equivalent to 0.5-1.5% in 2014 and 0.7-1.8% in 2019 of the Portuguese GDP in those years. Considering all the depression cases, from mild to severe, the indirect costs would rise to around 1,257 and 3,666 million EUR in 2014 and 2,1190 and 5,500 million EUR in 2019, representing 0.7-2.1% in 2014 and 1.0-2.6% in 2019 of the Portuguese GDP in those years. Nevertheless, they would only represent around 60% of the total costs (13). To obtain the total indirect costs, the mortality costs of suicide and the costs of unemployment and early retirement due to depression would still need to be included. Further to the indirect costs, the direct costs incurred would also need to be considered in order to calculate the total costs of the disease.

Therefore, depression assumes an utmost importance role when considering the investment in the mental care planning. Not only its prevalence is high, but also the disability it causes in productivity generates great societal losses.

6. Conclusion

Literature about depression in the Portuguese context is scarce. The present study provided additional and updated information on the prevalence of depression and its associated indirect costs to the Portuguese population.

Despite the study limitations, important trends for future research were identified. Although there was an economic growth observed from 2014 to 2019 in Portugal, the reported prevalence of depression was higher in 2019, indicating the complexity of the disease and of the factors that may contribute to its development. Furthermore, this study revealed that depression is significantly associated with more days of work absence, leading to substantially higher costs. The mean individual cost with work absence in those with depression was at least twice the cost for the non-depressed. An increase in the excess work absence was also observed from 2014 to 2019 (10.3-33.0 and 15.2-41.0 days per worker, respectively), elevating the economic burden to the Portuguese society from 163-524 million EUR to 294-790 million EUR, respectively. In a rough estimation based on data from literature(12,69) and using costs from absenteeism obtained in this study, presenteeism and absenteeism might be responsible for indirect costs equivalent to about 0.5 to 1.8% of the Portuguese GDP.

The results of this study have allowed to quantify the indirect costs generated by depression to the society in the recent years. Knowing the costs of depression will support the comparisons of interventions in the mental healthcare sector and choosing the most cost-beneficial intervention. Taking in account the identified decreasing trend of the occurrence of episodes of major depressive symptoms and less severe symptoms, and the observed increase in the number of work absence days from 2014 to 2019, the author hypothesizes that the awareness of the disease might have increased among the Portuguese population although they might not be receiving the appropriate care either because they are not seeking it or not receiving the most appropriate care.

The presented costs represent a considerable economic burden that may justify an intervention to implement more effective and preventive measures to improve population's mental health. Frias and Pinto da Costa identified some of the limitations of the Portuguese Mental Health System (144) and Perelman et al. proposed some interventions and an incentive-based payment model(146). Since the later was published few as changed and the proposed interventions still remain valid(147).

Further data will be required to confirm and investigate the trends identified in this study and the hypothesis raised by the author. Prospective studies would be the best approach to study depression and better understand the incidence, prevalence, disease dynamics,

risk factors, care received throughout time and the economic burden it represents to the society, either through morbidity and mortality, and the use of healthcare resources.

7. References

1. Langlieb AM, Depaulo JR. Etiology of Depression and Implications on Work Environment. J Occup Environ Med. 2008;50(4):391–5.
2. Sicras-Mainar A, Blanca-Tamayo M, Gutiérrez-Nicuesa L, Salvatella-Pasant J, Navarro-Artieda R. Impact of morbidity, resource use and costs on maintenance of remission of major depression in Spain: a longitudinal study in a population setting. Gac Sanit. 2010;24(1):13–9.
3. World Health Organization. The global burden of disease: 2004 update. Geneva: World Health Organization; 2008.
4. Malhi GS, Mann JJ. Depression. Lancet. 2018;392(10161):2299–312.
5. Liu Q, He H, Yang J, Feng X, Zhao F, Lyu J. Changes in the global burden of depression from 1990 to 2017: Findings from the Global Burden of Disease study. J Psychiatr Res. 2020;126:134–40.
6. Caldas de Almeida J, Xavier M. Estudo epidemiológico nacional de saúde mental. Lisboa: Faculdade de Ciências Médicas, Universidade Nova de Lisboa; 2013.
7. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health. 2013;34:119–38.
8. Lerner D, Henke RM. What does research tell us about depression, job performance, and work productivity? J Occup Environ Med. 2008;50(4):401–10.
9. Lerner D, Adler DA, Chang H, Lapitsky L, Hood MY, Perissinotto C, et al. Unemployment, job retention, and productivity loss among employees with depression. Psychiatr Serv. 2004;55(12):1371–8.
10. Riihimäki K, Vuorilehto M, Isometsä E. A 5-year prospective study of predictors for functional and work disability among primary care patients with depressive disorders. Eur Psychiatry. 2015;30(1):51–7.
11. Schofield DJ, Shrestha RN, Percival R, Passey ME, Callander EJ, Kelly SJ. The personal and national costs of mental health conditions: impacts on income, taxes, government support payments due to lost labour force participation. BMC Psychiatry. 2011;11(72).
12. Evans-Lacko S, Knapp M. Global patterns of workplace productivity for people with depression: absenteeism and presenteeism costs across eight diverse countries. Soc Psychiatry Psychiatr Epidemiol. 2016;51(11):1525–37.

13. Donohue JM, Pincus HA. Reducing the societal burden of depression. A review of economic costs , quality of care and effects of treatment. Pharmacoeconomics. 2007;25(1):7–24.

14. König H, König H-H, Konnopka A. The excess costs of depression: a systematic review and meta-analysis. Epidemiol Psychiatr Sci. 2020;29(e30):1–16.

15. Luppa M, Heinrich S, Angermeyer MC, König H-H, Riedel-Heller SG. Cost-of-illness studies of depression: A systematic review. J Affect Disord. 2007;98(1–2):29–43.

16. Beck A, Crain L, Solberg L, Unützer J, Glasgow R, Maciosek M, et al. The effect of depression treatment on work productivity. Am J Manag Care. 2014;20(8):e294–301.

17. Organization for Economic Co-operation and Development/European Union. Health at a Glance: Europe 2018: State of Health in the EU Cycle. Paris: OECD Publishing; 2018.

18. Rehm J, Shield KD. Global Burden of Disease and the Impact of Mental and Addictive Disorders. 2019;1–7.

19. Schaefer JD, Belsky DW, Harrington H, Houts R, Horwood LJ, Hussong A, et al. Enduring mental health: Prevalence and prediction. J Abnorm Psychol. 2017;126(2):212–24.

20. Institute for Health Metrics and Evaluation. Global Burden of Disease Study 2019 (GBD 2019) results. [Internet]. Global Burden of Disease Collaborative Network. 2020 [cited 2021 May 9]. Available from: http://ghdx.healthdata.org/gbd-results-tool

21. World Health Organization. Depression and other common mental disorders: Global health estimates. Geneva: World Health Organization; 2017.

22. Bromet E, Andrade LH, Hwang I, Sampson NA, Alonso J, Girolamo G De, et al. Cross-national epidemiology of DSM-IV major depressive episode. BMC Med. 2011;9(90).

23. Lim GY, Tam WW, Lu Y, Ho CS, Zhang MW, Ho RC. Prevalence of depression in the community from 30 countries between 1994 and 2014. Sci Rep. 2018;8(2861).

24. Lim D, Sanderson K, Andrews G. Lost productivity among full-time workers with mental disorders. J Ment Health Policy Econ. 2000;3(3):139–46.

25. Wang PS, Beck AL, Berglund P, Mckenas DK, Pronk NP, Simon GE, et al. Effects of Major Depression on Moment-in-Time Work Performance. Am J Psychiatry. 2004;161(10):1885–91.

26. Bailey R, Sharpe D, Kwiatkowski T, Watson S, Samuels AD, Hall J. Mental health care disparities now and in the future. J Racial Ethn Heal Disparities. 2018;5:351–356.

27. Zuelke AE, Luck T, Schroeter ML, Witte AV, Hinz A, Engel C, et al. The association between unemployment and depression–Results from the population-based LIFE-adult-study. J Affect Disord. 2018;235:399–406.

28. Honkonen T, Virtanen M, Ahola K, Kivimäki M, Pirkola S, Isometsä E, et al. Employment status, mental disorders and service use in the working age population. Scand J Work Environ Health. 2007;33(1):29–36.

29. Lallukka T, Kronholm E, Pekkala J, Jäppinen S, Blomgren J, Pietiläinen O. Work participation trajectories among 1 , 098 , 748 Finns : reasons for premature labour market exit and the incidence of sickness absence due to mental disorders and musculoskeletal diseases. BMC Public Health. 2019;19(1418):1–13.

30. Tannenbau C, Lexchin J, Tamblyn R, Romans S. Indicators for measuring mental health: Towards better surveillance. Healthc Policy. 2009;5(2):e177–86.

31. Fried EI. The 52 symptoms of major depression: lack of content overlap among seven common depression scales. J Affect Disord. 2017;208:191–7.

32. Santor DA, Gregus M, Welch A. Eight Decades of Measurement in Depression. Meas Interdiscip Res Perspect. 2006;4(3):135–55.

33. Mitchell AJ, Yadegarfar M, Gill J, Stubbs B. Case finding and screening clinical utility of the Patient Health Questionnaire (PHQ-9 and PHQ-2) for depression in primary care: a diagnostic meta- analysis of 40 studies. BJPsych Open. 2016;2(2):127–38.

34. Dam NT Van, Earleywine M. Validation of the Center for Epidemiologic Studies Depression Scale — Revised (CESD-R): Pragmatic depression assessment in the general population. Psychiatry Res. 2011;186(1):128–32.

35. Trajkovi G, Star V, Latas M, Le M, Ille T, Bukumiri Z, et al. Reliability of the Hamilton Rating Scale for Depression : A meta-analysis over a period of 49 years. Psychiatry Res. 2011;189(1):1–9.

36. Beck AT, Steer RA, Ball R, Ranieri WF. Comparison of Beck Depression Inventories-IA and-II in psychiatric outpatients. J Pers Assess. 1996;67(3):588–97.

37. Kroenke K, D M, Spitzer RL, D M, Williams JBW, W DS, et al. The Patient Health Questionnaire Somatic , Anxiety , and Depressive Symptom Scales : a systematic review. Gen Hosp Psychiatry. 2010;32(4):345–59.

38. Wang J, Wu X, Lai W, Long E, Zhang X, Li W, et al. Prevalence of depression and depressive symptoms among outpatients: a systematic review and meta-analysis. BMJ Open. 2017;7(8):e017173.

39. Sjöberg L, Karlsson B, Atti AR, Skoog I, Fratiglioni L, Wang HX. Prevalence of depression: Comparisons of different depression definitions in population-based samples of older adults. J Affect Disord. 2017;221:123–31.

40. Kessler RC, Calabrese PA, Farley MJ, Gruber MA, Jewell MA, Katon W, et al. Composite International Diagnostic Interview screening scales for DSM-IV anxiety and mood disorders. Psychol Med. 2013;43(8):1625–37.

41. Kessler RC, Üstün TB. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res. 2006;13(2):93–121.

42. World Health Organization. International Statistical Classification of Diseases an Related Health Problems.-10th Revision, edition 2010. 4th ed. Geneva: World Health Organization; 2010.

43. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-IV.- 4th ed. American Psychiatric Association, editor. Washington, DC: American Psychiatric Association; 1994.

44. Li Z, Page A, Martin G, Taylor R. Attributable risk of psychiatric and socio-economic factors for suicide from individual-level, population-based studies: A systematic review. Soc Sci Med. 2011;72(4):608–16.

45. Ichimura A, Matsumoto H, Aoki T, Andoh H, Yano H, Nakagawa Y, et al. Characteristics of suicide attempters with depressive disorders. Psychiatry Clin Neurosci. 2005;59(5):590–4.

46. Luo Y, Zhang S, Zheng R, Xu L, Wu J. Effects of depression on heart rate variability in elderly patients with stable coronary artery disease. J Evid Based Med. 2018;11(4):242–5.

47. Scott KM, Lim C, Al-Hamzawi A, Alonso J, Bruffaerts R, Caldas-de-almeida JM, et al. Association of mental disorders with subsequent chronic physical conditions: World Mental Health Surveys from 17 countries. JAMA Psychiatry. 2016;73(2):150–8.

48. Subramaniam M, Mahesh MV, Peh CX, Tan J, Fauziana R, Satghare P, et al. Hazardous alcohol use among patients with schizophrenia and depression. Alcohol. 2017;65:63–9.

49. Charlson F, Baxter A, Dua T, Degenhardt L, Whiteford H, Vos T. Excess Mortality from Mental, Neurological, and Substance Use Disorders in the Global Burden of Disease Study 2010. In: Disease Control Priorities, Third Edition (Volume 4): Mental, Neurological, and Substance Use Disorders. 2016. p. 145–61.

50. Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJL, et al. Burden of pepressive disorders by country, sex, age, and year: Findings from the global burden of Disease study 2010. PLoS Med. 2013;10(11):e1001547.

51. Cuijpers P, Smit F. Excess mortality in depression : a meta-analysis of community studies. J Affect Disord. 2002;72(3):227–36.

52. Eaton WW, Martins SS, Nestadt G, Bienvenu OJ, Alexandre P. The burden of mental disorders. Epidemiol Rev. 2008;30(1):1–14.

53. Spijker J, De Graaf R, Bijl R V, Beekman ATF, Ormel J, Nolen WA. Functional disability and depression in the general population . Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). Acta Psychiatr Scand. 2004;110(3):208–14.

54. Antunes A, Frasquilho D, Azeredo-Lopes S, Neto D, Silva M, Cardoso G, et al. Disability and common mental disorders: Results from the World Mental Health Survey Initiative Portugal. Eur Psychiatry. 2018;49:56–61.

55. Meng X, Brunet A, Turecki G, Liu A, D'Arcy C, Caron J. Risk factor modifications and depression incidence : a 4-year longitudinal Canadian cohort of the Montreal Catchment Area Study. BMJ Open. 2017;7(8):e015156.

56. Fushimi M, Saito S, Shimizu T. Prevalence of depressive symptoms and related factors in Japanese rmployees as measured by the Center for Epidemiologic Studies Depression Scale (CES-D). Community Ment Health J. 2013;49(2):236–42.

57. Pirkola SP, Isometsä E, Suvisaari J, Aro H, Joukamaa M, Poikolainen K, et al.

DSM-IV mood- , anxiety- and alcohol use disorders and their comorbidity in the Finnish general population Results from the Health 2000 Study. Soc Psychiatry Psychiatr Epidemiol. 2005;40:1–10.

58. Kessler RC, Birnbaum H, Shahly V, Bromet E, Hwang I, Mclaughlin KA, et al. Age differences in the prevalence and comorbidity of DSM-IV major depressive episodes: Results from the WHO World Mental Health Survey Initiative. Depress Anxiety. 2010;27(4):351–64.

59. Bulloch AGM, Williams JVA, Lavorato DH, Patten SB. The depression and marital status relationship is modified by both age and gender. J Affect Disord. 2017;223:65–8.

60. Annequin M, Weill A, Thomas F, Chaix B. Environmental and individual characteristics associated with depressive disorders and mental health care use. Ann Epidemiol. 2015;25(8):605–12.

61. Rodrigues AP, Sousa-Uva M, Fonseca R, Marques S, Pina N, Matias-Dias C. Depression and unemployment incidence rate evolution in Portugal, 1995-2013: General Practitioner Sentinel Network data. Rev Saude Publica. 2017;51(98).

62. Niedzwiedz CL, Thomson KH, Bambra C, Pearce JR. Regional employment and individual worklessness during the Great Recession and the health of the working-age population: Cross-national analysis of 16 European countries. Soc Sci Med. 2020;267:112377.

63. Coelho IL, Sousa-Uva M, Pina N, Marques S, Matias-Dias C, Rodrigues AP. Economic crisis in Portugal: Trajectory of the incidence of depression and correlation with unemployment. Acta Med Port. 2021;34(4):278–82.

64. Kim I, Choi C, Urbanoski K, Park J, Kim J. Is job insecurity worse for mental health than having a part-time job in Canada? J Prev Med Public Heal. 2021;54(2):110–8.

65. Theorell T, Hammarström A, Aronsson G, Bendz LT, Grape T, Hogstedt C, et al. A systematic review including meta-analysis of work environment and depressive symptoms. BMC Public Health. 2015;15(738).

66. Madsen IEH, Nyberg ST, Magnusson Hanson LL, Ferrie JE, Ahola K, Alfredsson L, et al. Job strain as a risk factor for clinical depression: Systematic review and meta-analysis with additional individual participant data. Psychol Med. 2017;47(8):1342–56.

67. Evans-Lacko S, Knapp M. Importance of social and cultural factors for attitudes,

disclosure and time off work for depression: findings from a seven country European study on depression in the workplace. PLoS One. 2014;9(3):e91053.

68. Kleppa E, Sanne B, Tell GS. Working overtime is associated with anxiety and depression : The Hordaland Health study. J Occup Environ Med. 2008;50(6):658–66.

69. Stewart WF, Ricci JA, Chee E, Hahn SR, Morganstein D. Cost of lost productive work time among US workers with depression. J Am Med Assoc. 2003;289(23):3135–44.

70. Richardson R, Westley T, Gariépy G, Austin N, Nandi A. Neighborhood socioeconomic conditions and depression : a systematic review and meta-analysis. Soc Psychiatry Psychiatr Epidemiol. 2015;50:1641–56.

71. Rautio N, Filatova S, Lehtiniemi H, Miettunen J. Living environment and its relationship to depressive mood : A systematic review. Int J Soc Psychiatry. 2018;64(1):92–103.

72. Charlson F, van Ommeren M, Flaxman A, Cornett J, Whiteford H, Saxena S. New WHO prevalence estimates of mental disorders in conflict settings: a systematic review and meta-analysis. Lancet. 2019;394(10194):240–8.

73. Hidaka BH. Depression as a disease of modernity: explanations for increasing prevalence. J Affect Disord. 2012;140(3):205–14.

74. Baglioni C, Battagliese G, Feige B, Spiegelhalder K, Nissen C, Voderholzer U, et al. Insomnia as a predictor of depression : A meta-analytic evaluation of longitudinal epidemiological studies. J Affect Disord. 2011;135(1–3):10–9.

75. Grosso G, Micek A, Castellano S, Pajak A, Galvano F. Coffee, tea, caffeine and risk of depression: A systematic review and dose-response meta-analysis of observational studies. Mol Nutr Food Res. 2016;60(1):223–34.

76. Zhang XC, Woud ML, Becker ES, Margraf J. Do health-related factors predict major depression? A longitudinal epidemiologic study. Clin Psychol Psychother. 2018;25(3):378–87.

77. Faith MS, Butryn M, Wadden TA, Fabricatore A, Nguyen AM, Heymsfield SB. Evidence for prospective associations among depression and obesity in population-based studies. Obes Rev. 2011;12(5):e438–53.

78. Li J, Wang H, Li M, Shen Q, Li X, Zhang Y, et al. Effect of alcohol use disorders and alcohol intake on the risk of subsequent depressive symptoms: a systematic

review and meta-analysis of cohort studies. Addiction. 2020;115(7):1224–43.

79. Pavkovic B, Zaric M, Markovic M, Klacar M, Huljic A. Double screening for dual disorder, alcoholism and depression. Psychiatry Res. 2018;270:483–9.

80. Rosenbaum S, Tiedemann A, Sherrington C, Curtis J, Ward PB. Physical activity interventions for people with mental illness: A systematic review and meta-analysis. J Clin Psychiatry. 2014;75(9):964–74.

81. Gianfredi V, Blandi L, Cacitti S, Minelli M, Signorelli C, Amerio A, et al. Depression and objectively measured physical activity : A systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(10):3738.

82. Read JR, Sharpe L, Modini M, Dear BF. Multimorbidity and depression: A systematic review and meta-analysis. J Affect Disord. 2017;221:36–46.

83. Burcusa SL, Iacono WG. Risk for recurrence in depression. Clin Psychol Rev. 2007;27(8):959–85.

84. Vigo D, Thornicroft G, Atun R. Estimating the true global burden of mental illness. The Lancet Psychiatry. 2016;3(2):171–8.

85. Alonso J, Petukhova M, Vilagut G, Chatterji S, Heeringa S, Üstün TB, et al. Days out of role due to common physical and mental conditions : results from the WHO World Mental Health surveys. Mol Psychiatry. 2011;16(12):1234–46.

86. Graaf R De, Tuithof M, Dorsselaer S Van, Have M ten. Comparing the effects on work performance of mental and physical disorders. Soc Psychiatry Psychiatr Epidemiol. 2012;47(11):1873–83.

87. Chong SA, Vaingankar JA, Abdin E, Subramaniam M. Mental disorders: employment and work productivity in Singapore. Soc Psychiatry Psychiatr Epidemiol. 2013;48:117–23.

88. Hilton MF, Scuffham PA, Sheridan J, Cleary CM, Whiteford HA. Mental ill-health and the differential effect of employee type on absenteeism and presenteeism. J Occup Environ Med. 2008;50(11):1228–43.

89. Kessler RC, Akiskal HS, Ames M, Birnbaum H, Greenberg P, Hirschfeld RMA, et al. Prevalence and effects of mood disorders on work performance in a nationally representative sample of US workers. Am J Psychiatry. 2006;163(9):1561–8.

90. Cardoso G, Xavier M, Vilagut G, Petukhova M, Alonso J, Kessler RC, et al. Days out of role due to common physical and mental conditions in Portugal: results

from the WHO World Mental Health Survey. BJPsych Open. 2017;3(1):15–21.

91. Shippee ND, Shah ND, Williams MD, Moriarty JP, Frye MA, Ziegenfuss JY. Differences in demographic composition and in work , social , and functional limitations among the populations with unipolar depression and bipolar disorder : results from a nationally representative sample. Health Qual Life Outcomes. 2011;9(90).

92. Chang SM, Hong J, Cho MJ. Economic burden of depression in South Korea. Soc Psychiatry Psychiatr Epidemiol. 2012;47:683–9.

93. Bruffaerts R, Vilagut G, Demyttenaere K, Alonso J, Alhamzawi A, Andrade LH, et al. Role of common mental and physical disorders in partial disability around the world. Br J Psychiatry. 2012;200(6):454–61.

94. Barbaglia G, Duran N, Vilagut G, García C, Maria J, Alonso J. Effects of common mental disorders and physical conditions on role functioning in Spain. Gac Sanit. 2013;27(6):480–6.

95. Adler DA, McLaughlin TJ, Rogers WH, Chang H, Lapitsky L, Lerner D. Job performance deficits due to depression. Am J Psychiatry. 2006;163(9):1569–76.

96. Lagerveld SE, Bültmann U, Franche RL, Van Dijk FJH, Vlasveld MC, Van Der Feltz-Cornelis CM, et al. Factors associated with work participation and work functioning in depressed workers: A systematic review. J Occup Rehabil. 2010;20(3):275–92.

97. Mattila-Holappa P, Ervasti J, Joensuu M, Ahola K, Pentti J, Oksanen T, et al. Do predictors of return to work and recurrence of work disability due to mental disorders vary by age? A cohort study. Scand J Public Health. 2017;45(2):178–84.

98. Veronese A, Ayuso-mateos JL, Cabello M, Chatterji S, Nuevo R. Work disability and depressive disorders: impact on the European population. Am J Phys Med Rehabil. 2012;91(2):S62–8.

99. Mousteri V, Daly M, Delaney L, Tynelius P, Rasmussen F. Adolescent mental health and unemployment over the lifespan: Population evidence from Sweden. Soc Sci Med. 2019;222:305–14.

100. Link BG, Phelan JC, Sullivan G. Mental and physical health consequences of the stigma associated with mental illnesses. In: Major B, Dovidio JF, Link BG, editors. The Oxford Handbook of Stigma, Discrimination, and Health. New York: Oxford University Press; 2018. p. 521–40.

101. Yin H, Wardenaar KJ, Xu G, Tian H, Schoevers RA. Mental health stigma and mental health knowledge in Chinese population : a cross- sectional study. 2020;1–10.

102. Angermeyer MC, Holzinger A, Matschinger H. Mental health literacy and attitude towards people with mental illness : A trend analysis based on population surveys in the eastern part of Germany. Eur Psychiatry. 2009;24(4):225–32.

103. Crisp AH, Gelder MG, Rix S, Meltzer HI, Rowlands OJ. Stigmatisation of people with mental illnesses. Br J Psychiatry. 2000;177(1):4–7.

104. Pescosolido BA, Medina TR, Martin JK, Long JS. The " Backbone " of Stigma : Identifying the Global Core of Public Prejudice Associated With Mental Illness. Am J Public Health. 2013;103(5):853–60.

105. Schomerus G, Matschinger H, Kenzin D, Breier P, Angermeyer MC. Public attitudes towards mental patients : a comparison between Novosibirsk , Bratislava and German cities. Eur Psychiatry. 2006;21:436–41.

106. Olesen SC, Butterworth P, Leach LS, Kelaher M, Pirkis J. Mental health affects future employment as job loss affects mental health: findings from a longitudinal population study. BMC Psychiatry. 2013;13(144).

107. Butterworth P, Leach LS, Pirkis J, Kelaher M. Poor mental health influences risk and duration of unemployment: a prospective study. Soc Psychiatry Psychiatr Epidemiol. 2012;47:1013–21.

108. Mojtabai R, Stuart EA, Hwang I, Susukida R, Eaton WW, Sampson N, et al. Long-Term Effects of Mental disorders on Employment In the National Comorbidity Survey Ten-Year Follow-up. Soc Psychiatry Psychiatr Epidemiol. 2015;50(11):1657–68.

109. Karpansalo M, Kauhanen J, Lakka T, Manninen P, Kaplan G, Salonen J. Depression and early retirement: prospective population based study in middle aged men. J Epidemiol Community Health. 2005;59:70–4.

110. Philipson A, Alaie I, Ssegonja R, Imberg H, Copeland W, Möller M, et al. Adolescent depression and subsequent earnings across early to middle adulthood: a 25-year longitudinal cohort study. Epidemiol Psychiatr Sci. 2020;29(e123):1–10.

111. Schofield DJ, Kelly SJ, Shrestha RN, Callander EJ, Percival R, Passey ME. How depression and other mental health problems can affect future living standards of those out of the labour force. Aging Ment Health. 2011;15(5):654–62.

112. Yeh H-H, Westphal J, Hu Y, Peterson EL, Williams LK, Prabhakar D, et al. Diagnosed mental health conditions and risk of suicide mortality. Psychiatr Serv. 2019 Sep 1;70(9):750–7.

113. Lasserre AM, Marti-Soler H, Strippoli MPF, Vaucher J, Glaus J, Vandeleur CL, et al. Clinical and course characteristics of depression and all-cause mortality: A prospective population-based study. J Affect Disord. 2016;189:17–24.

114. Thornicroft G, Chatterji S, Evans-Lacko S, Gruber M, Sampson N, Aguilar-Gaxiola S, et al. Undertreatment of people with major depressive disorder in 21 countries. Br J Psychiatry. 2017;210(2):119–24.

115. Luber MP, Hollenberg JP, Williams-Russo P, Didomenico TN, Meyers BS, Alexopoulos GS, et al. Diagnosis, treatment, comorbidity, and resource utilization of depressed patients in a general medical practice. Int J Psychiatry Med. 2000;30(1):1–13.

116. Simo B, Bamvita J, Caron J, Fleury M-J. Predictors of mental health service use among individuals with high psychological distress and mental disorders. Psychiatry Res. 2018;270:1122–30.

117. Frasquilho D, Matos MG, Salonna F, Guerreiro D, Storti CC, Gaspar T, et al. Mental health outcomes in times of economic recession: a systematic literature review. BMC Public Health. 2016;16(115).

118. Anderson P, Jané-Llopis E, Hosman C. Reducing the silent burden of impaired mental health. Health Promot Int. 2011;26(S1):i4–9.

119. Silva M, Resurrección DM, Antunes A, Frasquilho D, Cardoso G. Impact of economic crises on mental health care: a systematic review. Epidemiol Psychiatr Sci. 2020;29(e7):1–13.

120. Antunes A, Frasquilho D, Silva M, Cardoso G. Changes in socioeconomic position among individuals with mental disorders during the economic recession in Portugal: a follow-up of the National Mental Health Survey. Epidemiol Psychiatr Sci. 2019;28(6):638–43.

121. Johnston KM, Powell LC, Anderson IM, Szabo S, Cline S. The burden of treatment-resistant depression: A systematic review of the economic and quality of life literature. J Affect Disord. 2019;242:195–210.

122. Mrazek DA, Hornberger JC, Altar CA, Degtiar I. A review of the clinical, economic, and societal burden of treatment-resistant depression: 1996-2013. Psychiatr Serv. 2014;65(8):977–87.

123. Ramos F, Sennfelt J, Amaral MJ, Valente P. Economia da saúde e saúde mental- os custos da depressão. Rev Port Saúde Pública. 1996;14(2):53–68.

124. Gustavsson A, Svensson M, Jacobi F, Allgulander C, Alonso J, Beghi E, et al. Cost of disorders of the brain in Europe 2010. Eur Neuropsychopharmacol. 2011;21(10):718–79.

125. Olesen J, Gustavsson A, Svensson M, Wittchen H-U, Jönsson B. The economic cost of brain disorders in Europe. Eur J Neurol. 2012;19(1):155–62.

126. Salvador-Carulla L, Bendeck M, Fernández A, Alberti C, Sabes-Figuera R, Molina C, et al. Costs of depression in Catalonia (Spain). J Affect Disord. 2011;132(1–2):130–8.

127. Cuijpers P, Smit F, Oostenbrink J, de Graaf R, ten Have M, Beekman A. Economic costs of minor depression: a population-based study. Acta Psychiatr Scand. 2007;115(3):229–36.

128. Thomas CM, Morris S. Cost of depression among adults in England in 2000. Br J Psychiatry. 2000;183(6):514–9.

129. Chisholm D, Diehr P, Knapp M, Patrick D, Treglia M, Simon G. Depression status, medical comorbidity and resource costs: Evidence from an international study of major depression in primary care (LIDO). Br J Psychiatry. 2003;183(2):121–31.

130. Lee Y, Chatterton M Lou, Magnus A, Mohebbi M, Le LK, Mihalopoulos C. Cost of high prevalence mental disorders: Findings from the 2007 Australian National Survey of Mental Health and Wellbeing. Aust New Zeal J Psychiatry. 2017;51(12):1198–211.

131. Instituto Nacional de Estatística. Ganho médio mensal (€) por Localização geográfica (NUTS - 2013); Anual [Internet]. MTSSS/GEP, Quadros de pessoal. 2020 [cited 2021 Feb 14]. Available from: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_indicadores&indOcorrCod=0009047&selTab=tab0

132. Instituto Nacional de Estatística. Documento Metodológico: Inquérito Nacional de Saúde. Instituto Nacional de Estatística; 2014.

133. Instituto Nacional de Estatística. Documento Metodológico: Inquérito Nacional de Saúde. Instituto Nacional de Estatística; 2020.

134. Instituto Nacional de Estatística. Inquérito Nacional de Saúde 2014. Lisboa:

Instituto Nacional de Estatística; 2016.

135. Góis E. Inquérito Nacional de Saúde 2019. In INE / Departamento de Estatísticas Sociais; 2020.

136. Instituto Nacional de Estatística. Atualização de valores com base no IPC [Internet]. Instituto Nacional de Estatística. 2020 [cited 2021 Feb 21]. Available from: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ipc

137. Kroenke K, Spitzer R, Williams J. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–13.

138. Lamela D, Soreira C, Matos P, Morais A. Systematic review of the factor structure and measurement invariance of the patient health questionnaire-9 (PHQ-9) and validation of the Portuguese version in community settings. J Affect Disord. 2020;276:220–33.

139. Kroenke K, Strine TW, Spitzer RL, Williams JBW, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord. 2009;114(1–3):163–73.

140. Department of Mental Health and Substance Dependence Noncommunicable Diseases and Mental Health Cluster. International Guide for Monitoring Alcohol Comsumption and Related Harm. World Health Organization, editor. Geneva; 2000.

141. Xavier M, Baptista H, Mendes JM, Magalhães P, Caldas-de-almeida JM. Implementing the World Mental Health Survey Initiative in Portugal – rationale , design and fieldwork procedures. Int J Ment Health Syst. 2013;7(19):1–10.

142. Gonçalves B, Fagulha T. Prevalência e diagnóstico da depressão em medicina geral e familiar. Rev Port Clínica Geral. 2004;20:13–27.

143. Steffen A, Thom J, Jacobi F, Holstiege J, Bätzing J. Trends in prevalence of depression in Germany between 2009 and 2017 based on nationwide ambulatory claims data. J Affect Disord. 2020;271:239–47.

144. Frias P, Pinto da Costa M. Community psychiatry in Portugal: a critical review. Consort Psychiatr. 2020;1(1):49–59.

145. Rost K, Smith JL, Dickinson M. The Effect of Improving Primary Care Depression Management on Employee Absenteeism and Productivity A Randomized Trial. Med Care. 2004;42(12):1202–10.

146. Perelman J, Chaves P, de Almeida JMC, Matias MA. Reforming the Portuguese

mental health system: An incentive-based approach. Int J Ment Health Syst. 2018;12(1):1–10.

147. Conselho Nacional da Saúde. Sem mais tempo a perder - Saúde mental em Portugal: um desafio para a próxima década. Lisboa: CNS; 2019.

8. Appendix

a. Literature Review of the Economic Cost of depression in Portugal

A literature search was performed on January 19th, 2021 on PubMed, Web of Science and Scopus for country-specific studies regarding the economic cost of depression to the Portuguese population. The following search algorithms were used, and the following results obtained:

PubMed search:

- ("Depression/economics"[Mesh]) OR "Depressive Disorder/economics"[Mesh] OR "Depressive Disorder, Major/economics"[Mesh]) AND "Portugal"[Mesh]: 2 documents
- ("Mental Health/economics"[Mesh]) AND "Portugal"[Mesh]: 2 documents

Web of Science, using All Databases, search:

- TOPIC:((depression OR "depressive disorder*") AND (economic OR costs) AND Portugal): 100 documents
- TOPIC: ("mental health" AND (economic OR costs) AND Portugal): 103 documents

Scopus search:

- (TITLE-ABS-KEY (depression OR "depressive disorder*") AND TITLE-ABS-KEY (economic OR costs) AND TITLE-ABS-KEY (portugal)): 77 documents
- (TITLE-ABS-KEY ("mental health") AND TITLE-ABS-KEY (economic OR costs) AND TITLE-ABS-KEY (portugal)) : 76 documents

After reviewing the titles and abstracts of the documents resulting from the search it was concluded that none of them presented a review of the costs of depression in Portugal. From the reading of additional literature on this field of interest regarding the Portuguese context, only an article was found referring to the estimated costs of depression in 1992 for the Portuguese society(123).

a. Complementary Tables

Appendix 1- *General adult population sample characteristics of NHS 2014 and 2019 on self-reported depression in the last 12 months and PHQ-8 depression prevalence and severity in the last 2 weeks.*

		Year	
		2014 (N=17,769)	**2019 (N=14,341)**
Variable		**n (%)**	**n (%)**
Self- reported Depression	**n**	n= 17,718	n= 14,197
	No	15,292 (86.3)	12,059 (84.9)
	Yes	2,426 (13.7) 95%CI= [13.2-14.2]	2,138 (15.1) 95%CI= [14.5-15.7]
Depression (PHQ-8)	**n**	n= 17,540	n= 13,853
	No	15,774 (89.9)	12,628 (91.2)
	Yes	1,766 (10.1) 95%CI= [9.6-10.5]	1,225 (8.8) 95%CI= [8.4-9.3]
Depression Severity (PHQ-8)	**n**	n= 17,540	n= 13,853
	None/Minimal	12,503 (71.3)	10,079 (72.8)
	Mild	3,271 (18.6)	2,549 (18.4)
	Moderate	1,104 (6.3)	744 (5.4)
	Moderately Severe	453 (2.6)	329 (2.4)
	Severe	209 (1.2)	152 (1.1)

Appendix 2- *General adult population sample demographic characteristics of NHS 2014 and 2019.*

		Year	
		2014 (N=17,769)	**2019 (N=14,341)**
Variable		**n (%)**	**n (%)**
Gender	**n**	n= 17,769	n= 14,341
	Female	10,038 (56.5)	8,146(56.8)
	Male	7,731 (43.5)	6,195 (43.2)
Age group (years)	**n**	n= 17,769	n= 14,341
	18-24	983 (5.5)	761 (5.3)
	25-34	1,843 (10.4)	1,101 (7.7)
	35-44	3,188 (17.9)	2,008 (14.0)
	45-54	3,023 (17.0)	2,357 (16.4)
	55-64	3,031 (17.1)	2,768 (19.3)
	>=65	5,701 (32.1)	5,346 (37.3)
Education Level	**n**	n= 17,769	n= 14,341
	No Education Level	2,349 (13.2)	1,501 (10.5)
	Primary Education	7,133 (40.1)	5,701 (39.8)
	Lower Secondary Education	2,754 (15.5)	2,190 (15.3)

		Year	
		2014 (N=17,769)	2019 (N=14,341)
Variable		**n (%)**	**n (%)**
	Upper Secondary Education	2,723 (15.3)	2,394 (16.7)
	Post-Secondary Non-Tertiary Education	162 (0.9)	165 (1.2)
	Tertiary Education	2,648 (14.9)	2,390 (16.7)
Marital Status	**n**	n= 17,769	n= 14,296
	Single	4,435 (22.7)	3,450 (24.1)
	Married	9,399 (52.9)	7,176 (50.2)
	Widow	2,615 (14.7)	2,231 (15.6)
	Divorced	1,708 (9.6)	1,439 (10.1)

Appendix 3- *General adult population sample economic characteristics of NHS 2014 and 2019.*

		Year	
		2014 (N=17,769)	2019 (N=14,341)
Variable		**n (%)**	**n (%)**
Employment Status	**n**	n= 17,754	n= 14,309
	Unemployed	2,066 (11.6)	1,004 (7.0)
	Employed	7,788 (43.9)	6,469 (45.2)
	Other Working Inactivity type	7,900 (44.5)	6,836 (47.8)
Income Range	**n**	n= 17,769	n= 14,341
	1st Quintile	3,878 (21.8)	2,631 (18.3)
	2nd Quintile	3,656 (20.6)	3,543 (24.7)
	3rd Quintile	3,517 (19.8)	2,971 (20.7)
	4th Quintile	3,372 (19.0)	2,588 (18.0)
	5th Quintile	3,346 (18.8)	2,608 (18.2)

Appendix 4- *General adult population sample health-related characteristics of NHS 2014 and 2019.*

		Year	
		2014 (N=17,769)	2019 (N=14,341)
Variable		**n (%)**	**n (%)**
Overweight	**n**	n= 17,769	n= 14,341
	No	7,672 (43.2)	6,077 (42.4)
	Yes	10,097 (56.8)	8,264 (57.6)
Tobacco Consumption	**n**	n= 17,758	n= 14,289
	Non-smoker	10,034 (58.2)	8,787 (61.5)
	Smoker	3,499 (19.7)	2,356 (16.5)

Variable		Year	
		2014 (N=17,769)	2019 (N=14,341)
		n (%)	n (%)
	Former Smoker	3,915 (22.0)	3,146 (22.0)
Alcohol Consumption	**n**	n= 17,684	n= 14,297
	Non-drinkers	10,561 (59.7)	8,839 (61.8)
	Non-high-risk drinkers	6,249 (35.3)	4,860 (34.0)
	High-risk drinkers	874 (4.9)	598 (4.2)
Physical Activity	**n**	n= 17,722	n= 14,119
	Non-regular	13,074 (72.8)	10,751 (76.1)
	Regular	4,648 (26.2)	3,568 (23.9)
Number of comorbidities (other than depression)	**n**	n= 17,655	n= 13,948
	0	6,464 (36.6)	4,290 (30.8)
	1-2	5,217 (29.5)	4,406 (31.6)
	3 or more	5,974 (33.8)	5,252 (37.7)
Healthcare resources utilization	**n**	n= 17,719	n= 14,156
	Mean	0.51	0.74
	Median	0.0	0.0
	Standard Deviation	0.01	0.01
	Min	0.0	0.0
	Max	624.0	20.0
	Interquartile Amplitude	1.0	1.0

Appendix 5- *Frequencies of PHQ-8 depression severity in the last 2 weeks in the general adult population with and without self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year			
		2014 (N=17,769)		2019 (N=14,341)	
		No Depression	Depression	No Depression	Depression
		n (%)	n (%)	n (%)	n (%)
Depression Severity (PHQ-8)	**n**	n= 17506		n= 13760	
	None/minimal	11,926(78.8)	558 (23.4)	9,459 (80.9)	573 (27.8)
	Mild	2,399 (15.9)	863 (36.2)	1,717 (14.7)	808 (39.2)
	Moderate	563 (3.7)	535 (22.5)	371 (3.2)	356 (17.3)
	Moderately Severe	173 (1.1)	280 (11.8)	109 (0.9)	217 (10.5)
	Severe	64 (0.4)	145 (6.1)	41(0.4)	109 (5.3)

Appendix 6- *Frequencies in general adult population with and without self-reported depression and associations of demographic characteristics with self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Gender	**n**	n=17,718			n= 14,197		
	Female	8117 (53.1)	1,892 (78.0)	ref.	6,421 (53.2)	1,636 (76.5)	ref.
	Male	7,175 (46.9)	534 (22.0)	0.319 [0.289-0.353]	5,638 (46.8)	502 (23.5)	0.349 [0.314-0.389]
Age group (years)	**n**	n=17,718			n= 14,197		
	18-24	955 (6.1)	26 (1.1)	ref.	718 (6.0)	36 (1.7)	ref.
	25-34	1,739 (11.4)	100 (4.1)	2.112 [1.362-3.275]	1,010 (8.4)	77 (3.6)	1.521 [1.012-2.285]
	35-44	2,924 (19.1)	256 (10.6)	3.216 [2.134-4.846]	1,799 (14.9)	181 (8.5)	2.007 [1.389-2.899]
	45-54	2,617 (17.1)	396 (16.3)	5.558 [3.712-8.322]	2,006 (16.6)	324 (15.2)	3.221 [2.259-4.593]
	55-64	2,450 (16.0)	566 (23.3)	8.486 [5.687-12.661]	2,263 (18.8)	488 (22.8)	4.301 [3.035-6.096]
	>=65	4,607 (30.1)	1,082 (44.6)	8.627 [5.811-12.807]	4,263 (35.4)	1,032 (48.3)	4.828 [3.431-6.794]
Education Level	**n**	n=17,718			n= 14,197		
	No Education Level	1,908 (12.5)	437 (18.0)	ref.	1166 (9.7)	320 (15.0)	ref.
	Primary Education	5,815 (38.0)	1,309 (54.0)	0.983 [0.872-1.108]	4,566 (37.9)	1,101 (51.5)	0.879 [0.764-1.011]
	Lower Secondary Education	2,447 (16.0)	297 (12.2)	0.530 [0.452-0.621]	1,873 (15.5)	293 (13.7)	0.570 [0.479-0.679]
	Upper Secondary Education	2,524 (16.5)	188 (7.7)	0.325 [0.271-0.390]	2151 (17.8)	213 (10.0)	0.361 [0.299-0.435]
	Post-Secondary Non-Tertiary Education	150 (1.0)	11 (0.5)	0.320 [0.172-0.596]	145 (1.2)	17 (0.8)	0.427 [0.255-0.717]

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
	Tertiary Education	2,448 (16.0)	184 (7.6)	0.328 [0.273-0.394]	2,158 (17.9)	194 (9.1)	0.328 [0.270-0.397]
Marital Status	**n**	n=17,707			n= 14,161		
	Single	3,713 (24.3)	311 (12.8)	ref.	3,069 (25.5)	341 (16.0)	ref.
	Married	8,104 (53.0)	1,267 (52.2)	1.867 [1.639-2.126]	6,100 (50.7)	1,020 (47.8)	1.505 [1.321-1.714]
	Widow	2,041 (13.4)	569 (23.5)	3.328 [2.869-3.861]	1,682 (14.0)	532 (24.9)	2.847 [2.454-3.302]
	Divorced	1,423 (9.3)	279 (11.5)	2.341 [1.969-2.782]	1,175 (9.8)	242 (11.3)	1.854 [1.551-2.215]

Legend: OR = unadjusted odds ratio.

Appendix 7- *Frequencies in general adult population with and without self-reported depression and associations of economic characteristics with self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Employment Status	**n**	n= 17,703			n= 14,171		
	Unemployed	1,759 (11.5)	300 (12.4)	ref.	805 (6.7)	190 (8.9)	ref.
	Employed	7,155 (46.8)	609 (25.1)	0.499 [0.431-0.579]	5,811 (48.3)	592 (27.7)	0.432 [0.361-0.516]
	Other Working Inactivity type	6,366 (41.7)	1,514 (62.5)	1.394 [1.219-1.595]	5,419 (45.0)	1,354 (63.4)	1.059 [0.894-1.253]
Income Range	**n**	n=17,718			n= 14,197		
	1st Quintile	3,215 (21.0)	655 (27.0)	ref.	2,107 (17.5)	501 (23.4)	ref.
	2nd Quintile	3,059 (20.0)	593 (24.4)	0.952 [0.843-1.075]	2,810 (23.3)	695 (32.5)	1.040 [0.915-1.182]

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
	3rd Quintile	2,991 (19.6)	513 (21.1)	0.842 [0.742-0.955]	2,532 (21.0)	418 (19.6)	0.694 [0.602-0.800]
	4th Quintile	2,958 (19.3)	402 (16.6)	0.667 [0.583-0.763]	2,268 (18.8)	292 (13.7)	0.541 [0.463-0.633]
	5th Quintile	3,069 (20.1)	263 (10.8)	0.421 [0.362-0.489]	2,342 (19.4)	232 (10.9)	0.417 [0.353-0.492]

Legend: OR = unadjusted odds ratio.

Appendix 8- *Frequencies in general adult population with and without self-reported depression and associations of health-related characteristics with self-reported depression in the last 12 months in 2014 and 2019.*

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Overweight	**n**	n=17,718			n= 14,197		
	No	6,741 (44.1)	904 (37.3)	ref.	5,280 (43.8)	719 (33.6)	ref.
	Yes	8,551 (55.9)	1,522(62.7)	1.327 [1.215-1.450]	6,779 (56.2)	1,419(66.4)	1.537 [1.396-1.693]
Tobacco Consumption	**n**	n=17,710			n= 14,165		
	Non-smoker	8,633(56.5)	1,682(69.4)	ref.	7,254 (60.3)	1,455(68.1)	ref.
	Smoker	3,129 (20.5)	365 (15.1)	0.599 [0.531-0.675]	2,027 (16.9)	312 (14.6)	0.767 [0.673-0.876]
	Former Smoker	3,523 (23.0)	378 (15.6)	0.551 [0.489-0.620]	2,748 (22.8)	369 (17.3)	0.669 [0.592-0.757]
Alcohol Consumption	**n**	n=17,636			n= 14,159		
	Non-drinkers	8,702 (57.2)	1,830(75.6)	ref.	7,137 (59.4)	1,608(75.3)	ref.
	Non-high-risk drinkers	5,698 (37.4)	534 (22.1)	0.446 [0.402-0.494]	4,329 (36.0)	489 (22.9)	0.501 [0.450-0.559]
	High-risk drinkers	816 (5.4)	56 (2.3)	0.326 [0.248-0.430]	557 (4.6)	39 (1.8)	0.311 [0.224-0.432]

Variable		Year					
		2014 (N=17,769)			2019 (N=14,341)		
		No Depression	Depression		No Depression	Depression	
		n (%)	n (%)	OR [95%CI]	n (%)	n (%)	OR [95%CI]
Physical Activity	**n**	n=17,679			n= 14,013		
	Non-regular	11,055(72.5)	1,990(82.1)	ref.	8,878 (74.6)	1,795(85.0)	ref.
	Regular	4,201 (27.5)	433 (17.9)	0.573 [0.513-0.639]	3,022 (25.4)	318 (15.0)	0.520 [0.459-0.590]
Number of comorbidities (other than depression)	**n**	n=17,626			n= 13,899		
	0	6,239 (41.0)	215 (8.9)	ref.	4,131 (34.9)	147 (7.2)	ref.
	1-2	4,679 (30.8)	534 (22.1)	3.312 [2.814-3.897]	3,907 (33.0)	483 (23.5)	3.474 [2.874-4.200]
	3 or more	4,295 (28.2)	1,664(69.0)	11.243[9.703-13.026]	3,807 (32.1)	1,424(69.3)	10.512[8.820-12.527]
Healthcare resources utilization	**n**	n=17,674			n= 14,034		
		2,417	15,257	1.395 [1.343-1.450]	11,923	2,111	1.244 [1.208-1.282]
	Mean	0.45	0.89		0.66	1.17	
	Median	0.0	1.0		0.0	1.0	
	Standard Deviation	0.01	0.03		0.01	0.04	
	Min	0.0	0.0		0.0	0.0	
	Max	20.0	24.0		20.0	18.0	
	Interquartile Amplitude	1.0	1.0		1.0	2.0	

Legend: OR = unadjusted odds ratio.

Appendix 9- *Frequencies for depression diagnosis and depression severity according to PHQ-8 in the last 2 weeks and other variables used in the logistic regression model in the employed adult population with and without any self-reported work absence due to a health condition in the last 12 months in 2014 and 2019.*

Variable		Year			
		2014 (N=7,788)		2019 (N=6,469)	
		No Absence	At Least 1 day	No Absence	At Least 1 day
		n (%)	n (%)	n (%)	n (%)
Depression (PHQ-8)	**n**	n= 7,706		n= 6,239	
	No	5,549(75.8)	1,771(24.2)	4,400(73.6)	1,575 (26.4)
	Yes	181(46.9)	205 (53.1)	112 (42.4)	152 (57.6)
Depression Severity (PHQ8)	n	n= 7,780		n= 6,239	
	None/minimal	4,911(78.7)	1,332(21.3)	3,930(76.8)	1,184 (23.2)
	Mild	638 (59.2)	439 (40.8)	470 (54.6)	391 (45.4)
	Moderate	132 (52.4)	120 (47.6)	82 (46.6)	94 (53.4)
	Moderately Severe	37 (41.6)	52 (58.4)	15 (26.8)	41 (73.2)
	Severe	12 (26.7)	33 (73.3)	15 (46.9)	17 (53.1)
Gender	**n**	n= 7,780		n= 6,440	
	Female	2,844(71.5)	1,132(28.5)	2,305(68.4)	1,065 (31.6)
	Male	2,935(77.2)	869 (22.8)	2,331(75.9)	739 (24.1)
Age group (years)	**n**	n= 7,780		n= 6,440	
	18-24	207(79.6)	53 (20.4)	198 (74.2)	1,575 (26.4)
	25-34	1,017(75.4)	332 (24.6)	595 (67.7)	152 (57.6)
	35-44	1,883(73.9)	665 (26.1)	1,252(73.3)	456 (26.7)
	45-54	1,603(74.6)	546 (25.4)	1,333(71.8)	1,184 (23.2)
	55-64	916 (71.7)	362 (28.3)	1,081(72.4)	391 (45.4)
	>=65	153 (78.1)	43 (21.9)	177 (75.3)	94 (53.4)
Tobacco Consumption	**n**	n= 7,775		n= 6,410	
	Non-smoker	2,944(75.2)	972 (24.8)	2,550(74.7)	865 (25.3)
	Smoker	1,525(72.9)	567 (27.1)	1,052(69.4)	463 (30.6)
	Former Smoker	1,307(74.0)	460 (26.0)	1,011(68.3)	469 (31.7)
Number of comorbidities (other than depression)	**n**	n= 7,731		n= 6,292	
	0	3,245(81.4)	743 (18.6)	2,305(81.3)	531 (18.7)
	1-2	1,743(71.8)	684 (28.2)	1,503(69.0)	674 (38.4)
	3 or more	762 (57.9)	554 (42.1)	727 (56.8)	552 (43.2)
Healthcare resources utilization	**n**	n= 7,752		n= 6,353	
		5,576	1993	4,588	1,765
	Mean	0.31	0.73	0.43	0.98
	Median	0.0	0.0	0.0	0.0
	Standard Deviation	0.01	0.03	0.01	0.04

Variable		Year			
		2014 (N=7,788)		2019 (N=6,469)	
		No Absence	At Least 1 day	No Absence	At Least 1 day
		n (%)	n (%)	n (%)	n (%)
	Min	0.0	0.0	0.0	0.0
	Max	9.0	24.0	15.0	20
	Interquartile Amplitude	0.0	1.0	1.0	1.0

Appendix 10- *Binary logistic regression model for the association of self-reported depression with any work absence due to a health condition in the last 12 months in 2014 and 2019 and adjusted by gender, age group, tobacco consumption, number of comorbidities and healthcare resources utilization.*

Variable		Year	
		2014 (N=7,788)	2019 (N=6,469)
		OR [95%CI]	OR [95%CI]
Self- reported Depression	**n**		
	No	ref.	ref.
	Yes	2.283 [1.898-2.746]	2.244 [1.851-2.721]
Gender	**n**	n= 7,780	n= 6,440
	Female	ref.	ref.
	Male	0.945 [0.842- 1.060]	0.838 [0.739-0.950]
Age group (years)	**n**	n= 7,780	n= 6,440
	18-24	ref.	ref.
	25-34	1.237 [0.884- 1.731]	1.342 [0.968- 1.860]
	35-44	1.178 [0.852-1.629]	0.863 [0.631-1.180]
	45-54	0.907 [0.652-1.261]	0.797 [0.583-1.089]
	55-64	0.894 [0.635-1.260]	0.647 [0.470-0.891]
	>=65	0.620 [0.384-1.000]	0.493 [0.317-0.767]
Tobacco Consumption	**n**	n= 7,775	n= 6,410
	Non-smoker	ref.	ref.
	Smoker	1.308 [1.147-1.493]	1.463 [1.260-1.698]
	Former Smoker	1.146 [0.996-1.317]	1.419 [1.223-1.646]
Number of comorbidities (other than depression)	**n**	n= 7,731	n= 6,292
	0	ref.	ref.
	1-2	1.637 [1.444-1.855]	1.850 [1.609-2.127]
	3 or more	2.799 [2.392-3.277]	2.919 [2.468-3.454]
Healthcare resources utilization	**n**	n= 7,752	n= 6,353
		1.575 [1.476-1.681]	1.424 [1.344-1.509]

Legend: OR = unadjusted odds ratio.

Appendix 11- *Binary logistic regression model for the association of PHQ-8 depression with any work absence due to a health condition in the last 12 months in 2014 and 2019 and adjusted by gender, age group, tobacco consumption, number of comorbidities and healthcare resources utilization.*

		Year	
		2014 (N=7,788)	2019 (N=6,469)
Variable		**OR [95%CI]**	**OR [95%CI]**
Depression (PHQ-8)	**n**		
	No	ref.	ref.
	Yes	2.239 [1.792-2.799]	2.357 [1.787-3.108]
Gender	**n**	n= 7,780	n= 6,440
	Female	ref.	ref.
	Male	0.916 [0.816- 1.027]	0.798 [0.703-0.904]
Age group (years)	**n**	n= 7,780	n= 6,440
	18-24	ref.	ref.
	25-34	1.258 [0.900- 1.760]	1.365 [0.983- 1.896]
	35-44	1.211 [0.876-1.674]	0.868 [0.634-1.190]
	45-54	0.937 [0.674-1.303]	0.787 [0.575-1.078]
	55-64	0.933 [0.662-1.314]	0.666 [0.483-0.919]
	>=65	0.665 [0.412-1.074]	0.493 [0.316-0.769]
Tobacco Consumption	**n**	n= 7,775	n= 6,410
	Non-smoker	ref.	ref.
	Smoker	1.308 [1.146-1.492]	1.497 [1.288-1.740]
	Former Smoker	1.139 [0.991-1.310]	1.433 [1.233-1.665]
Number of comorbidities (other than depression)	**n**	n= 7,731	n= 6,292
	0	ref.	ref.
	1-2	1.660 [1.465-1.881]	1.933 [1.680-2.225]
	3 or more	2.947 [2.521-3.444]	3.121 [2.639-3.690]
Healthcare resources utilization	**n**	n= 7,752	n= 6,353
		1.548 [1.449-1.653]	1.431 [1.349-1.517]

Legend: OR = unadjusted odds ratio.

Appendix 12- *Binary logistic regression model for the association of PHQ-8 depression severity with any work absence due to a health condition in the last 12 months in 2014 and 2019 and adjusted by gender, age group, tobacco consumption, number of comorbidities and healthcare resources utilization.*

		Year	
		2014 (N=7788)	2019 (N=6469)
Variable		OR [95%CI]	OR [95%CI]
Depression Severity (PHQ8)	n	n=7,706	n= 6,239
	None/minimal	ref.	ref.
	Mild	1.964 [1.696-2.274]	2.066 [1.755-2.432]
	Moderate	2.193 [1.670-2.879]	2.434 [1.749-3.388]
	Moderately Severe	3.265 [2.084-5.116]	5.928 [3.119-11.267]
	Severe	6.075 [3.055-12.081]	1.790 [0.818-3.917]
Gender	n	n= 7,780	n= 6,440
	Female	ref.	ref.
	Male	0.993 [0.883- 1.116]	0.845 [0.744-0.960]
Age group (years)	n	n= 7,780	n= 6,440
	18-24	ref.	ref.
	25-34	1.252 [0.894- 1.754]	1.340 [0.963- 1.865]
	35-44	1.203 [0.869-1.665]	0.854 [0.622-1.173]
	45-54	0.928 [0.667-1.292]	0.767 [0.558-1.052]
	55-64	0.927 [0.657-1.308]	0.665 [0.481-0.920]
	>=65	0.676 [0.418-1.092]	0.492 [0.315-0.771]
Tobacco Consumption	n	n= 7,775	n= 6,410
	Non-smoker	ref.	ref.
	Smoker	1.282 [1.123-1.464]	1.440 [1.237-1.676]
	Former Smoker	1.149 [0.998-1.322]	1.433 [1.232-1.688]
Number of comorbidities (other than depression)	n	n= 7,731	n= 6,292
	0	ref.	ref.
	1-2	1.575 [1.388-1.787]	1.840 [1.597-2.121]
	3 or more	2.584 [2.202-3.031]	2.741 [2.310-3.254]
Healthcare resources utilization	n	n= 7,752	n= 6,353
		1.548 [1.449-1.653]	1.412 [1.332-1.498]

Legend: OR = unadjusted odds ratio.