Undiagnosed Depression:

An Epidemiologic Study in Three European Countries

PhD Thesis

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Abbreviations

MDE	Major Depressive Episode
MDD	Major Depressive Disorder
DUI	Duration of Untreated Illness
AOO	Age of Onset
WHO	World Health Organization
CIDI	Composite International Diagnostic Interview
ICD	International Classification of Diseases
WMH Survey	World Mental Health Survey
GBD	Global Burden of Disease
YLL	Years of Life Lost
DALY	Disability Adjusted Life Year
YLD	Years of Life Lived with Disability
DIS	Diagnostic Interview Schedule
OR	Odds Ratio
RCT	Randomized Control Trial
GP	General Practitioner
ECNP	European College of Neuropsychopharmacology
EBC	European Brain Council
ECA	Epidemiologic Catchment Area
ICPE	International Consortium in Psychiatric Epidemiology
PVHI	Private Voluntary Health Insurance
ELSA	English Longitudinal Study of Aging
GHS	Gutenberg Health Study
CI.	Confidence Interval

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Abstract

Introduction

Depression represents the most prevalent mental disorder that has high societal burden. However, high proportion of people are not treated or even diagnosed formally by the health system though they report the presence of a depressive episode. The aim of this study is to explore undiagnosed depression, its prevalence and associated factors.

Methods

The Collaborative Research on Aging in Europe (COURAGE in Europe) was a cross-sectional survey, conducted in three European countries; Spain, Finland and Poland. The total sample was divided into two samples; the first one included those who were depressed either diagnosed by formal health care or identified by World Health Organization - Composite International Diagnostic Interview (WHO-CIDI), and the second sample represented the formally non-depressed population that included those who did not present depression according to the health care system. Undiagnosed depression was studied in both populations as dependent factor in logistic regression models. Independent factors included sociodemographic and economic variables, private financing and utilization of health care, healthy life style behaviors, clinical conditions, and variables of well-being, loneliness and disability.

Results

For the total formally non-depressed population; being in the age group between 18 and 49 years, widowed and less educated were associated with presence of undiagnosed depressive episode. Other associated factors included having financial problem, frequent outpatient visits, higher levels of disability and loneliness, and lower levels of experienced well-being. For the total depressed population, being undiagnosed was associated with being

male, widowed and employed compared to both retired and unemployed. Other associated factors in this population included having sedentary life style and lower disability levels. Results for each country were reported separately in both populations.

Conclusions

The presence of undiagnosed depressive episode in the formally non-depressed population was associated with factors that had been studied comprehensively in the literature, related to education, financial burden and disability, well-being and loneliness measures. However, the associations varied when studying the depressed population showing different barriers to help-seeking behavior that included resilient factors such as lower levels of disability.

Resumen

Introducción

La depresión representa el trastorno mental más prevalente, con una alta carga social. No obstante, existe una alta proporción de personas que no reciben tratamiento, ni siquiera están formalmente diagnosticadas por los sistemas de salud, a pesar de presentar episodios depresivos. El objetivo de este estudio es la exploración de la depresión no diagnosticada, su prevalencia y factores asociados.

Métodos

El estudio Colaborativo de Envejecimiento en Europa (COURAGE en Europa) fue una encuesta transversal, realizada en tres países europeos: España, Finlandia y Polonia. La muestra total se dividió en dos submuestras; la primera submuestra incluía a los sujetos con depresión, ya sean oficialmente diagnosticados por el sistema de salud o identificados por la Entrevista Internacional Diagnóstica Compuesta (CIDI) desarrollada por la Organización Mundial de la Salud; la segunda submuestra representaba la población formalmente sin depresión, incluyendo aquellos que no sufrían depresión según los servicios de salud.

La depresión no diagnosticada fue estudiada en ambas submuestras como variable dependiente en los modelos de regresión logística. Las variables independientes incluyeron variables sociodemográficas, económicas, financiación privada de salud y utilización de los servicios de asistencia sanitaria, los comportamientos propios de un estilo de vida saludable, las condiciones clínicas, y variables de bienestar, discapacidad y soledad.

Resultados

Para la población sin depresión formal, tener entre 18 y 49 años, ser viudo y tener un nivel educativo inferior estaba relacionado con la presencia de un mayor número de episodios depresivos no diagnosticados. Los otros factores asociados incluían problemas financieros, mayor frecuencia de visitas de atención ambulatoria, mayor nivel de discapacidad, soledad más acuciante, y bajos niveles de bienestar. Para la población con depresión, no estar diagnosticado estuvo asociado con el hecho de ser varón, viudo y empleado, en comparación con jubilados y desempleados. Otros factores asociados en esta población incluían tener un estilo de vida sedentario y un nivel bajo de discapacidad. Los resultados de cada país fueron reportados por separado en ambos grupos.

Conclusiones

La presencia de episodios depresivos no diagnosticados en la submuestra que fue formalmente considerada como sin depresión, estuvo asociada con factores que habían sido estudiados de forma exhaustiva en la literatura, comprendiendo el nivel de educación, la carga financiera, la discapacidad, el bienestar y la soledad. Sin embargo, las asociaciones variaban al estudiar al grupo con depresión, mostrando diferentes barreras al proceso de buscar ayuda en la asistencia sanitaria, e incluyendo factores de resiliencia tales como los niveles bajos de discapacidad.

1. Introduction

1.1 Depression Burden

Almost one in three of all years of life lost (YLL) due to premature mortality in women, and almost one in four in men are due to disorders of the brain which have high cost (1). The total cost of brain disorders (mental and neurologic disorders) in Europe in 2010 was 797,725 million euros. The majority of the estimated cost of brain disorders was direct cost, 60%, divided into direct health care cost and direct non-medical cost (nursing homes etc.). Indirect cost (absenteeism from work, pensions etc.) constituted the remaining 40% (2).

For mental disorders alone, it is estimated conservatively in Europe that 27% of the total adult population aged between 18 and 65 years is affected by a mental disorder every year, then the prevalence declines in the elderly population. Mental disorders are costly, not because of its high direct treatment costs, but because of its indirect costs (3). In a review study about brain disorders in Europe published in 2011, coordinated by the European College of Neuropsychopharmacology and the European Brain Council (ECNP/EBC Report) mood disorders were the second most frequent group of disorders (7.8%), dominated by major depression (6.9%) (1). The world mental health surveys (WMH Surveys) (4) show lifetime prevalence estimates of any mood disorder averaging approximately 12% and 12-month prevalence estimates averaging approximately 6%. Lifetime prevalence estimate of Major depressive disorder (MDD) is usually in the 4-10% range and 12-month prevalence estimate is in the 3- 6% range (5). MDD has high costs that result from its relatively high prevalence and the moderate-to-severe level of disability associated with it (6).

The global burden rankings of MDD in the global burden of disease (GBD) cause list would have increased from eleventh to eighth place, surpassing

road injury, chronic obstructive pulmonary disease, and preterm birth complications (7). One review suggested that depressive disorder raises the risk of all-cause mortality by about 70 percent (6). Though the most disabling diseases differed markedly by gender and age group; overall, the first most disabling single condition, among brain disorders, was depression in the ECNP/EBC report (1).

The disability adjusted life years (DALYs) consists of two classes, YLL due to premature mortality and the years of life lived with disability (YLD, adjusted for severity of disability) (8). MDD accounted for 2.5% of global DALYs. Higher estimates of DALYs in depression were found in females, and adults in working age. MDD was ranked as the leading cause of global DALYs in 2010 and the second leading cause of YLDs after low back pain explaining 8.2% of all YLDs (7). Even the low back pain itself has outcomes that are worsened by symptoms of depression at baseline (9). Within the mental and substance abuse disorders group, depressive disorders had the highest proportion of total burden across all regions, accounted for most DALYs (40.5%), contributed most of the non-fatal burden of these diseases (10). As suicide and ischemic heart disease are linked to depression, it was estimated that close to half (46.1%) of DALYs originally allocated to suicide, included as intentional injuries in the GBD cause list, could be reattributed to MDD. In addition to this, 2.9% of ischemic heart disease DALYs (3.8 million DALYs of which 93.5% were YLLs) was attributable to MDD (7).This adds a substantial additional proportion of fatal burden by quantifying the proportion of death attributable to mental disorders as risk factors for other health outcomes from comparative risk assessment method (10).

1.2 Treatment Delay

The World Mental Health (WMH) data showed that only a small minority of people with even seriously impairing mental disorders receive treatment in most countries and that even fewer receive high-quality treatment (5).

According to two reviews (1, 3), no indications for improved care and treatment were found from 2005 to 2010; less than one third of all cases received any treatment, suggesting a considerable level of unmet needs. The marginalization and stigma attached to some disorders of the brain have been identified as barriers to a wider recognition of the core relevance of mental disorders. There is a difference between its true prevalence and its treated prevalence, which means the difference between total cases and those cases receiving care (11).

Figure 1: Relationship between true prevalence and treated prevalence.
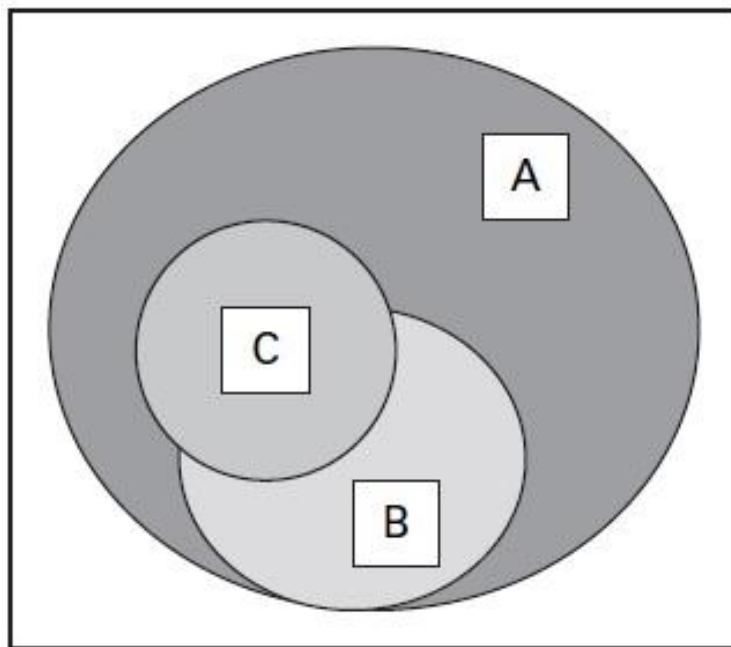
Note: This figure appears as figure 2.1 in Book titled "Better Mental Health Care", page 10 (11). Key: A = total adult population, B = true prevalence, C = treated prevalence.

Less than a half of depressed patients might be recognized and treated (12), and the majority of those recognized reported considerable delay before seeking treatment. The proportional treatment contact in the year of onset ranged from 28% to 47% (13, 14) and the median duration of delay in

treatment ranged from 2 to 8 years according to some previous studies (13, 14).

It is important to recognize the first episode as early as possible. Studies included in a systematic review (15) confirmed the importance of reducing delays in the treatment of depression in order to prevent the risk of worse outcomes and chronicity, in particular inpatients presenting with a first episode of depression.

However, seeking help remains an important factor as studies concluded that less than half of patients experiencing a first episode of depression may actively seek help in the first year of onset (13) and that early-onset disorders are consistently associated with a longer delay prior to seeking treatment (13). Clinical studies showed that a substantial proportion of people who seek treatment for major depression have a chronic-recurrent course of illness (16, 17).

This duration of untreated depression is called the duration of untreated illness (DUI) which is the interval between the first life time onset of symptoms of depression (not necessarily satisfying all five of the nine items for an episode of major depression according to DSM-IV) and the first adequate treatment (18). Longer DUI is associated with worse outcomes and the shorter DUI is associated with a better response to treatment in the first episode of depression (15). Moreover, pooled data (15) from two studies (19, 20) showed the overall positive effect that a shorter DUI have on the response to treatment, and pooled data (15) of three studies (19-21), about the effect of DUI on remission, indicated the positive effect of shorter DUI, bearing in mind the difference of follow-up time of these studies.

The WMH surveys showed that treatment rates are low in many developed countries and consistently much lower in developing countries (22). This undiagnosed depression can be identified in the general population by

screening instruments such as the World Health Organization (WHO)-Composite International Diagnostic Interview (CIDI) (23).

1.3 CIDI Screening Instrument

The CIDI is a fully structured diagnostic interview, administered by well-trained interviewers without clinical experience, based on the Diagnostic Interview Schedule (DIS) which was designed in a large survey in the US, called the Epidemiologic Catchment Area (ECA) to examine the prevalences and correlates of mental disorders. In the mid-1980s the WHO collaborated with the US Public Health Service to expand the use of the DIS and form an international group to modify it by including the criteria of the International Classification of Diseases (ICD) and develop the CIDI. Subsequent revision to include DSM IV criteria was done. The CIDI was used in different countries and the WHO created a coordinating consortium – the WHO international Consortium in Psychiatric Epidemiology (ICPE) - for this wide use in comparative analysis internationally. Reliability and validity were tested cross-nationally by field trials (24).

Recently, a newer version of the CIDI has been used in the WMH surveys (4). Diagnoses by the CIDI have been confirmed by independent clinical diagnoses in probability sub-samples. Good concordance with the CIDI has been shown in the methodological studies of these clinical reappraisal interviews (5).

The CIDI instrument has an average sensitivity of 85% and an specificity of 92% (25). The sensitivity of the screening test is the proportion of patients diagnosed as having depression who were correctly identified as "positive" at screening (26). The specificity is the proportion of patients, expressed as a percentage, without a diagnosis of depression, who were correctly identified with as "negative" by the screening test (26).

However, the wide variability in lifetime and 12-month prevalence estimates of major depression is presumably due to measurement factors (cultural differences in the acceptance and meaning of items, and the psychometric properties of the instrument) as well as substantive factors (genetic vulnerability and environmental risk factors) (27).

The CIDI includes three screening questions about sadness/depressed mood, feelings of discouragement, and loss of interest lasting several days or longer. Respondents endorsing one or more of these questions (screen-positives) were given the remainder of the major depressive episode (MDE) module. DSM-IV MDE requires the presence of five of nine cardinal symptoms that persist for 2 weeks or longer, are present for most of the day nearly every day, and cause significant distress or impairment. These symptoms are depressed mood and markedly diminished interest or pleasure (one of these must be present to meet the criteria for diagnosis), and clinically significant weight gain/loss or appetite disturbance, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished ability to concentrate or think clearly, and recurrent thoughts of death or suicide. MDE is defined without organic exclusions and without diagnostic hierarchy rules.

Though depression can be identified by screening, it is a controversial recommendation as the evidence is divided into studies that are in favor of screening provided that it is linked to treatment (28) including a meta-analysis (29) that led the United States Preventive Service Task Force to recommend screening (30) and those studies that are against it such as the meta-analysis (31, 32) conducted in 2005 and updated in 2008 and found no reduction in depression prevalence or improvement of depressive symptoms due to depression screening. Potential disadvantage to screening is the number of false positives (28, 33) with potential "nocebo" effect of causing a patient to develop depressive symptoms by labeling him with a false diagnosis (34). Mitchel et al. (35) suggested a simple way of managing a high false-positive

rate on initial screening found in their meta-analysis about depression diagnosis in primary care. The suggestion is a multistep assessment process applied to routine clinical examinations as a second assessment allows re-examination of not just true positives but also false positives (35).

Being undiagnosed may be affected by a number of factors that can be classified as patient, provider and system factors. Patients may internalize negative perceptions held by the others towards their mental illness so the "public stigma" becomes "self-stigma" (36). Other patient factors include doubts about the effectiveness of treatment, the depression effect on their daily lives and the belief that depression would not last very long (37). In case of contacting the health care services, patient factors include physical representation of symptoms that may not lead to paying attention to mental health (38-40) and patients may explain their symptoms by somatic causes so higher recognition rates are found for those having psychologizing attributable style (41, 42). Provider barriers include worries about patient stigma (43, 44), belief that depression diagnosis has high burden (45) and limited time of short consultations (44). The general practitioner (GP) may not consider patient as depressed especially when they are infrequent attenders at health services (46), having insufficient physician patient relationship (43). Lack of competence with care of mental disorders (47) and orientation regarding the psychosocial aspect of care (48-50) and the insufficient knowledge about cultural variations of clinical presentation of mental disorders (51) are also contributing factors. Moreover, physicians may not have sufficient knowledge about diagnostic criteria and treatment choices (52), and may be uncertain about the diagnosis (53). They may question the clinical significance of depression symptoms (46, 54, 55), underestimating its level (56) so reliable diagnosis may be made for more severe form of depression (39, 57-63) and when psychiatric comorbidity exists (57). It was suggested that non-depressed individuals in primary care who thought by the GP to have a psychiatric disorder were more likely to develop depression within one year compared

with those not identified as psychiatric case (64). System barriers include limited coverage of mental health including restrictions on drugs, specialists, and psychotherapy (44) , and financing of care (43).

1.4 Factors that may be associated with undiagnosed depression

The following lines describe factors related to overall health state, depression and undiagnosed depression; health care financing factors and patient factors. These factors may have associations with both diagnosed and undiagnosed depression.

1.4.1 Financing of health care

Financing of health care may be public or private. Private financing is either out of pocket payments or private voluntary insurance and may affect access to health care which contributes to health care utilization and consequently to depression diagnosis and treatment.

1.4.1.1 Out of Pocket Payments

Out of pocket payments include (65) direct payments of the uncovered services of the public insurance, indirect payments which represents patient cost sharing under the public insurance schemes (66) and informal payments (67). Studies show different terms for informal out of pocket payments such as bribes/bribe payments, envelope payments, gratitude payments, informal payments, red packages/envelopes, under-the-table payments and unofficial payments/fees (68).The burden of out of pocket payments may be an obstacle to utilization of the health care services for the patients with low socioeconomic status (69) and diagnosis of the mental illnesses including depression (70) and other comorbid conditions. A systematic review divided the included thirty eight studies into three categories: those reporting direct, out of pocket, costs (medical and/or non-medical); studies of the indirect costs associated with illness (such as wage or income loss); and papers reporting

general financial or economic burdens secondary to illness. More affluent people have greater out of pocket costs, but are less financially burdened by illness, compared with older adults from lower socioeconomic backgrounds. Disadvantaged patients and families are more likely to report experiences of financial hardship, and spend a higher proportion of their income on all expenses related to their diagnoses (70). Regarding the use of preventive services, the results of a systematic literature review (71) suggested that out of pocket payments can create a financial barrier and can decrease the use of preventive services and the uptake of preventive medications. These results are consistent with the three factors mentioned in WHO report (69) that have to be present for catastrophic payments to arise: the availability of health services requiring out of pocket payments; low household capacity to pay; and lack of prepayment mechanisms for risk pooling.

1.4.1.2 Voluntary Health Insurance

The second form of private financing is the voluntary insurance which is either substitutive, complementary or supplementary (72) and those people who do not have private insurance may have less choices of mental health care however this insurance may represent a financial burden at the same time. An example of the evidence comes from Australia (73), suggesting that private health insurance was not associated with access to a mental health professional in the past 12 months, however individuals with a mental health problem were less likely to have private health insurance than those without a mental health problem.

1.4.2 Patient Factors

Patient factors include healthy lifestyle behavior habits that indicates self-care; such as physical activity, sedentary behavior and smoking. Other patient factors include disabilities, comorbidities, service use, loneliness, well-being and sociodemographic factors.

1.4.2.1 Healthy Life style behavior

1.4.2.1.1 Physical activity

In most of the countries inactivity is higher in women than in men, and older adults are less active than younger adults (74). A systematic review of 25 prospective studies (75) showed that baseline physical activity was negatively associated with a risk of subsequent depression. The majority of these studies were of high methodologic quality, providing consistent evidence that physical activity may prevent future depression. There is promising evidence that any level of physical activity, including low levels, can prevent future depression (75).

In the literature there is an evidence of the other temporal sequence of the relationship that the exercise can be an intervention for depression. According to a meta-analysis of seven studies (76), exercise was associated with significantly lower depression severity, irrespective of whether participant eligibility was determined by clinical diagnosis or symptom checklist. Two reviews (77, 78) regarding the effect of exercise on depression among the elderly showed that exercise was effective in treating depression among those suffering from minor or major depression and in reducing depressive symptoms among those with a high amount of depressive symptoms at baseline. The results of another review (79) based on 12 Randomized Control Trials (RCTs) indicated that both the mindful and non-mindful physical exercises were effective in their short-term effect in reducing depression levels or depressive symptoms. This short term effect was supported by another review (80). In a Cochrane review (81), for the thirty five trials (a total of 1,356 participants, after adding up the sample sizes corresponding to the samples recruited in each trial) comparing exercise with no treatment or a control intervention, exercise had a moderate clinical effect.

1.4.2.1.2 Sedentary behavior

Sedentary behavior affects overall health status. An overview of systematic reviews (82) found strong evidence of a relationship between sedentary behavior and all-cause mortality, fatal and non-fatal cardiovascular disease, type 2 diabetes and metabolic syndrome. Another evidence synthesis of forty eight articles (83) indicated a consistent relationship of self-reported sedentary behavior with mortality and with weight gain from childhood to the adult years. This finding is supported by a systematic review (84) showing that greater sedentary time was related to an increased risk of all-cause mortality in the older adults, however the finding regarding mental health outcomes remained insufficient to draw conclusions. In a review about sedentary behavior and depression among adults (85), seven observational studies found positive associations between sedentary behavior and risk of depression, while intervention studies showed contradictory results. Regarding the opposite direction, baseline depression may be a significant risk factor for the development of sedentary lifestyle or decreased level of physical exercise (86).

1.4.2.1.3 Smoking

Three primary mechanisms, identified by a recent review (87), explained persistent smoking among depressed smokers: low positive affect, high negative affect and cognitive impairment. However, the findings from the study of the consortium for Causal Analysis Research in Tobacco and Alcohol (CARTA) (88) did not support a causal role of smoking heaviness in the development of depression.

Smoking cessation, according to a review and meta-analysis of 26 studies (89), was associated with reduced depression and improved positive mood and quality of life compared with continuing to smoke. The strength of association was similar for both the general population and clinical populations, including those with mental health disorders (89).

With regard to management of depression in addition to smoking cessation attempts, a Cochrane review (90) showed a significant positive effect for adding psychosocial mood management to a standard smoking cessation intervention when compared with standard smoking cessation intervention alone and 44 trials in another meta-analysis (91) showed that an antidepressant, bupropion, significantly increased long-term cessation when added to nicotine replacement therapy (NRT). An evidence synthesis (92) showed that depression had a greater impact on treatment outcomes for women than for men.

1.4.2.2 Disabilities

As shown in a study by Scott et al. (93) investigating the WMH survey, the odds of severe disability were generally greater for mental disorder in the absence of a given physical condition than they were for any of the physical conditions in the absence of mental disorder. Based on the same survey (27), the mean level of impairment for respondents with current MDE ranged between five and eight times as high as respondents without MDE, in high and low-to middle- income countries, respectively. As the degree of the impairment increased with recency of MDE in most countries, respondents with MDE in the past year (but not currently) reported impairment scores, less than those reported for current patients with MDE, between approximately twofold (high-income) and fourfold (low to middle income) that of non-MDE group (27).

As reported by Simon et al. (94) in a study conducted in 15 primary care centres in 14 countries, depression was associated with lower levels of impairment at higher prevalence centres. This negative relation between prevalence and levels of impairment was different from that positive one suggested by Scott et al. (27) when investigating profiles of general population regarding depression and impairment. However, they argued that the different studied population in the other study may induce selection bias regarding

seeking help on the basis of either distress or impairment might lead to more negative association in the primary care sample.

In the WMH surveys, 62,971 respondents across 24 countries were interviewed for a wide range of disorders as well as for days in which they were unable to work or carry out other normal daily activities (95). Depression was the most impacting disorder among mental disorders at the societal level and was associated with 5.1% of all days out of role and represented the fourth highest population-attributable risk proportion of all the considered disorders (95). Not only full disability is affected by depression, but also functional limitations in daily activities that represent partial disability (96) taking into account that partial disability may be a predictor of full disability (97). Compared with mental disorders, depression had greatest impact on partial disability at the societal level in addition to its third rank of impact at the individual level (96).

Ormel et al. (98) showed that depression had the second rank of mean disability rating and proportion of severely disabled among various mental and physical conditions, preceded only by bipolar disorder. This study used Sheehan disability scale that has four domains; home management, ability to work, social life, and forming and maintaining close relationships.

Another study (99) compared MDD with 18 physical and mental disorders to predict a summary measure of perceived health, depression was rated as the third most severe at the individual level after neurological conditions and insomnia. The impact of depression on perceived health was mediated partially by disability dimensions (100). Role functioning was the most important mediator in addition to stigma and family burden (100). Cognition and embarrassment were relatively important for depression as shown in another study (101).

Depression has a documented influence on cognition even at its first episode according to a meta-analysis (102), showing that significant cognitive deficits during the first MDE were identified (small to medium effect sizes) for psychomotor speed, attention, visual learning and memory, and all aspects of executive functioning.

Disability is also affected by comorbidity. There are two models of comorbidity that explain its association with disability. The first one is the additive model that suggests the combined effect is approximately equal to the sum of the parts and this model was suggested by some studies (96). The second model is the interactive model that suggests the presence of one disorder modifies the association of the other disorder with disability so the odds of severe disability of both mental and physical disorders are greater than the sums of the odds for the single condition as shown in Scott et al. (93) and the impairment is higher than expected on the basis of an additive model as reported by Kessler et al. (103). The synergetic effect of this interactive model was suggested by other studies (104, 105) investigating depression and various chronic conditions in USA and Canada and also by an American study (105) investigating depression and comorbid diabetes.

1.4.2.3 Comorbidities

Depression prevalence is higher in people with chronic diseases. Moussavi et al. (106) summarized data on depressive episodes in participants in the WHO World Health Survey used in 60 countries, showing that the 1-year prevalence was 3.2% in participants without comorbid physical disease, and ranged between 9.3% and 23.0% in participants with chronic conditions. In addition, a recent meta-analysis (107) of population data from 190,593 people across 43 low- and middle-income countries based on the world health survey showed that two, three and four or more physical health conditions were present in 7.4, 2.4 and 0.9% of non-depressive individuals compared with 17.7, 9.1 and 4.9% among people with any depressive episode, respectively.

In addition, significant positive association was observed in 42 of the 43 countries between multimorbidity and any depression; subsyndromal depression or brief depressive episode or depressive episode.

The relationship between depression and physical diseases may be bi-directional (108, 109). MDD is significantly associated with many chronic physical disorders (110-116). It was suggested to be a risk factor for cardiovascular diseases (117-120) and a predictor of its subsequent onset (121-125) as well as the onset of diabetes (126) and cancer (127).

Several behavioral and biologic mechanisms were suggested to explain the associations of MDD with different disorders (108, 128-131). These include poor health life style behaviors which are known to be linked to MDD, such as smoking, low levels of physical activity, poor diet (131), elevated rates of substance use disorders (132), obesity, and increased central body fat (133). A variety of biological dysregulations were observed, such as alterations in the mechanisms of the autonomic nervous system (131), impaired immune function such as increased production of cytokines (109, 131), hypothalamic-pituitary-adrenal hyperactivity (131), and hippocampal volume reduction especially if the illness has long duration and more than one episode and the degree of reduction may be related to the number of episodes (134-136). Other mechanisms, related to cardiovascular risk, include coagulation abnormalities (131), increased prothrombotic factors and C reactive protein (133), and vascular endothelial dysfunction (131). Low bone density and deficiency of omega 3 fatty acids were also linked to depression (131, 133).

Some studies referred to an underlying shared pathophysiology between chronic diseases and depression through the allostatic load as response and adaptation to stressors which refers to the cumulative wear and tear on the body that occurs through dysregulation of stress mediators which are turned on and off in an inadequate way (137-139). The proposed biologic mechanisms of depression support the kindling hypothesis (140) suggesting

that the depressogenic effect of stressful life events declined with increasing episode number and the onset of depressive episodes may become increasingly autonomous and less related to environmental adversity.

In presence of comorbid depression, the physical symptoms become more burdensome, the medical costs increase (130) and patients have more hospital admissions (141) as depression is often associated with non-compliance with treatment regimens and recommendations such as adherence to inhaled steroids in asthma (142) and life style changes after myocardial infarction (143). Depression interferes with adjustment to physical condition (144), pain perception and appraisal, and coping ability (145). In addition, comorbid depression is likely to be associated with a worse course of the physical disorder such as outcomes of asthma, diabetes and rehabilitation after stroke (146-148).

The evidence about the effect of comorbid chronic conditions on recognition of depression is provided by a systematic review (149), where four of the included studies showed that higher chronic physical comorbidity burden negatively affected primary care providers' ability to recognize depression. In contrast, two studies in this review reported higher rates of recognition in patients with higher comorbidity burden and seven studies reported no differences in recognition between comorbidity groups.

The negative comorbidity burden-recognition relationship may be due to brief medical consultations where the GP may prioritize physical diseases over patients' psychological problems as both are competing demands for the attention of clinicians when there is no enough time for each demand (150) and the severity of physical problems decreased the odds that patients initiated depression therapy according to Nutting et al. (151). GP may also have difficulty recognizing symptoms of depression when they mirror symptoms of physical disease such as fatigue or weight loss or when patients with chronic disease emphasize their physical complaints during consultations

(152, 153). GP may think that patients experience normal distress as a temporary adjustment reaction or an understandable and inevitable consequence to physical disease so the depression may be normalized in presence of long term conditions in primary care and does not require a specific treatment (152, 154, 155). In addition, applying label of having depression is a challenge to the clinicians when they are uncertain how to negotiate this label in vulnerable patients that may have difficulties accepting additional diagnosis considering depression as a sign of weakness (154, 156).

The positive comorbidity-recognition pattern may be due to increased contacts with health system that allow more opportunities to discuss psychological problems. For instance the depression of patients, with diabetes or hypertension, was more likely to be detected in a study by Borowsky et al. (157). Another study (155) showed that older adults with comorbid heart failure were identified as depressed more than those without the condition. However, a study by Nuyen et al. (57) indicated that in patients with somatic condition, only having psychiatric comorbidity increase the likelihood of receiving depression diagnosis and another study by Menear et al. (158) showed that patients with psychiatric comorbidity with or without physical condition were more likely to be diagnosed with depression than those with physical morbidity only.

This association between depression and physical diseases requires devotion of health professionals to mental health care, integrated collaborative care based on guidelines and algorithms, more frequent consultations and proactive follow-up by the medical staff, patient centred treatment regimens and individualized care plans, and support for patients' self-care (158-160).

1.4.2.4 Service Use

Pooled effects of 16 studies included in a meta-analysis (161) indicated that depression was associated with a 49% increase in the odds of urgent healthcare utilisation by people with long term conditions.

According to a review study (162) of evidence between 1990 and 2016, the prevalence of depression ranged from 5% to 60%, with a median of 33%, among hospitalized patients. A systematic review (163) conducted in 2015 showed that a positive association between depressive symptoms and non-psychiatric hospitalization was found in only half of the included studies. Additionally, in the same study (163), there was a significant association between depressive symptoms and both longer length of stay and readmission risk. However the authors suggested that comorbidity, disability and functional limitations, age and gender were likely to be true confounders while the majority of studies focused on old age groups and any association of depressive symptoms with hospital admission may be due to underlying medical conditions and depressive symptoms increase the risk by exacerbating the symptoms and increasing the service utilization. One study (164) sub-divided depressive symptoms by increasing severity, reporting increasing hazard ratios for increasing scores on the geriatric depression scale (GDS). This increased risk of hospitalization may be due to biologic mechanisms, delayed access to care, poor adherence to treatment and direct influence on disability (130, 164-166). So depressive symptoms are associated with high healthcare costs (167-170). This increased utilization can be managed partially by primary care interventions that when they were modelled for 14 subregions of the world they would reduce the burden of depression between 10% and 30% (171).

1.4.2.5 Loneliness

A recent meta-analysis (172) provided quantitative data on mortality as affected by loneliness and living alone corresponding to an average of 26%, and 32% increased likelihood of mortality, respectively. Feeling of loneliness

was associated with increased risk of mortality in the English Longitudinal Study of Ageing (ELSA) (173), however, the effect of loneliness was not independent of demographic characteristics or health problems. In Netherlands, in the Amsterdam Study of the Elderly (174), feelings of loneliness were found to be a major risk factor for increasing mortality in older men. In the ELSA study, loneliness was associated with an increase in difficulties with activities of daily living (175) and with smoking (176) while in the Gutenberg Health Study (GHS) (177), lonely participants also smoked more and visited physicians more frequently. In addition, feeling lonely was associated with dementia (178) and was also associated with suicidal ideation (177, 179) and attempts (179).

A study (180), based on the Adult Psychiatric Morbidity Survey in England 2007, showed that loneliness was associated with all mental disorders, especially depression. Similarly, loneliness was associated with depression in a recent literature review (181), in the GHS study (177) and others (182) .

In a cohort study (183) of two years follow-up, loneliness was independently associated with more severe depressive symptoms at follow-up and very severe loneliness was negatively associated with remission after 2 years compared with no loneliness. Favorable course of depression was shown in other studies (184, 185) when feelings of loneliness were limited. Regarding marital status and living arrangements, loneliness may explain the excess risk of depression in the widowed (186) and in another study (187) participants living alone with absence of depression had a threefold higher chance of not feeling lonely. In a Swedish study (188), depression increment and recent widowhood were significant predictors of loneliness that increased with age. Another Swedish study (189) showed that an association between the odds to have a depressive disorder and loneliness was found and only one in four reported that they used antidepressant medication.

1.4.2.6 Well-being

A meta-analyses (190) showed that positive psychological well-being was associated with reduced mortality in both the healthy population and the disease population. In addition, both positive affect (e.g., emotional well-being, positive mood, joy, happiness, vigor, energy) and positive trait-like dispositions (e.g., life satisfaction, hopefulness, optimism, sense of humor) were associated with reduced mortality in healthy population studies. This finding regarding general population was supported by another more recent meta-analysis (191) showing that although the impact of subjective well-being on survival was significant in both men and women, it was slightly more protective in men. Mediation analysis in another study (192) determined that the effect of psychological well-being on adverse physical health outcomes was fully mediated by depression. Additionally, well-being therapy has proven efficacy in acting as a buffer against the development of some negative affective states improving the lives of persons living with disability and chronic illness (193) and decreased vulnerability to depression in high-risk populations (194, 195)

Regarding the other direction as shown in another study (196) good health significantly predicted subsequent levels of positive affect and according to a systematic review (197), psychotherapeutic interventions resulted in significantly increased positive affect and significantly decreased negative affect in depressed adults.

1.4.2.7 Sociodemographic Factors

According to a Chinese study (198), undetected depression was significantly associated with female gender, low income, low levels of education and occupation, and living in a rural area. The following part reviews the evidence regarding the relation between sociodemographic factors and depression.

1.4.2.7.1 Gender

Women have a two times increased risk of MDE compared with men (199). Two retrospective studies (200, 201) found an association between the duration of untreated depression and gender. They found that patients with a longer DUI were more frequently women.

1.4.2.7.2 Age

In the WMH surveys, the median retrospectively reported age of onset (AOO) of MDE ranged from twenty to twenty five years in most of the countries (24).

According to the WMH Survey (27), in six high-income countries and in Brazil, respondents in the youngest age group (18 to 34) were 3 to 5.5 times as likely to have MDE as those in the oldest age group (65+). Studies conducted in western countries showed that the rate of depression generally decreases with age (24, 202). In other countries, not monotonic age pattern was found or the association was reversed with depression increasing with age (203, 204).

Mid-life (ages 50 to 64) is a period of transition from work to retirement in many countries and this age group may face difficulties adjusting to retirement with subsequent depression feelings. Compared with respondents age 65+, participants in this group had an increased risk of MDE in some of high income countries and Brazil (27).

A qualitative meta-analyses (205) of cross-sectional and longitudinal studies showed that older age groups generally have a significantly higher risk for depression, compared with younger participants. Regarding the development of depression in older adults, a review of 181 studies (206) showed that subthreshold depression was generally at least 2-3 times more prevalent than major depression and approximately 8-10% of older persons with subthreshold depression developed major depression per year. Risk factors included female gender, medical burden, disability, and low social

support; consequences included increased disability, greater healthcare utilization, and increased suicidal ideation.

With regard to being undiagnosed, an association between a longer DUI and an earlier illness-onset age was found in two studies (200, 201), leading the authors to think that the results of previous studies that showed an association between earlier onset and worse outcomes of illness might be considered an effect of the longer DUI. However, in primary health care patients' sample (207), one of the contributing factors to persistence of symptoms was the older age, as well as DUI, unexplained somatic symptoms at the baseline, and psychiatric symptoms scores.

1.4.2.7.3 Income

The association between income and MDE in higher-income countries was statistically significant in the WMH surveys, unlike that in the low to middle-income countries where income was not significantly related to MDE. In some high income countries such as the United States, the poorest respondents to had about two times increased odds of MDE compared with those in the highest income group (27). Income inequality, which is greater in high than in low- to middle-income countries, may lead to various chronic conditions including depression (208). This is consistent with the finding that inequalities across income groups existed in accessing specialists in high income countries such as France (209).

The incomes, either individual or household, of people with MDD are lower than those of people without depression (210-215) and reduced income earnings in adulthood were documented in some studies investigating the effect of depression in childhood and adolescence (216, 217). Regarding the other direction, low income has an impact on developing depression as shown in studies investigating the effects of unemployment and job loss (218). In addition, the evidence (219) from UK showed a strong inverse dose-response

association between wealth and depressive symptoms among people with disability.

1.4.2.7.4 Education

Low education was significantly associated with MDE in few non-Asian countries. In Asian countries, Indian respondents with the lowest education were 14 times as likely to have MDE as those with the highest education. In Japan and China, the reverse pattern was found (27). However this result for China is different from a meta- analysis (220) suggesting that lower educational level of older Chinese people was associated with higher rates of depression, which confirms with findings from previous studies (221, 222). Similarly, a meta-analysis about education and late life depression in Chinese people concluded that less education was associated with increased risk of late life depression (223).

In France, persons with primary education were less likely to directly access specialists than their more educated counterparts (209) and it was documented that early onset mental disorders including depression has an association with termination of education (224-230) with an elevated odds of failure to complete secondary school (231).

Similarly, a cross-sectional survey (232) of 10 European countries of population older than 50 years showed an inverse association between educational attainment and depression that remains significant independent of all other sociodemographic variables. On the other hand, one study (233) examining 25 European countries from human capital approach showed diminishing mental health returns to education and that overeducated people report more depression symptoms.

1.4.2.7.5 Marital Status

As shown by Kessler et al. (231), studies emphasized that depression, which is an early onset disorder, predicts low probability of ever marrying and is either positively associated with (234) or unrelated to (235) the marriage before age 18, which is not healthy. In addition, marital dissatisfaction are strongly related to depressive symptoms (236) and negative effects of clinical depression on marital functioning were reported in previous studies (237-239). Regarding the marital status, there were stronger associations in WMH Survey of being separated and never married with depression in high-income countries, and stronger associations of being divorced and widowed with depression in low- to middle-income countries (27). On the other hand, living arrangements per se were more modestly associated with MDE. This association was significant in eight of the high-income countries and in Ukraine and China (27). However, a meta-analysis (240) of the relationship between living arrangements and late life depression showed that older people living alone had a higher risk of depression than those not living alone.

1.4.2.7.6 Employment

Depression before completing schooling may lead to increased unemployment especially in higher and upper middle income countries (241). A meta-analysis (242) of cohort studies showed that unemployment was significantly related to a higher risk of depressive symptoms while retirement had a beneficial effect on mental health according to a systematic review (243) of 22 longitudinal studies. According to an American study (244), retirement was found to improve mental health of older Americans and women exhibit better psychological well-being than men following retirement.

With regard to the health of the employed, a meta-analysis (245) of 33 cohort studies showed the protective effect of employment on health and concluded that pooled effect sizes showed favorable effects on depression.

However, an American study investigating the National Comorbidity Survey Replication found that only about half of depressed workers received treatment and fewer than half of treated workers received care consistent with published treatment guidelines (246). An analysis of the same data set showed that MDD severity is significantly associated with increased treatment usage (247).

1.4.2.7.7 Residential Setting and Neighborhood

According to a meta-analysis (248), rates of mood disorders were higher in urban than in rural settings and the same pattern was specifically found for depression in other studies (249-251). This is consistent with the finding of The Netherlands Mental Health Survey and Incidence Study (NEMESIS) (252) which used the Composite International Diagnostic Interview (CIDI) to determine the prevalence of psychiatric disorders in a sample of 7,076 people aged 18-64. It found that the prevalence gradually increased over five levels of urbanization. This finding is supported by another recent study (253) from Canada, synthesizing a series of 11 Canadian national cross-sectional studies from 2000 to 2014 showing that urban regions had approximately 18% higher MDE prevalence than rural regions.

A systematic review (254) showed that 27 of 29 included studies found statistically significant association between mental health and at least one measure of neighborhood characteristics, after adjusting for individual factors. This association was evident for all types of neighborhood features, varying from sociodemographic characteristics to physical environment, and from objective to subjective measures. Similarly, 11 of 14 longitudinal studies, included in an evidence synthesis (254), observed a significant relationship between depression and at least one of the following neighborhood-level variables: neighborhood deprivation, disorder, instability, and social ties. A recent meta-analysis (255) showed that among studies with less than 5 years

of follow-up, there was a significant association between neighborhood socioeconomic conditions and depression.

Regarding human resources of health services, a recent review (256) from the US has indicated that rural physicians had fewer resources, an increased workload, and longer hours when compared to their urban counterparts. These factors contributed to lower job satisfaction, poor retention rates, and decreased physician wellness. This study can be seen in line with another one (257) showing that US adults with depressive symptoms that lived in rural area were more likely to report at least one health deficit during the last 12 months. This deficit depended on four factors: not having health insurance, not having a health care provider, deferring medical care because of cost and not having a routine medical exam.

2. Objectives and hypothesis

2.1 Objectives

The first general objective is to study factors that may be associated with undiagnosed depression overall and separately in three European countries; Spain, Poland and Finland.

The second general objective is to explore factors that may be related to being undiagnosed without regard to the depressive episode itself.

The specific objectives are the followings:

- To determine the prevalence of undiagnosed depression in the formally non-depressed (those who did not present depression according to the health care system) and the depressed populations in the three countries considered, overall and separately by country.

- To assess whether private financing and utilization of health care may have a relationship with the undiagnosed depression.

- To study the healthy lifestyle behavior habits that may be associated with undiagnosed depression.

- To investigate the economic factors including presence of financial burden, employment status and health benefits provided by the employer that may be associated with undiagnosed depression.

- To analyze the relationship of chronic diseases and disability with undiagnosed depression.

- To explore the relationship between both well-being and loneliness, and undiagnosed depression.

- To identify the sociodemographic factors that may be related to undiagnosed depression.

- To evaluate whether disability and well-being have relationships with being undiagnosed or not.

- To analyze the pattern of health care utilization related to being undiagnosed.

- To differentiate factors, related to undiagnosed depressive episode and others related to being undiagnosed, according to each country considered.

2.2 Hypothesis

- Prevalence of undiagnosed depression will be lower in those who pay more for health care, such as for voluntary insurance, than in those who pay less.

- Private health care financing, either having voluntary insurance or spending high out of pocket expenditure, will be associated with the absence of undiagnosed depression, even after controlling for potential confounders.

- Prevalence of undiagnosed depression is lower in people with private utilization of health care than in those with public utilization.

- Prevalence of undiagnosed depression is lower in people who have better healthy lifestyle behaviors.

- Presence of financial burden is associated with undiagnosed depression.

- Unemployment and employment conditions including no health care benefits are associated with undiagnosed depression.

- People with higher scores in disability, presence of chronic disease, less experienced well-being and higher scores in loneliness will have a higher prevalence of undiagnosed depression.

- The distribution of sociodemographic factors is different in people with undiagnosed depression, compared to the population not diagnosed by the health system and the depressed population.

- The depression of people who have less health care utilization is more likely to be undiagnosed.

- A better well-being and a low level of disability are associated with being undiagnosed, as resilient factors for not seeking formal treatment.

- Factors associated with development of undiagnosed depressive episode are different from factors associated with being undiagnosed only.

3. Methodology

3.1 Study Design

The Collaborative Research on Ageing in Europe (COURAGE in Europe) (258) was a cross-sectional household survey of a probabilistic sample representative of the non-institutionalized adult population of Finland, Poland and Spain. These countries were selected to give a broad representation of several European regions, representing Northern, Eastern and Southern Europe according to the classification of the United Nations (259), and different demographic, cultural, socioeconomic and health characteristics, as well as different social welfare systems (260).

The COURAGE in Europe questionnaire included several sections such as

- Sociodemographic characteristics.
- Work history and benefits.
- Risk factors and preventive health behaviors.
- Chronic conditions and health services coverage.
- Health care utilization.
- Subjective well-being and quality of life.

The information was collected with a face-to-face structured interview carried out at respondents' homes, via Computer-Assisted Personal Interviewing, between 8 April 2011 and 8 May 2012. The interviewers had participated in a training course for the administration of the survey. The questionnaires were based on the ones used in the WHO Study on Global Ageing and Adult Health (SAGE) (261) and they were translated from English into Finnish, Polish and Spanish following the WHO translation guidelines for assessment instruments (262). The translated questionnaires were piloted in 2010 in the countries and based on the feedback from the interviewers some

changes and corrections were made. Quality assurance procedures were implemented during fieldwork (263).

3.2 Sample and Participants

A multistage clustered design was used to obtain nationally representative samples. In Poland and Spain, a stratified multistage random sampling method was used and strata were created according to the geographical administrative regions and number of people living in the habitat. Age strata were used to select households according to the age structure of the population. The respondents were randomly selected among inhabitants of a household from a certain age group. In Finland, the design was a stratified two-stage cluster sampling design, and strata were created based on the largest towns and university hospital regions. A systematic sampling of people was conducted so that the sample size in each stratum was proportional to the corresponding population base. Specific details about sampling design in the COURAGE in Europe project are described elsewhere (264).

A total of 10,800 individuals participated: 1,976 from Finland, 4,071 from Poland and 4,753 from Spain. The countries' response rates were 53.4%, 66.5% and 69.9% respectively

3.3 Ethical Approval

Ethical approvals from the Ethics Review Committee, National Public Health Institute, Helsinki, Finland; the Bioethical Committee, Jagiellonian University, Krakow, Poland; Ethics Review Committee, Parc Sanitari Sant Joan de Déu, Barcelona, Spain; Ethics Review Committee, La Princesa University Hospital, Madrid, Spain were obtained. Informed consent from each participant was also obtained.

3.4 Measures

To be considered as part of the depressed population, the interviewee was asked whether he/she had been diagnosed with depression and had taken medication or received any other treatment (e.g. psychotherapy) for their symptoms during the previous 12 months. Additionally an algorithm of a set of questions, previously used in the WMH survey version (23) and based on the ICD-10 classification of mental and behavioral disorders (265), was employed to include the non-diagnosed cases.

The participants who reported two or more diagnostic stem symptoms in addition to four or more other depression symptoms during the last 12 months and had not been ever formally diagnosed by the health system were considered to have undiagnosed depression.

On the other hand, the formally non-depressed population excluded the diagnosed cases of depression and was composed of the people without depression and those having undiagnosed symptomatic depression.

Depression diagnostic stem symptoms were as follows:

- Feeling sad, empty, depressed most of the day for more than two weeks.
- Loss of interest in most things the interviewee usually enjoy such as personal relationships, work or hobbies/recreation and also decrease of interest in sex.
- Decrease of energy and feeling tiredness all the time for several days.

Other depression symptoms during the two weeks of depressive episode included:

- Negative perception of oneself or loss of confidence.
- Feeling anxious, worried and restless or jittery most days.
- Suicide ideation and attempt.
- Slowness in thinking and difficulty in concentrating.

- Slowness in movement around.

- Problems falling asleep and waking up too early.

- Loss of appetite.

3.4.1 Other Key Variables:

3.4.1.1 Sociodemographic Variables

Participants provided sociodemographic information (age, sex, marital status, residential setting, years of education and employment status).

Age was categorized in the following age groups: 18-49, 50-64 or 65+. For marital status, three categories were considered: married or in partnership, not in partnership and widowed. "Married or in partnership" category included married and those who live together. "Not in partnership" category included single, separated and divorced persons. Residential setting was categorised as urban and rural. Employment status was considered as a four category variable: employed, retired/ disabled, homemaker/ in unpaid work and unemployed.

3.4.1.2 Financial burden

Participants were asked if their household had any financial problems with paying for bills (electricity, central heating, phone bills, etc.). A dichotomous variable (yes/no) was considered to assess this.

3.4.1.3 Voluntary Health Insurance

Voluntary health care coverage was assessed asking the participants if they have private / voluntary health insurance coverage. A dichotomous variable (yes/no) was considered.

3.4.1.4 Out of Pocket Expenditure

Information about household out of pocket spending during the previous month was obtained by asking a series of questions about participants' spending on health care such as:

- Registration and consultation fees by doctors, nurses, or trained midwives that did not require an overnight stay.
- Diagnostic and laboratory tests such as X-rays or blood tests.
- Medications or drugs (prescription, non-prescription, traditional, homeopathic…).
- Dentists or dental care.
- Ambulance.
- Health care by traditional or alternative healers.
- And any other health care products or services that were not included above.

The sum of all these payments (in Euros) represented the out of pocket expenditure during the previous thirty days.

3.4.1.5 Occupational Health Benefits

A dichotomous variable (yes/no) was considered as the response of the participants when they were asked for receiving any benefit from their main employer regarding medical service or health care, in addition to their payment in cash or in kind.

3.4.1.6 Most Frequent Health Facility

Participants were asked about the type of the most frequent health facility they had visited for consultation when being sick during the last three years.

The answers were recoded into two categories: public facility (clinic and hospital) and private (doctor's office, clinic and hospital). Other types such as

charities, traditional healers and going directly to the pharmacies were ignored in the analysis.

3.4.1.7 Presence of Chronic Comorbidity

The following chronic conditions were assessed in the present study: hypertension, diabetes, angina, asthma and arthritis.

Participants were also asked if they had a medical diagnosis in the previous 12 months of angina, arthritis, hypertension, diabetes and asthma. For diabetes, only self-reported diagnosis was considered, while the presence of hypertension was based on the presence of systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg using the average of two times measures at the time of the interview (266, 267). Additional symptom questions were asked to detect undiagnosed cases for arthritis, asthma and angina, implementing algorithms for these chronic conditions as described in Garin et al. (268). The participant was considered to have one of these conditions if he/she fulfilled at least the self-reported diagnosis or the diagnosis made according to the symptoms.

3.4.1.8 Hospitalization

Hospitalization was defined as the presence of overnight stay in health facilities during the previous year. A dichotomous variable (yes/no) was considered.

3.4.1.9 Outpatient visits

Outpatient visits were registered as the number of visits to health care facilities without any hospitalization during the previous year.

3.4.1.10 Daily Smoking

A dichotomous variable (daily smoker / not daily smoker) was considered. "Not daily smoker" category included those who smoke occasionally and not in a daily basis, previous smokers and those that had never smoked.

3.4.1.11 Physical Activity

The Global Physical Activity Questionnaire (269) was developed by WHO for physical activity surveillance comprising 16 questions and collecting information on physical activity participation in three settings: activity at work, travel to and from places and recreational activities. Based on these domains, physical activity was dichotomized, considering two levels a) moderate and higher physical activity; and b) low physical activity.

"Moderate and higher physical activity" includes participants matching one of the following three cases a) three or more days of vigorous-intensity activity of at least 20 minutes per day; b) five or more days of moderate-intensity activity or walking of at least 30 minutes per day; c) five or more days of any combination of walking, moderate or vigorous intensity activities achieving a minimum of at least 600 MET-minutes per week.

A person not meeting any of the above mentioned criteria was considered to have a low level of physical activity.

3.4.1.12 Sedentarism

Sedentary behavior was measured as the period of time (in hours) that participants usually spent sitting or reclining on a typical day.

3.4.1.13 Disability

The WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) (270) is an instrument to measure disability as the interaction of a health condition with contextual factors (271). It was grounded in the conceptual framework of the International Classification of Functioning, Disability and Health (ICF) (272). It

integrates an individual's level of functioning in major life domains and directly corresponded with ICF's 'activity and participation' dimensions. The 12-item version was used in the COURAGE in Europe project; this short version is useful generally for brief assessments of overall functioning in surveys. A global score can be obtained, ranging from 0 to 100, with higher values indicating higher disability. The WHODAS 2.0 domains are cognition, mobility, affect, domestic life and work, and interpersonal activities.

3.4.1.14 Experienced Well-being

Experienced well-being was assessed with an abbreviated version of the Day Reconstruction Method (273), owing to its application in general population surveys (274, 275). Participants reconstructed a portion of their previous day's activities and reported the extent to which they experienced seven emotions on a seven-point response scale ranging from 0 (not at all) to 6 (very much).

Net affect (276) was defined as the average of the two positive emotions (calm/relaxed and enjoying) minus the average of the five negative ones (worried, rushed, irritated/angry, depressed, and tense/stressed), i.e., positive affect minus negative affect. Individual net affect was calculated adding up the net-affect in each activity performed, and weighting the sum by the duration of each activity. Net affect scores ranged from -6 to 6, with higher scores representing a better affective state.

3.4.1.15 Loneliness

Loneliness was assessed by means of the three-item UCLA Loneliness Scale (277). This scale comprises the following items: "How often do you feel that you lack companionship?", "How often do you feel left out?" and "How often do you feel isolated from others?", which have been measured on a three-point scale (1 = hardly ever; 2 = some of the time; 3 = often). The UCLA

Loneliness Scale has shown satisfactory reliability and both concurrent and discriminant validity (277).

The scores for each item were added up to produce a loneliness score ranging from 3 to 9, with higher scores indicating a higher perception of loneliness.

3.4.2 Statistical Analysis

3.4.2.1 Descriptive analysis and prevalence estimates

All data were weighted to account for sampling design in each country and to generalize the study sample to the reference population. Weights were used to adjust for differential probabilities of selection within households, and post-stratification weights to match the samples to population sociodemographic distributions. Post-stratification corrections were made to the weights to adjust for the population distribution obtained from the national census in each country, and for non-response (106).

Prevalence rates of undiagnosed and diagnosed depression were calculated using these weights and standardizing by age. One year prevalence estimates based on different categories were calculated. Prevalence refers to the total number of cases in a given population at a specific time (8). Significance tests for differences in the prevalence by sociodemographic characteristics and other variables were conducted for the entire population and separated by country, using the Rao–Scott chi-square statistic, which adjusts for complex sample design (278).

Unweighted proportions were used for descriptive analysis conducted over the categorical variables including sociodemographic, socioeconomic, life style behavior and use of services variables. In order to assess potential differences across the three countries considered, chi-squared tests were conducted over

the categorical variables, while ANOVA tests were conducted over the continuous sociodemographic ones.

Weighted and age-standardized means were also reported to describe other quantitative covariates (e.g., loneliness, well-being, disability, etc.) included in the analysis. Mean scores were compared in each pair of countries, using unpaired t-tests. Bonferroni's correction was employed for pairwise comparisons.

Effect size measures such as Cramer's V, Hedges'g and Cohen's f were reported. Cohen's guidelines (279) were used as standard to evaluate the magnitude of the effect size. Cramer's V values of 0.10, 0.30, and 0.50 constitute small, medium, and large effect sizes; whereas these values are 0.10, 0.25, and 0.40, respectively, for Cohen's f. Hedges' g values of 0.20, 0.50, and 0.80, constitute small, medium, and large effect sizes, respectively.

The confidence level was established at 95% for the hypotheses tests considered in this work. 95% confidence intervals (CIs) were generated for the parameters estimated.

3.4.2.2 Logistic Regression

Logistic regression models (280-285) were used for the main analyses conducted in the present study. In these models, considered as generalizations of the chi-squared test, factors associated with the probability of an event happening represent the result.

 "Success" and "failure" are the terms that can describe presence and absence of the dependent variable. . Logistic regression separates the effects of several independent variables on a binary dependent variable to test hypotheses about their relationships. A logarithmic transformation is used to allow modelling of a linear relationship. A set of regression coefficients

represents the relationship between each independent variable and the binary dependent one, after adjusting for all the other variables in the model.

It fits a model of the form:

$log_e [p/(1–p)] = b_0 + b_1x_1 + b_2x_2 + b_3x_3 + b_4x_4 + …$where:

p is the proportion with the dependent variable.

$log_e [p/(1–p)]$ is the transformation of the probability, or risk, of the dependent variable into the log odds. It is called the log function or the logit transformation.

$x_1, x_2 …$ are the independent variables.

b_0 is the intercept and $b_1, b_2, b_3,$ etc. are the regression coefficients for the variables $x_1, x_2, x_3,$ etc. representing the independent effects of the corresponding covariate. The odds ratios (ORs) are the results of the backtransformation of these the regression coefficient from the log scale to the natural scale.

A series of ORs is the result of this model. One OR for each independent factor is generated taking into consideration the effect of all other factors on the dependent variable at the same time. The OR coefficient contains the exponentials of the logistic regression coefficients and the 95% CIs are generated by exponentiating the CIs on the log scale.

For binary variables, OR is the odds of the dependent variable in one group divided by the odds in the other group, while for categorical variables it estimates the odds ratios for each non-reference group compared to the reference group established. This approach does not consider the ordering of the exposure variable.

Regarding the continuous independent variables, OR is the change in odds of the dependent variable for a unit change in the continuous independent variable, based on the assumption that the relationship between the dependent and the independent variable is linear on the logit scale for continuous independent variables.

A detailed description of logistic regression can be found elsewhere (286, 287).

Logistic regression models were conducted in the current study to assess the relationships between different variables and the presence of undiagnosed depression, identified by CIDI screening but not diagnosed by the health system. The analyses were done for the overall population and, separately, by country. Sociodemographic variables, presence of financial burden, voluntary health care coverage, household out of pocket spending, occupational health benefits, type of frequent facility visited for the last three years, presence of chronic comorbidity, number of outpatient visits, presence of hospitalization during the last year, healthy lifestyle behaviors such as sedentarism and daily smoking, degree of disability, net affect and loneliness were included as covariates in the models in order to assess their association with undiagnosed depression and to control for their potential confounder effect (288). ORs, 95% CIs and p-values were reported for the logistic regression models considered.

The different logistic regression models were generated overall and separately for each country, for two different populations; the first one was the formally non-depressed population; who neither reported receiving treatment nor had history of formal depression diagnosis, and the dependent variable in this case was the development of an undiagnosed depressive episode, while the second population represented the depressed population that included: (a) those who had history of formal diagnosis and treatment by health professionals during the previous year, and (b) those who reported the presence of depression symptoms according to CIDI diagnosis. Presence of

depression symptoms may be common in the second population diagnosed by health system or identified by administering CIDI and consequently number of depression symptoms was included only in the models of this depressed population to control for its effect. As a result, the dependent factor in this case was being undiagnosed rather than the depressive episode itself (Figure 2).

Figure 2: Illustration of study analysis
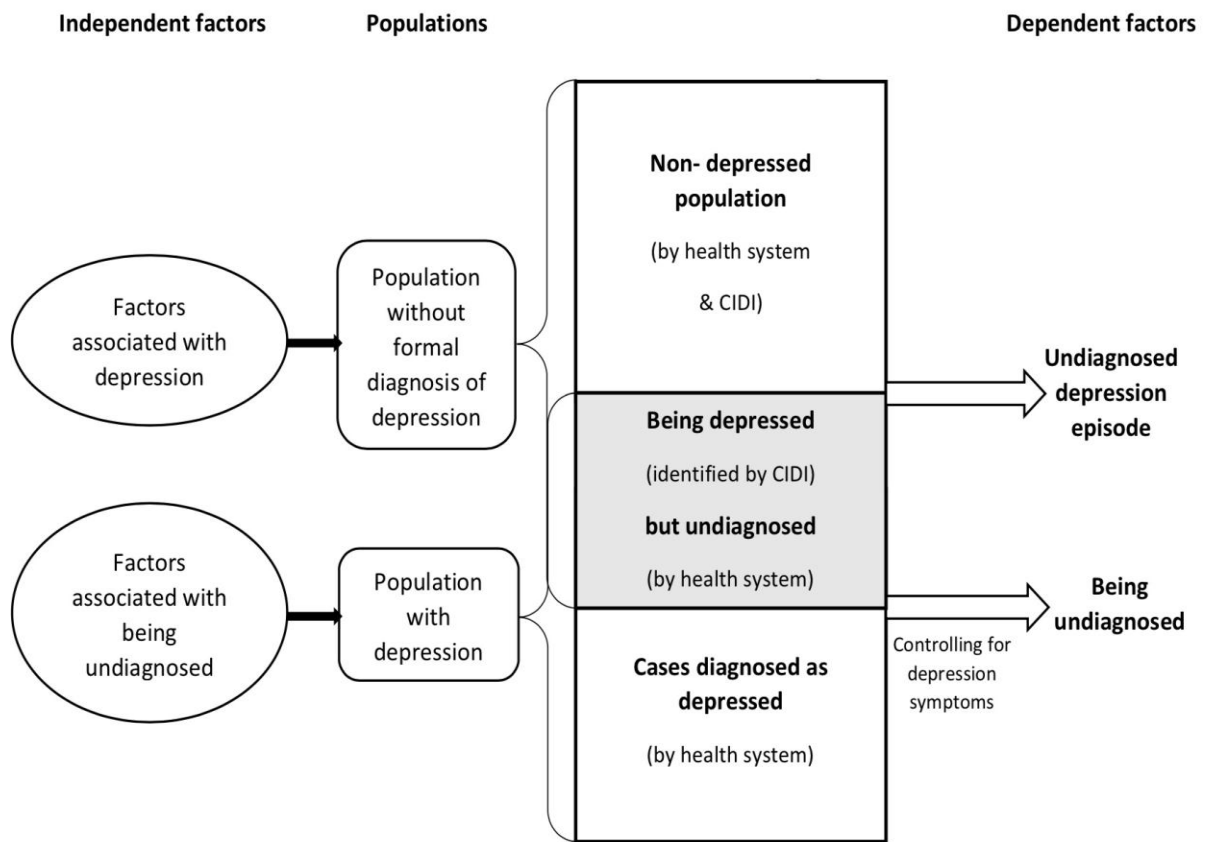
3.4.2.3 Software

Statistical analysis was conducted by using statistical packages such as Stata (289) and IBM Statistical Package for Social Sciences (SPSS) (290). Both Stata and SPSS are integrated statistical software packages that satisfy the user's need for data analysis, data management and graphics. Stata's

survey command (svy), which fits statistical models for complex survey data, was employed for weighted analysis.

4. Results

4.1 Overview of Prevalence of Undiagnosed Depression

The one year prevalence of undiagnosed depression in the formally non-depressed population was 3.96% [95%CI.= (3.44, 4.48)], whereas in the depressed population was 35.70% [95%CI.= (31.30, 40.09)].

When comparing the three countries, the highest prevalence estimate of undiagnosed depression in the formally non-depressed population was found in Spain (4.63%) followed by Poland (3.61%) and Finland (3.45%). The difference in percentages across countries was statistically significant ($p=$ 0.048) while the prevalence estimate of undiagnosed depression in the depressed population was higher in Poland (46.83%) than in Finland (31.82%) and Spain (30.78%) with a statistically significant difference ($p< 0.001$).

Table 1: One year prevalence* of undiagnosed depression (95% CI.)		
	Among the formally non-depressed population (n=9505)	**Among the depressed population** (n=1422)
Total	3.96 (3.44, 4.48)	35.70 (31.30, 40.09)
Spain	4.63 (3.81, 5.44)	30.78 (25.13 , 36.44)
Finland	3.45 (2.34, 4.55)	31.82 (23.46, 40.19)
Poland	3.61 (2.75, 4.48)	46.83 (39.84, 53.83)
Rao-Scott χ^2	6.12	16.64
_p_	0.048	< 0.001

*Weighted and age-standardized data

4.2 General Profile of the Formally Non-depressed Population

Table 2 shows the sociodemographic characteristics of the population separately by each country. The total population consisted of slightly higher proportion of women than men in all countries and the mean age differed slightly across countries: 61.48 years (s.d.= 14.63) in Spain, 59.17 years (s.d.= 15.96) in Finland and 58.66 years (s.d.= 16.45) in Poland. Those who were in partnership represented the highest proportion. Significant differences across countries in all the sociodemographic characteristics ($p < 0.001$) were found though the effect size for each factor was generally small except for the residential setting which was medium (Cramer's $V = 0.31$).

The percentage of people with financial problems was higher in Spain (11.71%) than in Poland (9.21%) and Finland (5.72%). This difference had a small associated effect size (Cramer's $V = 0.07$), as can be seen in Table 3. The highest proportion of people having voluntary health insurance was found in Finland (42.82%). The effect size associated to the differences in the percentage of people with voluntary health insurance was moderate (Cramer's $V = 0.21$).

The same pattern of significant difference and small effect size applied to clinical and use of services variables (Table 4) except the occupational health benefits which had a large associated effect size (Cramer's $V = 0.73$). In Finland the 76.58% of the population had occupational health benefits and this percentage decreased substantially in Poland (18.53%) and Spain (2.43%). Also Finland had the highest proportion of having at least one chronic disease. The majority in the three countries used public facilities and had no history of hospitalization during the last year.

Regarding healthy lifestyle behaviors, Table 5 shows that the majority in the three countries were not daily smokers and had moderate to high physical

activity. The differences were significant in both cases ($p<0.001$) and the associated effect sizes were small, according to the Cramer's V values.

Table 2: Sociodemographic characteristics across countries in the formally non-depressed population					
	Spain	**Finland**	**Poland**	**p**	**Effect Size***
Age Groups, n (%)				< 0.001	0.05
18-49	898 (21.41)	456 (25.10)	984 (26.48)		
50-64	1541 (36.73)	684 (37.64)	1446 (38.91)		
65+	1756 (41.86)	677 (37.26)	1286 (34.61)		
Gender, n (%)				< 0.001	0.06
Male	2009 (47.89)	793 (43.64)	1532 (41.23)		
Female	2186 (52.11)	1024 (56.36)	2184 (58.77)		
Marital Status, n (%)				< 0.001	0.06
Not in Partnership	903 (21.53)	440 (24.22)	893 (24.03)		
In Partnership	2570 (61.26)	1154 (63.51)	2076 (55.87)		
Widowed	722 (17.21)	223 (12.27)	747 (20.10)		
Residential Setting, n (%)				< 0.001	0.31
Urban	3633 (86.60)	1407 (77.44)	2091 (56.27)		
Rural	562 (13.40)	410 (22.56)	1625 (43.73)		
Employment Status, n (%)				< 0.001	0.19
Employed	1311 (33.47)	855 (48.80)	1420 (42.17)		
Retired	1415 (36.12)	790 (45.09)	1543 (45.83)		
Home Maker/ Not Working for Paid	751 (19.17)	50 (2.85)	263 (7.81)		
Unemployed	440 (11.23)	57 (3.25)	141 (4.19)		
Years of Education, mean (SD)	11.01 (6.34)	12.21 (4.26)	11.75 (3.81)	< 0.001	0.09

*Cramer's V was calculated for chi-squared tests conducted over categorical variables, while Cohen's f was calculated for ANOVA tests of continuous ones.

Table 3: Socioeconomic characteristics across countries in the formally non-depressed population					
	Spain	**Finland**	**Poland**	**p**	**Effect Size***
Financial Problems, n (%)				< 0.001	0.07
No	3598 (88.29)	1699 (94.28)	3283 (90.79)		
Yes	477 (11.71)	103 (5.72)	333 (9.21)		
Private / Voluntary Health Insurance, n (%)				< 0.001	0.21
No	3428 (81.76)	1003 (57.18)	2837 (78.96)		
Yes	765 (18.24)	751 (42.82)	756 (21.04)		

*Cramer's V was calculated for chi-squared tests.

Table 4: Clinical and use of services characteristics across countries in the formally non-depressed population					
	Spain	**Finland**	**Poland**	**p**	**Effect Size***
Occupational Health Benefits, n (%)				< 0.001	0.73
No	4093 (97.57)	418 (23.42)	1086 (81.47)		
Yes	102 (2.43)	1367 (76.58)	247 (18.53)		
Frequent Facility, n (%)				< 0.001	0.15
Public	3109 (76.61)	970 (75.25)	2500 (88.43)		
Private	949 (23.39)	319 (24.75)	327 (11.57)		
Physical Comorbidity, n (%)				< 0.001	0.06
No	1869 (44.55)	666 (36.65)	1630 (43.86)		
Yes	2326 (55.45)	1151 (63.35)	2086 (56.14)		
1 year Hospitalization, n (%)				< 0.001	0.11
No	3603 (87.03)	1531 (85.06)	2228 (77.82)		
Yes	537 (12.97)	269 (14.94)	635 (22.18)		

*Cramer's V was calculated for chi-squared tests.

Table 5: Life style characteristics across countries in the formally non-depressed population					
	Spain	**Finland**	**Poland**	**p**	**Effect Size***
Daily Smoking, n (%)				< 0.001	0.09
No	3145 (77.18)	1567 (86.24)	2764 (76.44)		
Yes	930 (22.82)	250 (13.76)	852 (23.56)		
Physical Activity, n (%)				< 0.001	0.06
Low	1190 (29.20)	429 (23.62)	1122 (31.03)		
Moderate or Higher	2885 (70.80)	1387 (76.38)	2494 (68.97)		

*Cramer's V was calculated for chi-squared tests.

Across the countries considered, there were significant differences in out of pocket expenditure, outpatient visits, sedentarism, disability, net affect and loneliness. Pairwise comparisons across countries indicated more outpatient visits and sedentary behavior in Finland, better experienced well-being in Spain, and more disability and loneliness in Poland. In addition, the mean of out of pocket expenditure was the highest (197 Euros) in Poland while in Finland was 95 and in Spain was 39. The significant differences across countries had small effect sizes except for the sedentary behavior, having moderate effect size for the difference between Finland and Poland (Hedges'g= 0.52), and between Finland and Spain (Hedges'g= 0.50) (Table 6).

Table 6: Mean estimates (95 % CI.) of quantitative economic, well-being and use of services variables and pairwise comparisons across countries in the formally non-depressed population						
				Effect Size (Hedges'g)		
	Spain	**Finland**	**Poland**	**FN-PL**	**FL-SP**	**PL-SP**
Out of Pocket Expenditure (ᶦin 1000 Euros)	0.039 (0.032, 0.046)	0.095 (0.082, 0.107)	0.197 (0.178, 0.217)	**0.23**	**0.15**	**0.36**
Outpatient Visits	2.77 (2.60, 2.93)	4.27 (3.65, 4.88)	2.64 (2.30, 2.99)	**0.11**	**0.12**	N.S.
Sedentarism in hours	4.61 (4.47, 4.75)	6.04 (5.84, 6.24)	4.45 (4.29, 4.62)	**0.52**	**0.50**	N.S.
WHO DAS	5.69 (5.33, 6.04)	5.78 (5.28, 6.29)	11.12 (10.51, 11.73)	**0.29**	N.S.	**0.29**
Net Affect	4.26 (4.18-4.34)	4.19 (4.09, 4.30)	3.94 (3.81, 4.06)	**0.13**	N.S.	**0.17**
UCLA Score	3.56 (3.51, 3.62)	3.44 (3.38, 3.49)	3.69 (3.63, 3.75)	**0.22**	**0.11**	**0.10**

Notes: FN= Finland, SP=Spain, PL= Poland, N.S. = not significant; Data were weighted and age-standardized; Effect sizes were reported for significant differences found in pairwise comparisons conducted across countries.

4.3 Prevalence of Undiagnosed Depression in the Formally Non-depressed Population

The one year prevalence estimates of undiagnosed depression by age groups, gender, marital status, residential setting, and employment status are shown in Table 7 for the total formally non-depressed population while Table 9 shows the prevalence for the same variables separately for each country.

The prevalence in the total population and in each country was higher in women, the widowed group, those who were living in rural areas and the unemployed people. Regarding age groups, the prevalence was higher in the older age group in the total population, Spain and Poland while in Finland it was higher in the younger age group (18-49).

In the formally non-depressed population, differences in the percentage of people with undiagnosed depression were found by age group ($p= 0.003$). The highest prevalence estimate of undiagnosed depression was found for the individuals older than 65 (5.43%) followed by those aged between 50 and 64 (4.14%) and those younger than 50 (3.35%). The same trend was observed in Spain (p= 0.008) and Poland ($p= 0.044$), as can be seen in Table 9.

As can be seen in Table 7, the prevalence of undiagnosed depression in women was significantly higher than the prevalence in men in the overall population (4.68% vs. 3.29%, $p = 0.005$), a result that was also found in Spain (5.61% vs. 3.94%, $p= 0.012$), as can be seen in Table 9. Regarding marital status, significant differences ($p< 0.001$) were found in the prevalence estimates of undiagnosed depression. The highest prevalence of undiagnosed depression was found in the widowed population (8.45%), followed by those who were not in partnership (4.53%) and those who were in partnership (3.03%). Differences across the occupation categories were also found ($p = 0.009$), with the highest prevalence of undiagnosed depression found for the home workers and those who were not working for paid (7.74%). Significant

differences in residential setting were not found in the overall population or across countries.

Table 8 shows the one year prevalence of undiagnosed depression by having financial problems, voluntary health insurance, occupational health benefits, type of frequent facility utilized, having physical comorbidity, being hospitalized during the last year, daily smoking and doing physical activity for the total formally non-depressed population and Table 10 shows the one year prevalence separately for each country.

Based on the formally non-depressed population, the prevalence estimate of undiagnosed depression was higher in people with financial problems (8.99%) than in those without financial problems (3.42%), with significant differences (Rao-Scott χ^2 = 29.71, p<0.001), as reported in Table 8. A similar trend can be observed in Spain and Poland, as can be seen in Table 10, while significant differences associated with having voluntary health insurance were reported only in Finland (3.97% vs. 2.43%, p= 0.030). Regarding occupational health benefits, there were significant differences only for the entire population (4.45 % vs. 3.10%, p= 0.037).

In relation to clinical status (Tables 8 and 10), the prevalence rates differed significantly according to having chronic comorbidity for the total population (4.60% for those with at least one comorbid condition vs. 3.05% for those without any condition, p< 0.001), in Spain (5.35% vs. 3.64%, p= 0.003) and Poland (4.20% vs. 2.86, p= 0.022), and also according to being hospitalized during the last year; for the total population (7.02% for those hospitalized at least once vs. 3.74% for those not hospitalized, p< 0.001) and for the Spanish population (5.39% vs. 4.44%, p= 0.037). More significant differences, associated with hospitalization, were found for the Polish population (9.19% vs. 2.83%, p< 0.001).

Regarding healthy lifestyle behaviors (Tables 8 and 10), significant differences were found, based on daily smoking and physical activity. Differences in daily smoking were found in the entire population (5.22% for daily smokers vs. 3.34% for non-daily smokers, $p= 0.004$), and in Poland (5.56% vs. 2.98%, $p= 0.037$) and Finland (7.89% vs. 2.83%, $p= 0.023$). Differences based on physical activity were found in the total population (3.69% in people with moderate or higher level of activity vs. 4.30% in people with low level of activity, $p= 0.034$) and specifically in Finland (2.83% vs. 6.62%, $p= 0.029$).

Table 7: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups according to sociodemographic variables in the formally non-depressed population

	Total
Age Groups	
18-49	3.35 (2.53, 4.18)
50-64	4.14 (3.43, 4.85)
65+	5.43 (4.59, 6.27)
Rao-Scott χ^2	12.64 p= 0.003
Gender	
Male	3.29 (2.53, 4.04)
Female	4.68 (3.95, 5.42)
Rao-Scott χ^2	7.90 p= 0.005
Marital Status	
Not in Partnership	4.53 (3.53, 5.54)
In Partnership	3.03 (2.49, 3.64)
Widowed	8.45 (4.94, 11.96)
Rao-Scott χ^2	43.43 p< 0.001
Residential Setting	
Urban	3.87 (3.30, 4.44)
Rural	4.19 (3.08, 5.31)
Rao-Scott χ^2	0.34 p= 0.56
Employment Status	
Employed	3.49 (2.63, 4.34)
Retired	3.47 (1.14, 5.79)
Home Worker/ Not Working for Paid	7.74 (4.33, 11.14)
Unemployed	6.00 (2.58, 9.42)
Rao-Scott χ^2	14.32 P= 0.009

* Weighted and age-standardized data.

Table 8: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups according to other relevant variables in the formally non-depressed population

	Total
Financial Problems	
No	3.42 (2.93, 3.92)
Yes	8.99 (6.22, 11.75)
Rao-Scott χ^2	29.71 p< 0.001
Private / Voluntary Health Insurance	
No	4.07 (3.45, 4.69)
Yes	3.66 (2.67, 4.65)
Rao-Scott χ^2	0.91 p= 0.34
Occupational Health Benefits	
No	3.10 (2.15, 4.05)
Yes	4.45 (3.74, 5.15)
Rao-Scott χ^2	4.36 p= 0.037
Frequent Facility	
Public	4.37 (3.63, 5.10)
Private	4.06 (2.96, 5.21)
Rao-Scott χ^2	0.42 p= 0.52
Physical Comorbidity	
No	3.05 (2.42, 3.68)
Yes	4.60 (3.65, 5.54)
Rao-Scott χ^2	15.06 p< 0.001
1 year Hospitalization	
No	3.74 (3.19, 4.30)
Yes	7.02 (4.51, 9.53)
Rao-Scott χ^2	11.64 p< 0.001
Daily Smoking	
No	3.34 (2.82, 3.86)
Yes	5.22 (3.93, 6.52)
Rao-Scott χ^2	8.46 p= 0.004
Physical Activity	
Low	4.30 (3.26, 5.35)
Moderate or Higher	3.69 (3.10, 4.28)
Rao-Scott χ^2	4.48 p= 0.034

* Weighted and age-standardized data.

Table 9: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups of the formally non-depressed population according to sociodemographic variables in each country			
	Spain	**Finland**	**Poland**
Age Groups			
18-49	3.77 (2.50, 5.04)	3.91 (2.08, 5.74)	2.77 (1.43, 4.12)
50-64	4.80 (3.61, 5.98)	3.14 (1.81, 4.78)	4.20 (3.03, 5.37)
65+	6.84 (5.48, 8.20)	2.52 (1.24, 3.79)	5.28 (3.74, 6.82)
Rao-Scott χ^2	10.57 p= 0.008	1.79 p= 0.40	6.77 p= 0.044
Gender			
Male	3.94 (2.74, 5.14)	2.42 (0.99, 3.86)	3.29 (1.98, 4.6)
Female	5.61 (4.39, 6.84)	4.42 (2.77, 6.07)	3.92 (2.84, 4.99)
Rao-Scott χ^2	6.34 p= 0.012	2.47 p= 0.12	0.79 p= 0.38
Marital Status			
Not in Partnership	4.57 (3.17, 5.97)	4.62 (1.85, 7.39)	5.02 (3.13, 6.91)
In Partnership	3.75 (2.71, 4.78)	2.63 (1.49, 3.76)	2.86 (1.74, 3.97)
Widowed	11.75 (3.56, 19.94)	4.48 (1.33, 7.64)	7.32 (3.38, 11.26)
Rao-Scott χ^2	28.47 p< 0.001	1.28 p= 0.49	15.73 p< 0.001
Residential Setting			
Urban	4.54 (3.66, 5.43)	3.24 (2.07, 4.41)	3.59 (2.48, 4.69)
Rural	5.37 (3.12, 7.62)	5.63 (1.47, 9.79)	3.76 (2.45, 5.08)
Rao-Scott χ^2	0.48 p= 0.49	0.25 p= 0.61	0.08 p= 0.78
Employment Status			
Employed	3.66 (2.40, 4.91)	2.63 (1.45, 3.81)	3.41 (2.16, 4.66)
Retired	6.19 (0.66, 11.72)	2.10 (0.41, 3.79)	2.46 (1.73, 3.20)
Home Worker/ Not Working for Paid	6.58 (3.76, 9.41)	5.64 (-0.68, 11.96)	5.27 (1.21, 9.34)
Unemployed	4.04 (2.15, 5.93)	4.14 (-0.99, 9.27)	7.10 (0.74, 13.47)
Rao-Scott χ^2	10.25 p=0.024	2.56 p=0.46	7.51 p=0.09

* Weighted and age-standardized data.

Table 10: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups of the formally non-depressed population according to other relevant variables in each country

	Spain	Finland	Poland
Financial Problems			
No	4.13 (3.29, 4.98)	3.21 (2.09, 4.32)	3.03 (2.25, 3.82)
Yes	8.15 (5.55, 10.78)	4.59 (1.09, 8.08)	10.27 (4.96, 15.59)
Rao-Scott χ^2	9.23 p= 0.002	2.41 p= 0.12	17.78 p< 0.001
Private / Voluntary Health Insurance			
No	4.83 (3.90, 5.75)	2.43 (1.15, 3.71)	3.82 (2.84, 4.81)
Yes	3.75 (2.12, 5.37)	3.97 (2.37, 5.58)	3.57 (1.25, 5.88)
Rao-Scott χ^2	1.48 p= 0.22	4.69 p= 0.030	0.97 p= 0.32
Occupational Health Benefits			
No	4.66 (3.83, 5.48)	4.45 (0.93, 7.97)	4.11 (2.43, 5.79)
Yes	3.45 (-0.76, 7.65)	3.34 (2.17, 4.50)	3.11 (0.58, 5.65)
Rao-Scott χ^2	0.11 p= 0.74	0.01 p= 0.92	1.19 p= 0.28
Frequent Facility			
Public	4.81 (3.82, 5.79)	4.26 (2.03, 6.48)	4.13 (2.92, 5.34)
Private	3.93 (2.52, 5.34)	7.39 (2.72, 12.05)	3.45 (0.95, 5.95)
Rao-Scott χ^2	1.10 p= 0.29	1.76 p= 0.18	0.62 p= 0.43
Physical Comorbidity			
No	3.64 (2.71, 4.57)	2.17 (0.98, 3.36)	2.86 (1.65, 4.07)
Yes	5.35 (3.58, 7.11)	4.76 (2.64, 6.88)	4.20 (2.76, 5.63)
Rao-Scott χ^2	8.65 p= 0.003	3.31 p= 0.07	5.26 p= 0.022
1 year Hospitalization			
No	4.44 (3.56, 5.31)	3.47 (2.25, 4.68)	2.83 (2.02, 3.63)
Yes	5.39 (3.41, 7.36)	3.57 (0.50, 6.65)	9.19 (4.65, 13.73)
Rao-Scott χ^2	4.35 p= 0.037	0.02 p= 0.89	17.53 p< 0.001
Daily Smoking			
No	3.95 (3.09, 4.81)	2.83 (1.86, 3.80)	2.98 (2.12, 3.85)
Yes	5.67 (3.92, 7.42)	7.89 (2.78, 13.01)	5.56 (2.99, 8.14)
Rao-Scott χ^2	1.37 p= 0.24	5.2 p= 0.023	4.36 p= 0.037
Physical Activity			
Low	5.30 (3.75, 6.85)	6.62 (2.49, 10.75)	3.23 (1.56, 4.90)
Moderate or Higher	4.30 (3.33, 5.27)	2.83 (1.82, 3.84)	3.54 (2.56, 4.52)
Rao-Scott χ^2	3.02 p= 0.08	4.77 p= 0.029	0.18 p= 0.67

* Weighted and age-standardized data.

4.4 General Profile of the Depressed Population

Table 11 shows the sociodemographic characteristics of the depressed population separately by each country. The percentage of women was higher than 70% in each country. The mean age was different across countries. Mean age in Spain was 64.11 years (s.d.=13.52), while in Poland and Finland was 62.26 (s.d.=14.64) and 56.26 years (s.d.= 15.19), respectively. The populations' statistics showed that the highest proportions in the three countries were those who were in partnership, people living in urban areas and the retired. The mean of years of education was significantly different across countries, with a small effect size (Cohen's F= 0.24).

Significant differences in sociodemographic characteristics among the populations corresponding to each country were also found regarding age groups, marital status, residential setting and employment status but not for gender. The highest value for the effect size was found for the residential setting (Cramer's V= 0.29), with a medium effect size.

The socioeconomic characteristics across countries are shown in Table 12 for the depressed population. The percentage of people with financial problems was similar, without significant differences across countries. Finland showed the highest proportion of people having voluntary insurance (36.26%), followed by Poland (17.93%) and Spain (14.02%). In the case of private/voluntary health insurance, the difference found across percentages was statistically significant ($p < 0.001$), with a small to moderate associated effect size (Cramer's $V = 0.19$).

Table 13 shows the clinical and use of services characteristics. The majority in the three countries used public facilities and had one or more chronic disease but did not get hospitalized during the last year. The highest percentage of using private facilities was found in Finland (21.17%) and the smallest percentage was found in Poland (9.80%). Significant differences

across countries were reported in using private health facilities as well as getting hospitalized; however, these differences were associated with small effect sizes while the difference regarding having occupational health benefits had a large effect size (Cramer's V= 0.74). In Finland, the 74.59% of the population had benefits and in Poland the percentage was 14.67% whereas in Spain only 1.62%.

Table 14 shows healthy lifestyle habits. The majority in the three countries were not daily smokers and exercised moderate to high physical activity. Significant differences in the percentage of people with a moderate or high level of physical activity were found across countries, although the effect size was small.

Table 11: Sociodemographic characteristics across countries in the depressed population					
	Spain	**Finland**	**Poland**	**p**	**Effect Size***
Age Groups, n (%)				< 0.001	0.11
18-49	117 (13.56)	52 (27.66)	63 (16.98)		
50-64	348 (40.32)	89 (47.34)	155 (41.78)		
65+	398 (46.12)	47 (25.00)	153 (41.24)		
Gender, n (%)				0.64	0.03
Male	232 (26.88)	50 (26.60)	109 (29.38)		
Female	631 (73.12)	138 (73.40)	262 (70.62)		
Marital Status, n (%)				< 0.001	0.10
Not in Partnership	194 (22.48)	72 (38.30)	96 (25.88)		
In Partnership	422 (48.90)	88 (46.81)	169 (45.55)		
Widowed	247 (28.62)	28 (14.89)	106 (28.57)		
Residential Setting, n (%)				< 0.001	0.29
Urban	726 (84.13)	154 (81.91)	206 (55.53)		
Rural	137 (15.87)	34 (18.09)	165 (44.47)		
Employment Status, n (%)				< 0.001	0.23
Employed	141 (17.69)	76 (42.70)	99 (29.29)		
Retired	339 (42.53)	78 (43.82)	193 (57.10)		
Home Maker/ Not Working for Paid	222 (27.85)	7 (3.93)	35 (10.36)		
Unemployed	95 (11.92)	17 (9.55)	11 (3.25)		
Years of Education, mean (SD)	8.97 (6.02)	12.45 (4.23)	11.04 (4.04)	< 0.001	0.24

* Cramer's V was calculated for chi-squared tests conducted over categorical variables, while Cohen's f was calculated for ANOVA tests of continuous ones.

Table 12: Socioeconomic characteristics across countries in the depressed population

	Spain	Finland	Poland	*p*	Effect Size*
Financial Problems, n (%)				0.81	0.02
No	645 (78.56)	147 (79.03)	275 (77.03)		
Yes	176 (21.44)	39 (20.97)	82 (22.97)		
Private / Voluntary Health Insurance, n (%)				< 0.001	0.19
No	742 (85.98)	116 (63.74)	293 (82.07)		
Yes	121 (14.02)	66 (36.26)	64 (17.93)		

*Cramer's V was calculated for chi-squared tests.

Table 13: Clinical and use of services characteristics across countries in the depressed population

	Spain	Finland	Poland	*p*	Effect Size*
Occupational Health Benefits, n (%)				< 0.001	0.74
No	849 (98.38)	47 (25.41)	128 (85.33)		
Yes	14 (1.62)	138 (74.59)	22 (14.67)		
Frequent Facility, n (%)				< 0.001	0.11
Public	673 (80.79)	108 (78.83)	276 (90.20)		
Private	160 (19.21)	29 (21.17)	30 (9.80)		
Physical Comorbidity, n (%)				0.07	0.06
No	284 (32.91)	55 (29.41)	98 (26.42)		
Yes	579 (67.09)	132 (70.59)	273 (73.58)		
1 year Hospitalization, n (%)				< 0.001	0.12
No	664 (77.39)	152 (81.28)	205 (66.13)		
Yes	194 (22.61)	35 (18.72)	105 (33.87)		

*Cramer's V was calculated for chi-squared tests.

Table 14: Life style characteristics across countries in the depressed population

	Spain	Finland	Poland	*p*	Effect Size*
Daily Smoking, n (%)				0.06	0.06
No	624 (76.00)	149 (79.26)	252 (70.79)		
Yes	197 (24.00)	39 (20.74)	104 (29.21)		
Physical Activity, n (%)				0.010	0.08
Low	328 (39.95)	56 (29.79)	119 (33.43)		
Moderate or Higher	493 (60.05)	132 (70.21)	237 (66.57)		

*Cramer's V was calculated for chi-squared tests.

Table 15 shows that statistically significant differences were detected when comparing countries with regard to out of pocket expenditure, outpatient visits, sedentarism, disability, net affect and loneliness but not to number of symptoms. Pairwise comparisons across countries indicated that Spain had the highest net affect, Finland had the highest sedentarism and outpatient visits, and Poland had the highest disability, loneliness and number of depression symptoms.   In addition, in Poland the mean of out of pocket expenditure was the highest (266 Euros) while in Finland was 133 and in Spain 50 Euros. All the significant differences had a small effect size except the differences between Poland and Spain in relation to the out of pocket expenditure (Hedges'g= 0.50) and net affect (Hedges'g= 0.55), and between Finland and Poland with regard to the net affect (Hedges'g= 0.50).

Table 15: Mean estimates (95 % CI.) of quantitative economic, well-being and use of services variables and pairwise comparisons across countries in the depressed population

	Spain	Finland	Poland	Effect Size (Hedges'g)		
				FN-PL	FL-SP	PL-SP
Out of Pocket Expenditure in 1000 Euros	0.050 (0.030, 0.070)	0.133 (0.086, 0.179)	0.266 (0.200, 0.333)	**0.34**	**0.20**	**0.50**
Outpatient Visits	6.13 (5.11, 7.15)	8.48 (6.27, 10.68)	4.96 (3.67, 6.26)	**0.24**	N.S	N.S.
Sedentarism in hours	4.79 (4.41, 5.16)	6.09 (5.62, 6.57)	4.77 (4.31, 5.23)	**0.41**	**0.39**	N.S.
WHO DAS	15.92 (14.40, 17.45)	19.43 (16.84, 22.01)	25.45 (22.17, 28.74)	**0.25**	**0.15**	**0.39**
Net Affect	3.47 (3.21, 3.74)	3.45 (3.10, 3.80)	2.15 (1.70, 2.60)	**0.50**	N.S.	**0.55**
UCLA Score	4.74 (4.49, 4.98)	4.45 (4.19, 4.72)	4.85 (4.57, 5.12)	N.S.	N.S.	N.S.
Number of Symptoms	6.29 (5.93, 6.65)	5.82 (5.32, 6.31)	6.33 (5.88, 6.79)	N.S.	N.S.	N.S.

Notes: FN= Finland, SP=Spain, PL= Poland, N.S. = not significant; Data were weighted and age-standardized; Effect sizes were reported for significant differences found in pairwise comparisons conducted across countries.

4.5 Prevalence of Undiagnosed Depression in the Depressed Population

The one year prevalence estimates of undiagnosed depression by age groups, gender, marital status, residential setting, and employment status are shown in Table 16 for the total depressed population and Table 18 shows the prevalence for the same variables separately for each country.

The prevalence in the total population was higher in men, younger age group (18-49), people who were in partnership, people living in rural areas and the employed.

The youngest age group had the highest prevalence of undiagnosed depression in the total population followed by the older than 65 and people aged between 50 and 64 years, with significant differences found across age groups (39.85%, 33.63% and 27.63%, $p= 0.011$). A similar trend was found in Spain (35.76%, 28.76% and 20.74%, $p= 0.012$).

The prevalence of undiagnosed depression was significantly higher in men than in women, in the entire population (45.91% vs. 30.29%, $p= 0.001$) and Spain (37.48% vs. 27.61%, $p= 0.048$), while significant differences were not found in Finland and Poland.

Regarding the employment, statistically significant differences were detected among groups of the entire population ($p= 0.004$). The employed had the highest prevalence (48.29%) followed by those not working for paid (40.74%) and the unemployed persons (33.46%), while the lowest prevalence was associated with retirement (13.41%). Similar results were observed in Spain. On the other hand, the highest prevalence was observed among those not working for paid in Finland and among the unemployed people in Poland. Retired people had the lowest prevalence in all countries. Differences in prevalence estimates among groups, according to employment status, were

significant in all countries. Finally, significant differences were not found in terms of marital status and residential setting.

Table 17 shows the one year prevalence of undiagnosed depression by having financial problems, voluntary health insurance, occupational health benefits, type of frequent facility utilized, having physical comorbidity, being hospitalized during the last year, daily smoking and doing physical activity for the total depressed population while Table 19 shows the one year prevalence in these groups separately for each country.

As can be seen in Table 17, significant differences were not found in the overall population. In Finland, the prevalence rates differed significantly according to the presence of financial burden (14.97% in people with financial problems vs. 36.90% in people without financial problems, $p= 0.022$) and having voluntary health insurance (47.87% in people with private or voluntary health insurance vs. 23.51% in people without private or voluntary health insurance, $p< 0.001$). In addition, based on frequent facility utilized in Finland, whether it was private or public, significant differences were reported (55.71% in people who used private facilities vs. 25.84% in people who used public facilities, $p= 0.005$). In Spain, significant differences in prevalence estimates associated with hospitalization during the last year were found (14.01% in the hospitalized group vs. 32.89% in the non-hospitalized group, $p= 0.001$).

Table 16: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups according to sociodemographic variables in the depressed population	
	Total
Age Groups	
18-49	39.85 (32.36, 47.34)
50-64	27.63 (23.37, 31.89)
65+	33.63 (29.12, 38.14)
Rao-Scott χ^2	10.34 p= 0.011
Gender	
Male	45.91 (38.55, 53.28)
Female	30.29 (25.15, 35.43)
Rao-Scott χ^2	10.80 p= 0.001
Marital Status	
Not in Partnership	33.12 (27.23, 39.00)
In Partnership	34.06 (28.30, 39.82)
Widowed	33.07 (24.98, 41.16)
Rao-Scott χ^2	0.48 p= 0.74
Residential Setting	
Urban	33.62 (28.75, 38.50)
Rural	41.65 (32.84, 50.46)
Rao-Scott χ^2	1.85 p= 0.17
Employment Status	
Employed	48.29 (39.31, 57.27)
Retired	13.41 (10.73, 16.09)
Home Worker/ Not Working for Paid	40.74 (31.53, 49.95)
Unemployed	33.46 (22.30, 44.61)
Rao-Scott χ^2	10.05 p= 0.036

 * Weighted and age-standardized data.

Table 17: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups according to other relevant variables in the depressed population	
	Total
Financial Problems	
No	37.10 (32.01, 42.18)
Yes	35.68 (25.98, 45.38)
Rao-Scott χ^2	0.02 p= 0.89
Private / Voluntary Health Insurance	
No	33.68 (28.50, 38.86)
Yes	41.01 (32.00, 50.02)
Rao-Scott χ^2	3.12 p= 0.08
Occupational Health Benefits	
No	33.45 (28.13, 38.76)
Yes	37.40 (28.78, 46.03)
Rao-Scott χ^2	0.23 p= 0.63
Frequent Facility	
Public	34.18 (29.23, 39.13)
Private	44.3 (34.82, 53.79)
Rao-Scott χ^2	0.69 p= 0.41
Physical Comorbidity	
No	33.87 (28.42, 39.31)
Yes	34.24 (27.04, 41.44)
Rao-Scott χ^2	1.29 p= 0.26
1 year Hospitalization	
No	34.50 (29.67, 39.33)
Yes	33.14 (26.20, 40.07)
Rao-Scott χ^2	0.42 p= 0.52
Daily Smoking	
No	33.62 (27.97, 39.27)
Yes	40.95 (33.77, 48.13)
Rao-Scott χ^2	2.59 p= 0.11
Physical Activity	
Low	32.25 (22.55, 41.95)
Moderate or Higher	37.63 (32.61, 42.65)
Rao-Scott χ^2	1.88 p= 0.17

 * Weighted and age-standardized data

	Spain	Finland	Poland
Table 18: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups of the depressed population according to sociodemographic variables in each country			
Age Groups			
18-49	35.76 (26.03, 45.49)	33.41 (19.82, 46.99)	48.54 (37.19, 59.89)
50-64	20.74 (15.76, 25.73)	24.69 (15.45, 33.92)	43.81 (34.40, 53.22)
65+	28.76 (23.55, 33.96)	35.85 (22.05, 49.65)	45.64 (35.87, 55.41)
Rao-Scott χ^2	10.14 p= 0.012	1.45 p= 0.47	0.50 p= 0.75
Gender			
Male	37.48 (27.00, 47.96)	42.08 (29.09, 55.08)	56.99 (50.21, 63.78)
Female	27.61 (20.90, 34.32)	27.87 (18.90, 36.83)	42.91 (34.62, 51.20)
Rao-Scott χ^2	3.92 p= 0.048	3.45 p= 0.07	2.60 p= 0.11
Marital Status			
Not in Partnership	27.16 (19.71, 34.61)	23.81 (12.80, 34.82)	51.92 (44.45, 59.40)
In Partnership	29.54 (23.32, 35.76)	36.09 (28.56, 43.61)	45.54 (33.97, 57.10)
Widowed	33.41 (18.82, 48.00)	19.36 (10.32, 28.40)	44.20 (33.84, 54.55)
Rao-Scott χ^2	0.14 p= 0.88	1.64 p= 0.43	3.75 p= 0.16
Residential Setting			
Urban	30.16 (23.98, 36.33)	29.92 (20.77, 39.08)	47.89 (39.13, 56.64)
Rural	35.29 (25.02, 45.56)	49.68 (37.21, 62.14)	47.12 (39.91, 54.34)
Rao-Scott χ^2	0.07 p= 0.80	2.17 p= 0.14	0.35 p= 0.55
Employment Status			
Employed	42.05 (34.68, 49.43)	40.77 (30.23, 51.32)	59.44 (49.65, 69.24)
Retired	10.46 (7.44, 13.49)	16.61 (10.21, 23.01)	29.59 (23.79, 35.39)
Home Worker/ Not Working for Paid	36.85 (26.92, 46.78)	48.99 (27.43, 70.54)	36.45 (25.43, 47.46)
Unemployed	32.1 (22.08, 42.13)	16.70 (3.83, 29.58)	64.28 (54.95, 73.60)
Rao-Scott χ^2	16.92 P=0.004	11.57 P=0.010	11.14 P= 0.020

* Weighted and age-standardized data.

Table 19: Prevalence estimates* (95% CI.) of undiagnosed depression among different groups of the depressed population according to other relevant variables in each country			
	Spain	**Finland**	**Poland**
Financial Problems			
No	28.84 (23.25, 34.44)	36.90 (26.10, 47.71)	51.92 (44.47, 59.37)
Yes	37.40 (27.89, 46.91)	14.97 (6.39, 23.54)	40.71 (32.65, 48.78)
Rao-Scott χ^2	0.42 $\quad$ p= 0.52	5.37 $\quad$ p= 0.022	0.03 $\quad$ p= 0.85
Private / Voluntary Health Insurance			
No	29.85 (23.73, 35.96)	23.51 (17.94, 29.09)	51.82 (42.47, 61.17)
Yes	34.20 (21.79, 46.60)	47.87 (32.21, 63.53)	41.43 (33.43, 49.43)
Rao-Scott χ^2	0.47 $\quad$ p= 0.49	12.09 $\quad$ p< 0.001	0.25 $\quad$ p= 0.62
Occupational Health Benefits			
No	30.65 (24.99, 36.32)	29.53 (18.15, 40.91)	66.10 (56.80, 75.40)
Yes	33.58 (10.57, 56.58)	33.86 (25.61, 42.12)	53.65 (46.01, 61.29)
Rao-Scott χ^2	0.04 $\quad$ p= 0.84	0.20 $\quad$ p= 0.65	0.02 $\quad$ p= 0.88
Frequent Facility			
Public	29.36 (23.29, 35.42)	25.84 (16.15, 35.54)	43.26 (35.77, 50.76)
Private	42.02 (35.31, 48.74)	55.71 (44.00, 67.41)	57.65 (44.07, 71.24)
Rao-Scott χ^2	0.19 $\quad$ p= 0.66	8.26 $\quad$ p= 0.005	1.50 $\quad$ p= 0.22
Physical Comorbidity			
No	30.63 (23.55, 37.70)	24.78 (13.00, 36.56)	43.53 (32.78, 54.28)
Yes	25.18 (15.37, 34.98)	34.24 (25.51, 42.98)	49.13 (39.96, 58.30)
Rao-Scott χ^2	2.14 $\quad$ p= 0.14	1.19 $\quad$ p= 0.28	0.88 $\quad$ p= 0.35
1 year Hospitalization			
No	32.89 (26.69, 39.09)	31.71 (22.66, 40.76)	44.15 (35.22, 53.08)
Yes	14.01 (8.43, 19.60)	33.71 (26.91, 40.50)	47.58 (38.05, 57.12)
Rao-Scott χ^2	10.87 $\quad$ p= 0.001	0.06 $\quad$ p= 0.81	2.41 $\quad$ p= 0.12
Daily Smoking			
No	29.03 (21.45, 36.61)	31.91 (22.29, 41.53)	51.41 (42.82, 60.00)
Yes	35.4 (26.58, 44.22)	27.03 (15.14, 38.93)	62.47 (53.91, 71.03)
Rao-Scott χ^2	1.23 $\quad$ p= 0.27	0.05 $\quad$ p= 0.83	0.63 $\quad$ p= 0.43
Physical Activity			
Low	25.98 (16.20, 35.75)	29.92 (19.84, 40.00)	47.73 (39.53, 55.93)
Moderate or Higher	32.63 (25.82, 39.43)	32.03 (22.65, 41.42)	47.61 (38.96, 56.27)
Rao-Scott χ^2	1.87 $\quad$ p= 0.17	0.54 $\quad$ p= 0.46	0.39 $\quad$ p= 0.54

*Weighted and age-standardized data.

4.6 Logistic Regression

Multiple logistic regression models were carried out to determine factors associated with undiagnosed depression in the total population as well as in each country for both the formally non-depressed and the depressed population.

Different logistic regression models were conducted for the overall population (Table 20), and separately for each country: Spain (Table 21), Finland (Table 22) and Poland (Table 23). The same factors were studied for both populations except the number of depressive symptoms, which was used for the purpose of controlling for its effect in the depressed population in order to examine potential factors associated with being undiagnosed rather than those associated with the depressive episode.

4.6.1 Associations with Sociodemographic Characteristics

The presence of undiagnosed depression was higher in people aged between 18 and 49 years than in those older than 65 [OR = 0.36, 95%CI. = (0.19, 0.69), p = 0.002] across the formally non-depressed population, as can be seen in Table 20. A similar trend was observed in Poland [OR = 0.12, 95% CI. = (0.04, 0.67), p = 0.012] and Finland [OR = 0.27, 95% CI. = (0.08, 0.94), p = 0.040], in the last case when comparing with the middle age group. A similar result was observed in the depressed population in Poland, when comparing the youngest age group with the group of people aged between 50 and 64 years [OR = 0.13, 95% CI. = (0.02, 0.77), p = 0.025] and older than 65 [OR = 0.10, 95% CI. = (0.01, 0.93), p = 0.043]. Also in the depressed population, men presented a lower probability of presenting undiagnosed depression than women in the overall sample [OR = 0.28, 95% CI. = (0.17, 0.49), p < 0.001] and Spain [OR = 0.28, 95% CI. = (0.14, 0.55), p < 0.001].

In terms of marital status, being widowed was associated with a higher probability of presence of undiagnosed depression in both the overall formally

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non-depressed population [OR = 2.12, 95% CI. = (1.17, 3.82), p = 0.013] and the overall depressed population [OR = 3.38, 95% CI. = (1.73, 6.60), p < 0.001]. By country, the significant association was found in the depressed population of Spain [OR = 3.23, 95% CI. = (1.41, 7.42), p = 0.006]. Significant differences were not found based on living in a rural or urban setting.

Considering employed people as reference category, the presence of undiagnosed depression was lower in those retired [OR = 0.26, 95% CI. = (0.13, 0.51), p < 0.001] and unemployed [OR = 0.40, 95% CI. = (0.17, 0.91), p = 0.029] in the depressed population. By country, the retired presented the lowest probability of being undiagnosed in Spain [OR = 0.14, 95% CI. = (0.05, 0.37), p < 0.001]. A lower number of years of education was related to the presence of undiagnosed depression in the total formally non-depressed population [OR = 0.95, 95% CI.= (0.91, 0.99), p= 0.030] and in Poland [OR = 0.87, 95% CI. = (0.76, 0.99), p= 0.037].

4.6.2 Associations with Socioeconomic Characteristics

In total formally non-depressed population, the presence of financial problems was associated with the presence of depressive episode [OR = 1.66; 95% CI.= (1.03, 2.66), p = 0.037]. In the depressed population, the relationship was found with a different sign in Finland: people with financial problems presented a lower probability of being undiagnosed [OR = 0.10, 95% CI.= (0.02, 0.46), p= 0.004]. Also in Finland, having a private or voluntary health insurance was related to the presence of undiagnosed depression in the formally non-depressed population [OR = 3.04; 95% CI.= (1.15, 8.04), p = 0.025] and the depressed population [OR = 13.62; 95% CI.= (2.43, 76.45), p = 0.003].

4.6.3 Associations with Clinical and Use of Services Characteristics

In Finland, out of pocket expenditure was positively associated with presence of depressive episode in the formally non-depressed population [OR

= 1.97, 95% CI.= (1.14, 3.40), *p*= 0.014] and with being undiagnosed in the depressed population [OR = 9.44; 95% CI.= (1.61, 55.21), *p*= 0.013]. In addition, in Finland, utilization of private facilities was associated with presence of depressive episode in formally non-depressed population [OR = 2.82; 95% CI. = (1.29, 6.16), *p* = 0.009]. Finally, there was a relationship between the presence of physical comorbidity and the presence of depressive episode [OR = 4.89; 95% CI.= (1.67, 14.33), *p* = 0.004], also in the formally non-depressed population.

A higher number of outpatient visits was associated with presence of depressive episode in the total formally non-depressed population [OR = 1.01; 95% CI.= (1.00, 1.02), *p* = 0.030]. This result was also found in Spain [OR = 1.05; 95% CI.= (1.02, 1.08), *p* < 0.001]; while in Poland a lower number of outpatient visits was associated with being undiagnosed within the depressed population [OR = 0.90; 95% CI.= (0.83, 0.97), *p* = 0.010].

4.6.4 Associations with Healthy Life Style Characteristics

In the overall population, sedentarism was associated with the presence of undiagnosed depression in the depressed population [OR = 1.08; 95% CI. = (1.01, 1.15), *p*= 0.031]. A similar result was found in Spain [OR = 1.09; 95% CI.= (1.00, 1.18), *p* = 0.037]; however, the sign of the result changed for Finland, where sedentarism was associated with a lower probability of being undiagnosed [OR = 0.71; 95% CI.= (0.52, 0.98), *p* = 0.035]. Non daily smoking was associated with being undiagnosed in Poland [OR = 0.25; 95% CI.= (0.08, 0.82), *p* = 0.022], in the depressed population.

4.6.5 Associations with Well-being, Loneliness and Disability

A higher score in disability was associated with presence of depressive episode in the total formally non-depressed population [OR = 1.03; 95% CI.= (1.02, 1.04), *p* < 0.001], and also separately in the three countries: in Spain [OR = 1.03; 95% CI.= (1.02, 1.04), *p* < 0.001], Finland [OR = 1.05; 95% CI. =

(1.03, 1.08), $p < 0.001$] and Poland [OR = 1.03; 95% CI.= (1.00, 1.05), $p=$ 0.018]. However, a higher score in disability was related to a lower probability of being undiagnosed in the overall depressed population [OR = 0.99; 95% CI. = (0.98, 1.00), p = 0.029].

Regarding the net affect, a global well-being variable, lower score was associated with presence of depressive episode in the total formally non-depressed population [OR = 0.84; 95% CI. = (0.76, 0.92), $p < 0.001$] and in the Spanish sample [OR = 0.80, 95% CI.= (0.70, 0.91), $p < 0.001$].

Regarding loneliness, a higher score of it was associated with presence of depressive episode in the total formally non-depressed population [OR = 1.41; 95% CI.= (1.27, 1.58), $p < 0.001$], in Spain [OR = 1.43; 95% CI.= (1.25, 1.63), $p < 0.001$] and Poland [OR = 1.73; 95% CI.= (1.27, 2.37), $p = 0.001$].

Table 20: Logistic regression models to examine factors associated with undiagnosed depression in both the total formally non-depressed and the total depressed population

	Formally Non-depressed Population			Depressed Population		
	OR (95% CI.)	*P*		OR (95% CI.)	*p*	
Age group Ref 18-49						
50-64	0.81 (0.52, 1.25)	0.35		0.71 (0.41, 1.21)	0.21	
65+	0.36 (0.19, 0.69)	**0.002**		1.35 (0.65, 2.81)	0.42	
Gender Ref Male	1.19 (0.76, 1.84)	0.44		0.28 (0.17, 0.49)	**< 0.001**	
Marital Status Ref Not in Partnership						
in Partnership	1.21 (0.74, 1.98)	0.44		1.61 (0.90, 2.88)	0.11	
Widowed	2.12 (1.17, 3.82)	**0.013**		3.38 (1.73, 6.60)	**< 0.001**	
Residential Setting Ref urban	0.97 (0.60, 1.56)	0.90		1.23 (0.72, 2.11)	0.46	
Employment Status Ref Employed						
Retired	0.80 (0.50, 1.29)	0.36		0.26 (0.13, 0.51)	**< 0.001**	
Home Maker/ Not Working for Paid	1.36 (0.74, 2.49)	0.32		0.79 (0.37, 1.69)	0.54	
Unemployed	0.87 (0.47, 1.60)	0.65		0.40 (0.17, 0.91)	**0.029**	
Years of Education	0.95 (0.91, 0.99)	**0.030**		0.99 (0.94, 1.04)	0.60	
Financial Problems Ref No	1.66 (1.03, 2.66)	**0.037**		1.36 (0.76, 2.43)	0.30	
Private / Voluntary Health Insurance Ref No	1.13 (0.73, 1.75)	0.58		1.67 (0.97, 2.88)	0.07	
Out of Pocket Expenditure	1.07 (0.80, 1.43)	0.65		0.95 (0.62, 1.47)	0.83	
Occupational Health Benefits Ref No	0.94 (0.51, 1.75)	0.86		1.41 (0.57, 3.49)	0.46	
Frequent Facility Ref Public	1.03 (0.67, 1.57)	0.90		1.55 (0.88, 2.71)	0.13	
Physical Comorbidity Ref No	1.34 (0.90, 1.99)	0.15		0.81 (0.48, 1.36)	0.42	
1 Year Hospitalization Ref No	0.96 (0.61, 1.53)	0.87		0.89 (0.51, 1.54)	0.67	
Outpatient Visits	1.01 (1.00, 1.02)	**0.030**		0.98 (0.95, 1.01)	0.13	
Daily Smoking Ref No	1.37 (0.88-2.15)	0.16		1.03 (0.58, 1.83)	0.93	
Physical Activity Ref Low	1.34 (0.92, 1.96)	0.13		1.25 (0.74, 2.11)	0.40	
Sedentarism in hours	1.03 (0.97, 1.09)	0.30		1.08 (1.01, 1.15)	**0.031**	
WHO DAS	1.03 (1.02, 1.04)	**< 0.001**		0.99 (0.98, 1.00)	**0.029**	
Net Affect	0.84 (0.76, 0.92)	**< 0.001**		1.02 (0.93, 1.12)	0.69	
UCLA Score	1.41 (1.27, 1.58)	**< 0.001**		0.96 (0.85, 1.09)	0.52	
Number of Symptoms	Not Included			1.36 (1.27, 1.46)	**< 0.001**	

In bold, significant *p*-values at the 95% confidence level.

Table 21: Logistic regression models to examine factors associated with undiagnosed depression in both the formally non-depressed and the depressed population in Spain

	Formally Non-depressed Population			Depressed Population		
	OR (95% CI.)		p	OR (95% CI.)		p
Age group Ref 18-49						
50-64	0.96 (0.54-1.70)		0.89	0.75 (0.39, 1.44)		0.39
65+	0.65 (0.27-1.54)		0.33	2.31 (0.96, 5.56)		0.06
Gender Ref Male	1.24 (0.69-2.24)		0.48	0.28 (0.14, 0.55)		**< 0.001**
Marital Status Ref Not in Partnership						
in Partnership	1.36 (0.71, 2.62)		0.36	1.80 (0.88, 3.71)		0.11
Widowed	1.84 (0.89, 3.81)		0.10	3.23 (1.41, 7.42)		**0.006**
Residential Setting Ref urban	0.96 (0.50, 1.86)		0.91	1.06 (0.54, 2.08)		0.88
Employment Status Ref Employed						
Retired	0.55 (0.29,1.04)		0.07	0.14 (0.05, 0.37)		**< 0.001**
Home Maker/ Not Working for Paid	1.08 (0.50, 2.34)		0.85	0.50 (0.19, 1.29)		0.15
Unemployed	0.88 (0.44, 1.74)		0.70	0.38 (0.14, 1.03)		0.06
Years of Education	0.96 (0.91, 1.01)		0.14	1.00 (0.94, 1.05)		0.91
Financial Problems Ref No	1.50 (0.79, 2.85)		0.21	1.82 (0.86, 3.88)		0.12
Private / Voluntary Health Insurance Ref No	0.97 (0.50, 1.87)		0.93	1.16 (0.57, 2.34)		0.69
Out of Pocket Expenditure	1.09 (0.80, 1.50)		0.57	0.93 (0.60, 1.43)		0.73
Occupational Health Benefits Ref No	1.51 (0.26, 8.64)		0.64	0.60 (0.08, 4.36)		0.62
Frequent Facility Ref Public	0.87 (0.53, 1.44)		0.58	1.40 (0.72-2.72)		0.32
Physical Comorbidity Ref No	1.17 (0.71, 1.94)		0.53	0.79 (0.42, 1.46)		0.45
1 Year Hospitalization Ref No	0.97 (0.58, 1.63)		0.92	0.92 (0.44-1.91)		0.81
Outpatient Visits	1.05 (1.02-1.08)		**< 0.001**	0.98 (0.94, 1.03)		0.48
Daily Smoking Ref No	1.50 (0.84-2.70)		0.17	1.01 (0.49, 2.10)		0.97
Physical Activity Ref Low	1.20 (0.76, 1.88)		0.44	1.27 (0.69, 2.33)		0.45
Sedentarism in hours	1.02 (0.95, 1.10)		0.52	1.09 (1.00, 1.18)		**0.037**
WHO DAS	1.03 (1.02, 1.04)		**< 0.001**	0.99 (0.97, 1.00)		0.07
Net Affect	0.80 (0.70, 0.91)		**< 0.001**	0.97 (0.86, 1.09)		0.57
UCLA Score	1.43 (1.25, 1.63)		**< 0.001**	0.98 (0.86, 1.12)		0.75
Number of Symptoms	Not Included			1.38 (1.27, 1.51)		**< 0.001**

In bold, significant *p*-values at the 95% confidence level.

Table 22: Logistic regression models to examine factors associated with undiagnosed depression in both the formally non-depressed and the depressed population in Finland

	Formally Non-depressed Population			Depressed Population		
	OR (95% CI.)		p	OR (95% CI.)		p
Age group Ref 18-49						
50-64	0.27 (0.08, 0.94)		**0.040**	0.08 (0.005, 1.19)		0.07
65+	0.21 (0.03, 1.64)		0.14	0.09 (0.002, 3.82)		0.21
Gender Ref Male	1.60 (0.67, 3.83)		0.29	1.66 (0.25, 11.02)		0.60
Marital Status Ref Not in Partnership						
in Partnership	1.46 (0.56, 3.81)		0.44	2.23 (0.46, 10.86)		0.32
Widowed	3.71 (0.75, 18.44)		0.11	6.30 (0.41, 96.73)		0.18
Residential Setting Ref urban	1.25 (0.55, 2.84)		0.59	3.18 (0.21, 48.65)		0.40
Employment Status Ref Employed						
Retired	0.48 (0.08, 3.06)		0.44	0.28 (0.01, 6.71)		0.43
Home Maker/ Not Working for Paid	2.01(0.35, 11.57)		0.43	0.19 (0.01, 3.66)		0.27
Unemployed	1.58 (0.39, 6.43)		0.52	0.01 (0.0004-0.45)		0.017
Years of Education	0.94 (0.82, 1.09)		0.43	1.12 (0.86, 1.46)		0.39
Financial Problems Ref No	1.67 (0.55, 5.08)		0.37	0.10 (0.02, 0.46)		**0.004**
Private / Voluntary Health Insurance Ref No	3.04 (1.15, 8.04)		**0.025**	13.62(2.43, 76.45)		**0.003**
Out of Pocket Expenditure	1.97 (1.14, 3.40)		**0.014**	9.44 (1.61, 55.21)		**0.013**
Occupational Health Benefits Ref No	1.45 (0.56, 3.78)		0.45	5.40 (0.71, 40.85)		0.10
Frequent Facility Ref Public	2.82 (1.29, 6.16)		**0.009**	1.23 (0.22, 6.87)		0.81
Physical Comorbidity Ref No	4.89(1.67, 14.33)		**0.004**	0.45 (0.04, 5.04)		0.52
1 Year Hospitalization Ref No	0.68 (0.19, 2.48)		0.56	0.57 (0.08, 3.82)		0.56
Outpatient Visits	1.00 (0.99, 1.01)		0.65	0.98 (0.90, 1.06)		0.55
Daily Smoking Ref No	1.68 (0.61, 4.60)		0.31	0.64 (0.14, 2.87)		0.56
Physical Activity Ref Low	1.31 (0.49, 3.52)		0.59	0.25 (0.02, 3.67)		0.31
Sedentarism in hours	0.95 (0.83, 1.09)		0.45	0.71 (0.52, 0.98)		**0.035**
WHO DAS	1.05 (1.03, 1.08)		**< 0.001**	0.96 (0.89, 1.04)		0.36
Net Affect	0.91 (0.74, 1.11)		0.34	1.88 (0.97, 3.64)		0.06
UCLA Score	1.24 (0.89, 1.72)		0.20	0.94 (0.42, 2.07)		0.87
Number of Symptoms	Not Included			1.80 (1.17, 2.79)		**0.009**

In bold, significant *p*-values at the 95% confidence level.

Table 23: Logistic regression models to examine factors associated with undiagnosed depression in both the formally non-depressed and the depressed population in Poland

	Formally Non-depressed Population			Depressed Population		
	OR (95% CI.)		p	OR (95% CI.)		p
Age group Ref 18-49						
50-64	0.68 (0.26,1.77)		0.43	0.13 (0.02, 0.77)		**0.025**
65+	0.16 (0.04, 0.67)		**0.012**	0.10 (0.01, 0.93)		**0.043**
Gender Ref Male	0.86 (0.30, 2.46)		0.78	0.26 (0.06, 1.05)		0.06
Marital Status Ref Not in Partnership						
in Partnership	0.74 (0.22, 2.45)		0.62	0.41 (0.09, 1.77)		0.23
Widowed	1.91 (0.64, 5.68)		0.24	1.72 (0.44, 6.76)		0.43
Residential Setting Ref urban	0.72 (0.24, 2.18)		0.56	1.96 (0.60, 6.33)		0.26
Employment Status Ref Employed						
Retired	1.90 (0.77, 4.69)		0.17	2.40 (0.48, 11.89)		0.28
Home Maker/ Not Working for Paid	2.62(0.40, 16.95)		0.31	5.92 (0.58, 60.45)		0.13
Unemployed	0.45 (0.04, 4.65)		0.50	1.03(0.005,232.25)		0.99
Years of Education	0.87 (0.76, 0.99)		**0.037**	0.88 (0.76, 1.03)		0.12
Financial Problems Ref No	1.34 (0.53, 3.37)		0.54	2.02 (0.51, 8.08)		0.32
Private / Voluntary Health Insurance Ref No	0.72 (0.28, 1.87)		0.50	0.77 (0.17, 3.48)		0.73
Out of Pocket Expenditure	1.13 (0.56, 2.28)		0.74	0.36 (0.05, 2.48)		0.30
Occupational Health Benefits Ref No	0.58 (0.25, 1.36)		0.21	1.77 (0.49, 6.42)		0.39
Frequent Facility Ref Public	0.58 (0.16, 2.10)		0.41	0.83 (0.11, 6.50)		0.86
Physical Comorbidity Ref No	0.97 (0.41, 2.27)		0.94	0.75 (0.20, 2.84)		0.67
1 Year Hospitalization Ref No	0.96 (0.30, 3.06)		0.95	1.04 (0.21, 5.14)		0.96
Outpatient Visits	0.95 (0.88, 1.04)		0.29	0.90 (0.83, 0.97)		**0.010**
Daily Smoking Ref No	0.76 (0.33, 1.72)		0.50	0.25 (0.08, 0.82)		0.022
Physical Activity Ref Low	1.74 (0.67, 4.52)		0.26	2.84 (0.64, 12.66)		0.17
Sedentarism in hours	1.12 (0.98, 1.28)		0.11	1.23 (1.00, 1.52)		0.06
WHO DAS	1.03 (1.00, 1.05)		**0.018**	1.00 (0.96, 1.04)		0.89
Net Affect	0.92 (0.77, 1.10)		0.37	1.26 (0.99, 1.58)		0.05
UCLA Score	1.73 (1.27, 2.37)		**0.001**	0.70 (0.44, 1.11)		0.13
Number of Symptoms	Not Included			1.38 (1.04, 1.82)		**0.026**

In bold, significant *p*-values at the 95% confidence level.

5. Discussion

This study has been based on a cross-sectional survey administered in three European countries, the "COURAGE in Europe" project. Its objective was to study factors that may be related to the development of undiagnosed depression overall and separately in Spain, Poland and Finland. In addition, another objective was to determine the prevalence of undiagnosed depression in these three countries.

5.1 Main Findings

For the total formally non-depressed population, those aged between 18 and 49 years, widowed and less educated were associated with presence of undiagnosed depressive episode. Other associated factors included having financial problem, frequent outpatient visits, higher levels of disability and loneliness, and lower levels of experienced well-being. For the total depressed population, being undiagnosed was associated with being male, widowed and employed compared to both retired and unemployed. Other associated factors in this population included having sedentary life style and lower disability levels.

The strongest association in the current study was found between higher levels of disability and presence of depressive episode in the overall formally non-depressed population. These results were also found when the analysis was conducted separately in each country. In line with the present study, depression was associated with considerable impairments in health-related quality-of-life according to a review (291) of ten randomized controlled trials, and there was significant association with significant disability in another systematic review (292). In addition, older people in the depressed trajectories had increased disability, relative to non-depressed older adults in a four-year cohort study (293).

For the depressed population, a low level of disability was associated with being undiagnosed in the depressed population. Alternative coping strategies may be the main factor for treatment delay and the principal barrier for seeking care (294).This finding is consistent with the finding of a study by Simon et al. (61) showing that more disabled patient got more recognition of their depression in primary care. In addition, factors related to disability such as difficulty in functioning (295) and activities (296) were associated with help-seeking for depression. Another study (297) showed an association between low level of resilience in general and seeking care. The positive cognitive triad, which includes having positive views toward the self, the world, and the future, could explain the relationship between resilience and depression (298), taking into account that the cognitive function is a component of disability (272).

Lower levels of experienced well-being were associated with the presence of undiagnosed depressive episode in the total formally non-depressed population and in Spain. In line with this result, people who had higher level of positive affect held more positive attentional bias and less negative attentional bias, and reported higher levels of psychological well-being and lower levels of depression (299). A study by Girz et al. (300) showed that depressed people had negative emotional bias and presence of depressive disorder predicted well-being in a cohort study (301). Positive affect was associated, in another study (302), with protective psychosocial factors such as greater social connectedness, perceived social support, optimism, and preference for adaptive coping responses. As a consequence, positive affect may be part of a broader profile of psychosocial resilience (302).

In a systematic review (303) of seven observational and cross-sectional studies, an inverse relationship between depression and resilience was found. This relationship may explain these associations in the formally non-depressed population between the undiagnosed depressive episode and both low level of experienced well-being and high level of disability since most people living with a disability may be more vulnerable and this situation can be

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understood from a positive psychology standpoint as a deficit of well-being (193).

The association between depressive symptoms and well-being was negative in a study based on a questionnaire (304); however, satisfactory levels of well-being were found in a substantial proportion of the participants with psychological symptoms since several of the personal strengths and resources had a positive main effect on well-being, having a buffering effect in face of psychopathology (304). This may explain the association of marginal significance between higher scores of well-being and being undiagnosed in the depressed population of Finland and Poland. An adequate resilience that leads to less treatment seeking may be the explanation (297).

In the present study, higher scores of loneliness were associated with presence of depressive episode in the total formally non-depressed population, and also specifically in Spain and Poland. Other studies (177, 180, 182, 305-313) found similar results indicating that depression was associated significantly with loneliness. In Sweden, the presence of depression predicted loneliness in a cohort study (188), however, the association between depression and loneliness decreased with increasing age, according to another study investigating the Swedish elderly (189). In addition, resilience was found to be related to loneliness as its low level was associated significantly with loneliness (305). Moreover, loneliness was a significant mediator in the majority of the associations between interpersonal stressors and depressive symptoms among older Irish adults (314).

Presence of financial burden was associated with development of depressive episode in the overall non-depressed population. According to comprehensive literature review (315), poverty can be considered as a risk factor for mental illness and wealth was inversely related to depression in another study (316) analyzing World Health Surveys. In addition, a previous meta-analysis (317) showed a dose-response relation between income and

depression. Richardson et al. (318) showed a significant relationship between debt and depression and Blazer et al. (319) showed in a ten-year longitudinal study that perceived inadequate basic needs predicted depressive symptoms.

In a Korean study (320), differences in the prevalence of depressive symptoms generally existed between individuals of the same income category, depending on perceived income adequacy. In addition, the person's rank of income or wealth group within a social comparison group, rather than income or wealth themselves, was associated with depressive symptoms (321) and related to different health outcomes (322, 323). The low social rank has negative effect that may be due to the associated negative cognitions (324) and may act as mediator between objective socioeconomic status and depressive symptoms (325).

Unlike the current study that did not find a significant association between presence of financial burden and depressive episode in Finland, significant association was reported over the time period 1979-2002 between self-reported depression and lowest household income category in thousands of participants of a Finnish study (326) and higher depressive symptoms were associated with lower future income and earnings in another Finnish study (327).

Absence of financial burden was associated with being undiagnosed in Finland. This finding is supported by a Japanese study (328) which showed that the prevalence of depression treatment in those with psychological distress was significantly lower in the highest income quintile than in all the other income groups, and they may be reluctant to consult professionals and receive medical treatment, despite their psychological distress.

Regarding help-seeking, perceived need at baseline significantly predicted use of psychotherapy during the follow-up period in a study by Bonabi et al. (329) and the results of the current study showed that perceived need was not

only related to the depressive symptoms but also to different measures related to well-being including disability levels as well as presence of financial burden. In addition, greater perceived stress was associated in another study with self-recognition of the disorder (295). In a study from Singapore (330), self-recognition was associated with less preference to seek informal help from family and friends for depression whilst increased preference to seek help from mental health professionals and services.

Being male was significantly associated with being undiagnosed in the total depressed population, and specifically in Spain. This finding is in accordance with other studies confirming that female gender was associated with help-seeking (295, 296, 331) as women were better recognizing depression symptoms and more likely to suggest seeing a doctor than men (332). This may be related to their better depression literacy (333) and their positive attitude concerning psychological openness (334). Findings of a study by Seidler et al. (335) suggested that conformity to traditional masculine norms has a threefold effect on men experiencing depression, impacting: i) their symptoms and expression of symptoms; ii) their attitudes to intention and actual help-seeking behavior; and iii) their symptom management. As shown in another study (36), conformity to dominant masculine gender norms ("boys don't cry") leads to self-stigmatization in depressed men who feel that they should be able to cope with their illness without professional help. As shown in a Canadian study (336), males would be embarrassed about seeking help for depression endorsing stigmatizing attitudes toward themselves if they were depressed, and stigmatizing views about male depression in general, compared to female respondents, describing it as unpredictable. Racial differences may exist regarding the effect of self-reliance of men as it was associated with fewer depressive symptoms in a sample of African American men except those aged between 30 and 39; however, high restrictive emotionality was associated with more symptoms in age group younger than 39 (337).

Regarding the relationship between age and undiagnosed depressive episode, the younger age group (18-49 years) had a positive association with the presence of a depressive episode, compared to the 50-64 age group in the Finnish formally non-depressed population. A similar result was found when comparing with those older than 65 in the formally non-depressed population, overall and in Poland. Data from WMH surveys showed that depression goes down with age in the developed countries (203). The evidence showed that although the elderly may experience vulnerability they may develop self-regulation strategies that lead to age-related decrease in stress reactivity (338).

The current study showed a marginally significant association between being undiagnosed and age group more than 65 (when comparing those older than 65 with those aged between 18 and 49 in the depressed population of Spain). This result can be supported by a study from Hungary where negative attitudes towards help-seeking were found among older people (339). Another study (340) referred to the belief of the older population that their symptoms are normal as a major barrier for old age help-seeking . Other major barriers, according to this study (340), were related to: self-reliance, cost of treatment, and fear of medication. In addition, higher levels of cognitive impairment in the old age may lead to less help-seeking (341).

A systematic review (342) may explain the result found in Poland, where the younger age group was associated with being undiagnosed, compared to middle and older age group. According to this review (342), the most important barriers to help-seeking of young people were perceived stigma and embarrassment, problems recognizing symptoms (poor mental health literacy), and a preference for self-reliance. Similarly, about a quarter of younger adults of a Portuguese sample failed to recognize depression (343). However, this finding is different from that found in China where recognition of depression was predicted by younger age (344). Embarrassment and lack of accurate psychiatric labelling by the young people were reported in studies of the

Australian National Survey (345, 346). Furthermore, the young age group may have lack of trust in the benefits of treatment and fear of the social consequences of help-seeking (347). As a result, they may use self-help interventions such as physical activity than to access professional help (348) and they may seek help from family and friends (349).

The association between widowhood and presence of depressive episode in the total non-depressed population is supported by a study by Vable et al. (350) indicating that recent and near widows had worse depressive symptoms than the married individuals though there was an evidence (351) that both men and women returned to their prewidowhood levels of depressive symptoms within 24 months of becoming widowed. However early, long-term widowhood was associated with worse outcomes compared with late widowhood in other studies (351, 352). According to a qualitative synthesis (353) of thirteen articles, the widows seemed overwhelmed by the need to overcome an unbearable emotional state.

The attitude of the older population that their symptoms are normal, which was considered as a barrier for help-seeking (340), may explain the association of being widowed with being undiagnosed. In addition to this attitude, other explanations may be the possible successful adaptation and the increase of people experiencing resilience and coping more than those vulnerable (354). However, the resilience process is experienced as a struggle, and the widowed require time to improve their well-being and self-management, according to a systematic review (353).

Low educational level, measured in the current study by counting years of education, was associated with presence of undiagnosed episode in the total non-depressed population and in Poland. In line with this result, late life depression was associated with this low educational level according to a meta-analysis (223). In another study (232) investigating 10 European countries, it had odds approximately twice as high among adults with less than a high

school education compared with those of greater educational background. Another meta-analysis (317) showed a dose response relationship between education and depression episodes. In addition, data from World Health Surveys (316) supported this inverse relationship; however, in a study (355) investigating a sample from 21 EU countries, the benefits of education in some of these countries were limited or even eliminated by education-labour market misfit. Another study (356) showed that people from disadvantaged backgrounds realized a greater protective effect of higher education, either completing some college or attaining a four-year degree, against depressive symptomology than people from advantaged backgrounds. Regarding the association of education with being undiagnosed, the present study showed no significant association unlike previous studies (296, 331, 339, 357).

The association found between being undiagnosed and those employed, in comparison with those retired in Spain and those unemployed and retired in the total depressed population, is supported by a study conducted by Menear et al. (158), which showed lower odds of minimally adequate treatment for patients working full time. This pattern may be related to the stigma of depression label which is more than the stigma associated with burnout label (358), though the circular causal relationship that may exist between burnout and depression. It was hypothesized that burnout may be a phase in the development of depression, but also that depression may negatively influence the experience of work and generate burnout. Interestingly, longitudinal studies reported bidirectional relationships (359). Burnout is a syndrome of three dimensions. In addition to its core component, emotional exhaustion, which was strongly related to depressive symptoms, the other two components are depersonalization and reduced professional efficacy (359).

The characteristics of the employment status may affect the development of depression in addition to the probability of being undiagnosed. Perception of adverse psychosocial factors in the workplace was related to an elevated risk of depressive symptoms or major depressive episode according to several

studies (360-362). In addition, a meta-analysis of work environment and depressive symptoms (363) showed that moderately strong evidence was found for job strain, low decision latitude and bullying, having a significant impact on the development of depressive symptoms.

Employment conditions include job insecurity. An extensive literature review (364) showed that significant associations between job insecurity and adverse health outcomes were reported in Southern and East European welfare systems such as Spain and Poland, more than in Scandinavian system such as Finland. In addition, adverse health effect of precarious employment was reported in Spain. However, the situation was different in Finland, where this might be related to the buffering effect of the egalitarian welfare policies of Scandinavian countries for those engaged in vulnerable forms of employment.

With regard to the burden of depression influencing the employment, MDD was found to be associated with significant declines in functioning according to a systematic review (292), while another one (365) showed that antidepressant treatments in MDD significantly improved functional outcomes and early treatment response predicted functional improvement.

Regarding the retirement, being retired in the present study was associated with lower probability of being undiagnosed in the depressed population and in Spain, in comparison with people who were employed. The evidence showed the relationship of retirement with depression but not with being undiagnosed or with seeking help. A substantial reduction in depressive symptoms of retirees was reported in a cohort study (366) examining the effect of retirement. Its effect included also improvement of self-perceived health according to another study based on the same cohort of French population (367). Among old-age retirees, according to a Finnish study (368), antidepressant medication use decreased during the transition period (one year after versus one year before retirement), and a decrease in

antidepressant medication was also reported for retirees due to mental health problems but not physical problems. In another Finnish study (369), purchases of antidepressants decreased after disability retirement. However, there was no significant association in the present study in Finland between retirement and development of depressive episode or being undiagnosed.

Age of retirees and whether the retirement is voluntary or not are important factors that may be related to depression (370-373) In addition, loneliness and socioeconomic factors may have an effect for easy transition into retirement, as lonely older workers were at increased risk for the experience of depressive symptoms following retirement in a study by Segel-Karpas et al. (374). Regarding socioeconomic factors, according to a study by Mein et al. (375), mental health functioning deteriorated among those who continued to work after age 60 and improved among the retired, however this improvement was restricted to those in higher employment grade. In addition, midlife adversities such as low occupational position, poor standard of living and high job strain had strong associations with post-retirement depressive symptoms, in a study by Virtanen et al. (376).

Despite the unhealthy effects of unemployment (377), the current study showed that unemployed respondents had a higher probability of being diagnosed than the employed respondents in the total depressed population. In line with this result of the present study, the prevalence of depression treatment was significantly lower in employed than in unemployed respondents in a national sample of Japanese adults (328).

The relationship between healthy lifestyle behaviors and being undiagnosed in the depressed sample showed contradictory results indicating that self-care was not related in a homogenous pattern to help-seeking. Not being a daily smoker was associated with being undiagnosed in Poland. In addition, a lower level of sedentary behavior was associated with being undiagnosed in Finland; however, the present study also showed an

association between a higher level of sedentary behavior and being undiagnosed in the total depressed population and in Spain. For the result of Finland, previous evidence showed that most frequent physical activity was not linearly associated with depressive symptoms (378).

The finding related to the association between undiagnosed episode and presence of chronic disease in the Finnish non-depressed population can be supported by a meta-analysis (379) of a series of Canadian surveys showing an association between MDE and most chronic conditions, especially those characterized by inflammation and pain. This result is consistent with an analysis (380) of World Mental Health Surveys from 2001 to the end of 2011 showing that depression was associated with an increased risk of onset of a wide range of chronic physical conditions. In addition, two meta-analyses (381, 382) showed that those with chronic disease had a higher risk for depression. The relationship between comorbidity and being diagnosed was not supported in the present study though a previous qualitative study (383) showed that multimorbidity may obscure symptom causation but it may also create time for GP to investigate causation and generate relationship through frequent presentations. However, the effect of multimorbidity may be related to disability as multimorbid patients attributed depressive symptoms to the loss of 'normal' roles and functionality in another qualitative study (384).

More frequent outpatient visits were associated with the presence of an undiagnosed depressive episode in the non-depressed population, overall and in Spain. This result may be an indicator of deteriorated health status. In this case, being undiagnosed cannot be ruled out and effectiveness of outpatient service may be questioned while less frequent outpatient visits were associated with being undiagnosed in the depressed population of Poland. This finding for Poland is not supported by an evidence (385) investigating the Polish primary care that showed relative weakness of its structure compared to that of Finland which was evaluated as medium, and compared to that of Spain which was strong. From patients' perception perspective, the Polish

perceived more improvement potential than the Finnish in accessibility, continuity, comprehensiveness, involvement and communication. Moreover, they perceived more potential than the Spanish in continuity and involvement and less potential regarding accessibility, comprehensiveness and communication (385).

In Finland, the development of a depressive episode in the formally non-depressed population was associated with private utilization of health care. In addition, having voluntary health insurance and spending more out of pocket payments were associated with both presence of depressive episode in the formally non-depressed population of Finland and being undiagnosed in the Finnish depressed population. The effectiveness of the Finnish health system, especially its private sector, to recognize depression may be questioned in this case. Review of the Finnish context is described in the following lines:

- The Finnish health care is financed by taxes, compulsory National Health Insurance (NHI) and co-payments (386). Finland has public, private and occupational provision of services. Public provision has many problems such as waiting times, limited choice of provider, insufficient accessibility and availability of human resources, and lack of availability of some services (386, 387). Modest user fees are charged for utilization of the public municipal health centers which are the only available option for the poor people that cannot afford fees of private sector and the unemployed people who lack access to occupational care. Fees of the public sector were estimated in 2009 as 8.9% of the total costs and catastrophic costs are prevented by annual ceiling on out-of-pocket spending (386).

- Prevention is the main function of occupational health care, however it may include access to primary care. It represented 13% of total GP consultations in mid-2000. It is either provided by the health care units of the employers or purchased from private or public providers. Employers pay more than half of the costs. The

complement is provided by the NHI, particularly its earned income insurance section which its contributions are collected from the employers (about two thirds of the revenues), the employees (about a quarter), and a state subsidy (5.5%) (386).

- Private provision accounts for 16% of total primary care consultations and 25-30% of specialist visits (386). Its advantages include wide choice among providers and direct access to specialists (386, 387). The obligatory public health insurance reimburses 20-30% of the costs. The role of the voluntary private health insurance (VPHI) is complementary since it covers the high co-payments resulting from utilization of private services in the context of this low rate of reimbursement of the public insurance, especially for medical diagnostics and treatments (387).

- About 20% of the Finnish population is covered by the VPHI, including those who need its advantages such as some of the elderly people who leave the coverage of occupational care. However, insurance companies may exclude some patients from having their insurance based on the case history regarding certain diseases. In addition, some services are not covered by the VPHI such as delivery. Moreover, some insurance companies may adopt policies of restricted utilization of health care services and the patients have to pay more out of pocket costs when choosing to use other providers (387).

Unlike the previous studies (295, 296, 388) showing that severity of depression was associated with help-seeking and seeking formal care, results of this study showed that the number of symptoms, which might be an indicator of severity, was associated with being undiagnosed in the depressed population, overall and separately in each of the countries considered (Spain, Finland and Poland). This may be attributed to being untreated thus subjects expressed more depression symptoms. This result is of interest as individuals

with less severe depressive symptoms had on average significantly higher utility scores in health related quality of life than individuals suffering from more severe depressive symptomatology (291).

5.2 Strengths

The present study is among few studies that contribute to a deeper understanding of undiagnosed depression. It tried to make a distinction between the episode development and being undiagnosed. Moreover, the study was conducted in nationally representative samples of three European countries that have diverse welfare regimes. In addition, the response rate in the current study was adequate.

Regarding the instruments employed to assess the measures considered in the present work, previous studies showed good validity and reliability of day reconstruction method questionnaire about experienced well-being (274, 275), and the three item UCLA loneliness scale (277). WHO questionnaires about physical activity (269) and disability (270) were also used.

Another strength is that the present study examined the relationship between a wide range of factors and undiagnosed depression. In addition, it adds interesting findings to the substantial evidence of depression research with particular focus on being undiagnosed by three different health care systems.

5.3 Limitations

The findings of this study should be interpreted taking into account several limitations. One of the limitations of the current study was its cross-sectional design that does not allow to infer causality nor temporal sequence. Hence, the results obtained should be interpreted with caution.

Self-report of depression symptoms was another limitation. Despite of the good specificity and sensitivity of CIDI diagnosis (25) and the concordance of this case identification with clinical diagnosis (389), self-report in general can lead to information bias because of recall bias when the recall is related to the independent or the dependent variables and participants rate past events, or exposures, based on their current health status (390). In addition self-report can lead to shared method variance when similar methods of measurement are used to establish the independent and the dependent variables. In this case, people with a pessimistic view on life may over-report negative psychosocial events and symptoms of disease, which would lead to an inaccurate relationship between the psychosocial events, including presence of financial burden, and development of disease especially when collecting information at one point of time and during the financial recession (390).

Additionally, in some epidemiologic studies of major depression including this study, bipolar disorders are not assessed. In this case, MDE is diagnosed rather than MDD without the assumption that a lifetime bipolar history has been ruled out. Prevalence estimates of major depression from such studies should be slightly higher than studies that have ruled out bipolar cases of depressive disorders (8).

Regarding the presence of chronic comorbidity, it relied on five conditions only and was based on self-report, instead of a formal clinical diagnosis and regardless its severity. However, good accordance between patients' self-report and medical records has been found in previous studies (391, 392).

The degree of seriousness can be questioned for the participants in community surveys such as that used in the current analysis compared to clinical interviews where the patients seek more seriously clinical outcomes for their conditions (393).

Another limitation was the building of the regression models conducted over the formally non-depressed populations, where the dependent variable was the presence of undiagnosed depressive episode. While the investigated variable was mainly the development of depression, being undiagnosed could not be ruled out completely.

5.4 Strategies for Undiagnosed Depression

5.4.1 Promoting Help-seeking Behavior

Stigma should be combated by the correction of the depressed patient image targeting both men and women. However, depression in men should be more targeted as shown in the present study and the evidence (336) of a suggested contradiction between masculinity and both depression perception and seeking care. Moreover, men may lack the mental health literacy more than women (333). Correction of depressed patient image can be done by psychoeducation through mental health literacy content that was effective in improving help-seeking attitudes in the majority of studies of a systematic review (394). Psychoeducation leads to correct self-recognition of depression which was related to seeking formal help as shown in a study by Picco et al. (330). In addition, psychoeducation should have broader audience than patients only, thus influencing the media and the public (329).

Focus on benefits of formal help should be improved. Benefits are not only for psychological health but also for general health as mentioned before in this thesis regarding the association between depression and both disability and comorbidity. An example of the evidence is an Italian study (395) showing that depressive symptoms were associated with poorer self-perceived health. Furthermore, depressive symptoms are related to well-being and loneliness as shown in the current study. In the same line, a study by Henshaw et al. (396) showed that when depression remained untreated it was associated with more negative character evaluation and greater social distance.

5.4.2 Improving Care

The present study emphasizes the relationship between frequent outpatient visits and the development of depression. Identification of depression by primary care physicians at baseline is an important factor for mental service use (397). This may be done by overcoming competing health demands (398) and enhancing competence and openness of physicians as well as patient-physician trust (399). Multi-component interventions were found to be effective in the literature (400, 401), including training of primary care physicians and implementation of guidelines, taking into account the local conditions of mental health systems. Depression representations across different groups of population should be considered; for instance major depression in older people may have a more somatic presentation, whereas feelings of guilt and loss of sexual function may be more prevalent in younger people (402).

5.4.3 Enhancing Resilience

Factors related to resilience such as low levels of disability should not be barriers to help-seeking as shown in the current study. Moreover, depression treatment should focus on personal resilience as there was an evidence (403) supporting an association between expanding inner resources and depression outcome. As a result, the more resilient patient can seek the treatment for enhancing self-regulation instead on self-reliance without seeking care. Resilience may interact with stigma as stigmatized individuals may feel compelled to take steps to develop their resilience including drawing on existing support networks and expanding on positive emotions and personal strengths in order to counteract this stigma (404). It is important to combine the treatment with both enhancing resilience and combating stigma.

5.5 Future lines of investigation

There is a need in the psychiatric research, especially depression, for shifting the focus from associations to generating and testing aetiological hypotheses through life course perspective, assessing accumulation of risks and critical periods, and using statistical modelling techniques (405). This can allow to draw more conclusions about risk, resilience and coping factors.

Longitudinal research and designs which allow for assessing the causal relationship between different factors and the undiagnosed depressive episodes, are needed to replicate the results obtained in the present cross-sectional study. Following the participants in the community surveys will be helpful for more robust analytical investigations.

The effect of employment status and its different conditions and benefits on help-seeking patterns should be studied comprehensively. Further attention is necessary for research investigating employment conditions and stigma in the work place. In addition, it is essential to investigate the effect of economic policies such as private financing and utilization of health care on these patterns.

6. Conclusions

The presence of an undiagnosed depressive episode was highly prevalent among the depressed population. About a half of episodes in Poland and about a third in Finland and Spain were not diagnosed by the health system. In the formally non-depressed population (those who did not present depression according to the health care system), the current study found the association of self-reported episodes with low levels of well-being and high levels of disability and loneliness. These findings are similar to those reported in the literature between cases identified clinically and these measures.

However, in the depressed population, self-reported undiagnosed episodes were associated with better scores in some of these measures such as low levels of disability. This may suggest that help-seeking was not related only to the burden of depressive symptoms but also to the burden of disability level. In addition, presence of financial burden was related to depressive episodes in the formally non-depressed population but its absence was related to being undiagnosed in the Finnish depressed population. These findings supported the role of resilience, in terms of a lower disability level and the absence of financial burden, on self-reliance. Patients may be reluctant to seek formal care though their undiagnosed episodes were associated with a higher number of depressive symptoms.

Regarding sociodemographic characteristics, being widowed was associated with both presence of depressive episode and being undiagnosed, and special programs should be directed towards this population. Programs for younger people and those with low educational levels should be also developed, based on the associations found in the formally non-depressed population between presence of depressive episode and these sociodemographic characteristics.

In addition, programs for the employed people should be improved to identify those depressed since there was an association between employment and being undiagnosed in the total depressed population. Special focus on gender should be taken into account while designing screening programs since being male was associated with being undiagnosed in the total depressed population.

6. Conclusiones

La presencia de un episodio depresivo no diagnosticado fue muy frecuente entre la población deprimida. Aproximadamente la mitad de los episodios en Polonia y cerca de un tercio en Finlandia y España no fueron diagnosticados por el sistema de salud. En el grupo de personas formalmente sin depresión (aquellos que no presentaban depresión de acuerdo al sistema de salud), los episodios auto-reportados estuvieron relacionados con bajos niveles de bienestar y altos niveles de discapacidad y soledad. Estos resultados son similares a los reportados en la bibliografía entre los casos clínicamente identificados.

Sin embargo, en el grupo de personas con depresión, los episodios auto-reportados pero no diagnosticados formalmente se asociaron con mejores puntuaciones en algunas de estas áreas, como los bajos niveles de discapacidad. Esto puede indicar que la búsqueda de ayuda oficial no sólo se relacionaba con la carga de los síntomas depresivos, sino también con la carga del nivel de discapacidad. Además, la presencia de carga económica se relacionó con la presencia de episodios depresivos en el grupo de personas sin depresión, mientras su ausencia se relacionó con la falta de diagnóstico en el grupo de personas con depresión de la muestra finlandesa. Estos hallazgos apoyaron el papel de la resiliencia, en términos de un menor nivel de discapacidad y la ausencia de carga económica, en la autoconfianza. Los pacientes pueden ser reacios a buscar atención en el sistema sanitario aunque sus episodios no diagnosticados se asocien con un mayor número de síntomas depresivos.

En cuanto a las características sociodemográficas, el estar viudo/a estuvo relacionado con la presencia de episodios depresivos sin estar diagnosticado, y programas especiales deberían ser dirigidos a esta población. Programas para los más jóvenes y aquellos con bajo nivel educativo deberían desarrollarse también, basadas en la asociación entre presencia de episodios

depresivos y estas características sociodemográficas, encontrada en la población formalmente sin depresión.

Además, se deberían mejorar los programas para las personas empleadas con el fin de identificar a personas con depresión, ya que se observó una asociación entre empleo y falta de diagnóstico en la población con depresión. Es importante considerar también el género al diseñar programas de detección precoz, dado que ser varón estuvo asociado con falta de diagnóstico en la población global con depresión.

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