Universitat de Girona

Relationship between socioeconomic deprivation and depressive symptomatology, in adults aged 50 years or more, among European countries

Data from the Survey of Health, Ageing and Retirement in Europe (SHARE)

- FINAL DEGREE PROJECT -
2010-2016

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Faculty of Medicine, November 2016

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1. ABSTRACT

Background

Depression is one of the diseases most prevalent and disabling worldwide. According to different studies, depression is related to socioeconomic deprivation which is a measure to asses if the individual is part of low socioeconomic position. Socioeconomic position has also been assessed using variables such income, occupation or education level, among others, but these types of variables consider only a single part of socioeconomic position unlike socioeconomic deprivation which takes into account other factors involved.

Objective

The main objective is to assess if the degree of the association between socioeconomic deprivation and the prevalence of clinically significant depressive symptomatology is different among European countries in adults aged 50 and over.

Methods

A cross-sectional study has been carried out using data of 14 European countries and 1 non-European country and that has been obtained from the 5th wave of the Survey of Health, Ageing and Retirement in Europe (SHARE). In order to measure the independent variable (socioeconomic deprivation) a multidimensional index of socioeconomic deprivation developed specially for the 5th wave of the SHARE has been used; the dependent variable (clinically significant depressive symptomatology) has been measured with the EURO-D scale and a cut-off point of 3 has been defined. Data of other variables associated with depression and socioeconomic deprivation have been collected: employment, gender, age groups, education, marital status, being medicated with anxiolytics or antidepressants, BMI, number of chronic diseases, history of affective emotional disorders and self-rated general health state.

Results

The countries with a higher proportion of people with socioeconomic deprivation have higher prevalence rates of clinically significant depressive symptomatology and those countries with a lower proportion of people with socioeconomic deprivation have lower prevalence rates of clinically significant depressive symptomatology. However, the association between the independent variable and the dependent variable is stronger in the countries with a lower proportion of people with socioeconomic deprivation. This can be explained with "the status anxiety hypothesis" which exposes that the perception of lower social status leads to poorer health because the people with socioeconomic deprivation tend to compare themselves with those in higher socioeconomic position and this comparison worsens when differences between people not socioeconomic deprived and people socioeconomic deprived are wider.

2. ABBREVIATIONS

5HT	5-hydroxytryptamine (serotonin)
APA	American Psychiatric Association
BDI-II	Beck Depression Inventory - second edition
BDNF	Brain-derived neurotrophic factor
BMI	Body Mass Index
CBT	Cognitive Behavioural Therapy
CES-D	Center for Epidemiological Studies - Depressive Scale
CIDI	Composite International Diagnostic Interview
CPRS	Comprehensive Psychopathological Rating Scale
DA	Dopamine
DALY	Disability-adjusted life year
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECT	Electroconvulsive therapy
GMS-AGECAT	Geriatric Mental State - AGECAT
HRSD (HAM-D)	Hamilton Rating Scale for Depression
ICD	International Classification of Diseases
IDS	Inventory of Depressive Symptomatology
ISCEN-97	International Standard Classification of Education-97
MADRS	Montgomery-Asberg Depression Rating Scale
MAO	Monoamine oxidase
MAOI	Monoamine oxidase inhibitor
MDD	Major Depressive Disorder
MDE	Major Depressive Episode
NA	Noradrenaline
NOS	Not Otherwise Specified
PHQ-9	Brief Patient Health Questionnaire
QIDS	Quick Inventory of Depressive Symptomatology
SES	Socioeconomic status
SEP	Socioeconomic position
SHARE	Survey of Health, Ageing and Retirement in Europe
SHORT-CARE	SHORT-Comprehensive Assessment and Referral Evaluation
SNRI	Serotonin-noradrenaline reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
WHO	World Health Organization
YLD	Years of life lived with disability
ZSDS	Zung Self Rating Depression Scale

3. INTRODUCTION

3.1. Depression

Depression is one of the most frequent diseases worldwide with more than 350 million people affected (1). The term of "depression" refers to an state of great sadness, loss of pleasure and/or loss of energy that affects the functioning of the individuals; however, it is unspecific and can be used either when referring to depressive symptomatology alone or to designate a concrete disorder in which depressive symptoms are the main problem (2). The present study focuses on clinically significant depressive symptomatology characterized by sad or irritable mood accompanied with other somatic and cognitive alterations that affect the daily life of the individual (3).

* *3.1.1. Epidemiology*

The Global Burden of Disease Study 2010 separated "unipolar depression" into major depressive disorder and dysthymia and found an estimated point prevalence of 4.37% and 1.55%, respectively (4); another study reported an average 12-month prevalence for major depressive episode of 5.5% in high-income countries and 5.9% in low-middle income countries (5). However, it's difficult to know the exact prevalence of depressive disorders because of its wide variability among studies (5–7). This variability can be due to either true differences in the epidemiology of depressive disorders, differences in the methodology used to capture data or in the study design (6). Regarding the incidence, one systematic review gave a global annual incidence of 3.0% but only 4 studies could be used to calculate it (6).

The studies have found that depression is more frequent in women than in men (4,6,7) and that its prevalence decreases with age in developed countries but not in developing countries, where it can even increase (8). According to a study from the WHO World Mental Health Survey Initiative, either the depression age-of-onset (with a mean of 29 years), the duration of a major depressive episode (with a 12-month duration's mean of 26-27 weeks) or the number of lifetime episodes, increases with age (8).

Depressive disorders are one of the leading contributors of world's burden; 85% of this burden is due to major depressive disorder which was ranked as the 11th leading cause of global DALYs (disability-adjusted life year) and as the 2nd leading cause of all YLDs (years of life lived with disability), after low back pain, in 2010; dysthymia, for its part, was ranked as the 51th leading cause of global DALYs and 19th leading cause of all YLDs (4).

* *3.1.2. Risk factors for depression*

Depression is a disorder related with many risk factors and not all of them have been identified. The study of the risk factors of depression has several limitations such as the

possible bidirectional association (a lot of the risk factors could be the cause or consequence), and the difficulty to know if the factor acts in the development of depression and/or in its persistence. The most relevant risk factors are explained below.

- *Gender*

  Women are twice as likely as men to develop unipolar depression but there are no clear differences in course or treatment response of MDD (3,9).

  It has been found the postpartum and the premenstrual period are seasons of greater risk for women (2).

- *Age*

  Some studies have found that in developed countries depression is less prevalent in the elderly but not in developing countries where the prevalence does not decrease with age or it even may increase (5,8). One study based on the first wave of the SHARE reported an increase of depressive symptoms with age that vanished for men, and even reversed for women, when controlling for other socio-demographic characteristics, health conditions and economic strains (10).

  Similar to what happens with gender, there are no clear effects of current age on the course of MDD or its treatment response; on the other hand, there are some symptom differences: hypersomnia and hyperphagia are more likely in younger individuals, and melancholic symptoms, particularly psychomotor disturbances, are more common in older individuals (3).

- *Education*

  The information about the relationship between the level education attained and depression is contradictory; for example, one study of the World Mental Health (WMH) survey initiative found that low education was associated with MDE in only some countries (2,5).

- *History of a previous depressive episode*

  Depression is frequently a recurrent disorder, therefore a person who already suffered from a depressive episode has a higher risk to develop another one in the future (9).

- *Chronic physical disorders*

  Various chronic physical disorders have been associated with the development of depression; furthermore, the depression tends to a more refractory course if it develops against the background of another disorder which is often also complicated in this context (3).

  Some of the physical disorders associated with depression are: certain neurological illnesses like migraine, cerebrovascular disease, Parkinson's disease, multiple

sclerosis and epilepsy; endocrinological disorders such as Cushing's syndrome, Addison's disease, diabetes and disorders of thyroid function (hypo or hypertiroidism); arthritis; asthma; cancer; hypertension; chronic respiratory disorders; cardiovascular diseases; and a variety of chronic pain conditions (5,9,11).

- *Other psychiatric disorders*

Depression is associated with other psychiatric disorders, specially anxiety disorders, substance misuse and borderline personality disorder, as well as to previous history of panic attacks, particularly in men (3,9,11).

Some personality traits such as neuroticism, obsessionality and impulsivity have been associated with an increased risk for depression (3,9).

- *Family history and Genetic factors*

First-degree family members of individuals with MDD have a risk for MDD two-to fourfold higher than that of the general population; second grade family members are also at risk but it is lower

The relationship between familiar history or genetic factors and early-onset depression is stronger than the relationship between familiar history or genetic factors an late-onset depression. Heritability is approximately 40% (3).

Many genetic variations have been studied; one example is the polymorphism of the gen that codifies the serotonin transporter; this polymorphism would produce a decrease of this neurotransmitter transporter (11).

- *Social and Environmental factors*

This group includes many factors associated with a higher risk of depression (2,5,9,11,12):

* Marital dissatisfaction and marital violence
* Life events such as family or friend death/illness, work problems or problems with the neighbor.
* Job loss or unemployment.
* Marital status (separated or never married persons have a higher risk in high-income countries and divorced or widowed individuals in low-middle income countries).
* Income (the poorest people in high-income countries have a higher prevalence of major depressive episodes; on the other hand, the income in the low-middle-income countries is not significantly related. Financial crisis has also been associated with major depression).
* Social support.
* Adverse childhood experiences (physical abuse, sexual abuse, lack of parental affection or overprotection).
* Social class (people with lower social class has more risk to develop depression).

* Geographical setting (living in an urban area increases the risk to develop depression versus living in a suburban area).

* *3.1.3. Etiology*

It is known that different biological, psychological and social factors operate in the etiology of depression although it has not yet been found how exactly they relate to one another. From the idea that there are various factors implicated in the development of the depression, the biopsychosocial model of depression has been created; according to this model there are precipitating factors or "life events" and vulnerability factors that modulate the impact of the first ones.

The different relevant factors in depression's etiology are summarized separately below (2,9).

BIOLOGICAL FACTORS

- *Genetics*

  The risk of developing depression is increased in those who have first-degree relatives affected by some mood disorder (bipolar disorder o depressive disorder); various twin and adoption studies have shown that this heritability is due to genetic factors as well as behavioral and environmental factors.

  It is believed that the genetic susceptibility to depression is polygenic and related to genetic polymorphism, but the exact mode of transmission is not known yet.

- *Neurochemistry*

  One of the most relevant theories in the etiology of depression is the monoamine theory which explains that depression is caused by the depletion of monoamine neurotransmitters like serotonin (5HT), noradrenaline (NA) and dopamine (DA); this concept was developed observing that depression could be induced by certain drugs that depleted some of these monoamines, while other drugs could increase their release and induce euphoria. However, the monoamine theory alone cannot explain the occurrence of the disorder; another hypothesis that has been postulated (the neurotransmitter receptor hypothesis) is that depression is related to abnormalities of the receptors of the monoamine neurotransmitters increasing their sensitivity and this, through a negative feedback, would cause the depletion of different monoamines.

  Janowsky and cols. (1972), in their cholinergic hypersensitivity theory, suggested that individuals with depression could have an imbalance between cholinergic and adrenergic systems, in favor of the first; this would be related to the shortening of REM sleep latency seen in certain depressions (13).

- *Neuroendocrinology*

Depression has been related with various endocrine alterations, especially with the hyperactivity of the hypothalamic-pituitary-adrenal axis (involved in the physiological response to stress) which causes an increase of cortisol that can either increase the levels of pro-inflammatory cytokines or suppress some aspects of cellular immunity; eventually, this hyperactivity can cause neuronal atrophy and therefore cognitive impairment.

Hypothyroidism has also been associated, in a way that patients with hypothyroidism frequently exhibit cognitive impairment and depression, and patients with depression have higher rates of hypothyroidism. Some studies have also found involvement of the hypothalamic-growth hormone axis.

- *Cellular factors*

The molecular and cellular theory of depression explains that stress and antidepressant treatments act via intracellular mechanisms causing a decrease or an increase of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), respectively; this neurotrophic factors are necessary for the survival and function of particular neurons so their depletion affects cellular resilience and it results in neuronal atrophy.

- *Neuroanatomy*

Nowadays depression has been associated with abnormalities in the neural systems related with emotion processing, reward seeking and regulation of emotion; various neuroimaging studies of major depressive disorder have found that there is an increased activity in neural systems related to emotion processing and a reduced activity in neural systems supporting regulation of emotion (14).

The structures involved in the pathophysiology of depression are the hippocampus which is important for memory, learning and mood regulation; amygdala involved in emotion and reward processing; prefrontal cortex whose functions are creating judgments, integrating feelings and controlling impulses and attention, among others; anterior cingulate cortex which includes the subgenual area related with motivation and emotion processing; nucleus accumbens, the area of reward and pleasure; the hypothalamus, important for its involvement with circadian rhythms and because it is a part of the hypothalamic-pituitary-adrenal axis which controls the physiological response to stress; and raphe nuclei containing the neuronal bodies that produce serotonin (14,15)

PSHYCOLOGICAL FACTORS

There are different psychological theories trying to explain depression; the most important one is **the cognitive-behavioral theory** which attribute depression to pessimistic views about oneself and the world (2,9).

This theory has its origin in the experiments in which electric shocks were given to dogs following a warning in a situation where the dogs could not escape; the dogs learned to accept the shocks and later, when they had the opportunity to escape of the electric shocks, they continued without doing anything. The hypothesis derived from this observation is the one called **"learned helplessness"** which exposes that there is an absence of adaptive behaviors because the association between an adaptive response and the relief of aversive stimuli is not recognized. Applied to humans it could be said that what brings a person to suffer depression are systematic failures to control the external reinforcing situations and this entails the feelings of hopelessness, insecurity and passivity common in depression.

Later on, in 1964, Beck defined the *"cognitive triad"* grouping the negative thoughts of depressed patients into three categories: about the self (pejorative conception of oneself), about present experiences (negative interpretations of the own experiences) and about the future (pessimistic vision of the future). He also developed the idea that in depression specific cognitive distortions are present contributing to the negative beliefs of the individual; according to Beck, this cognitive distortions are: overgeneralization; magnification of bad events and minimization of good events; assuming responsibility for bad events that were in reality outside the person's control; selective abstraction (focusing on the bad things and ignoring the good ones); and arbitrary interference (drawing conclusions when there is little evidence to support them) (16).

SOCIAL FACTORS

Lately the social factors and their role in the development of depression has gained importance; it has been found through several studies that situations such as unemployment, being of a lower social status, childhood traumas, being unmarried or divorced and some "life events" like parental loss, among others, increase the risk to suffer depression (12).

* *3.1.4. Clinical course*

Depression is characterized by depressed mood, loss of interest or pleasure and fatigue or decreased energy but it can also be presented with other symptoms (9). Depressive symptomatology is usually classified into several groups:

- *Affective symptoms*

  One of the most typical symptoms in depression is a depressed mood described by the person as depressed, sad, hopeless or discouraged and that can be expressed

with tearfulness; however, some individuals, especially children and adolescents, manifest irritability rather than sadness. Anxiety may also be present and in some people this is the main symptom.

Loss of interest in activities and anhedonia are also frequent; anhedonia can either be presented as the inability to experience pleasure, as the inability to find and anticipate pleasure or both. It is usual in people with depression to stop doing activities that they previously liked and there are persons who express a reduction of sexual interest or desire (2,3).

Another common feature of depression is the diminished emotional reactivity or apathy (lack of feeling or emotions; indifference) (2,9)

- *Biological symptoms*

One characteristic of depression is the diurnal variation of the depressed mood which normally improves as the day progresses (9) and it is also relevant that some depressions have a periodic presentation, being spring and autumn the most critical seasons (2).

Sleep disturbance is often the presenting complaint, frequently in form of middle insomnia (waking up during the night and then having difficulty returning to sleep) or terminal insomnia (waking too early and being unable to return to sleep). There are some individuals who present initial insomnia (difficulty falling asleep) or hypersomnia (prolonged sleep episodes at night or increased daytime sleep) but these are not so frequent. Other symptoms usually seen in depressed individuals are fatigue and asthenia (lack or loss of strength and energy) (3).

Many people who suffer this disease exhibit changes in appetite or weight; usually is a decreased appetite accompanied with weight loss, but in atypical depressions tend to be an increased appetite with weight gain (3,9).

The main complaints for some individuals and in some cultures are somatic symptoms rather than feelings of sadness (3); there are not specific symptoms but the more frequents are body aches or pains such as headache, paresthesias and gastrointestinal, neurological or autonomic disorders such as constipation (2,9).

- *Cognitive symptoms and Depressive cognitions*

During major depressive episodes there is an impairment of cognitive functions; the person experiences memory difficulties, slowness of thought processes or bradypsychia, decline in executive functions and difficulties concentrating, maintaining attention and in making decisions (3,17). These alterations usually disappear once the depressive episode is successfully treated (2,3,17); however, in some individuals, particularly elderly persons, major depressive episode is the initial presentation of an irreversible dementia and the deficits may not completely disappear after recovery (3).

Pessimism thoughts with feelings of guilt, hopelessness, helplessness or worthlessness are typical of depression and associated with loss of confidence and low self-esteem; this pessimism can lead to recurrent thoughts of death or suicidal ideation (3,9).

Psychotic symptoms may be present in severe depressive episodes; these appear as hallucinations (usually auditory although other modalities are possible) or delusions (they usually are mood-congruent and its content includes thoughts of guilt, poverty, persecution and illness) (9).

- *Behavior*

People who have depression often neglect social life and themselves adopting self-destructive behaviors such as alcoholism, bulimia, smoking, exposition to dangerous situations or low compliance with treatment regimens (2,5,9). What is also common in this disorder are psychomotor disturbances that include agitation (inability to sit still, pacing, hand-wringing; the pulling or rubbing of the skin, clothing or other objects; or reduced facial expression) and retardation (slowed speech or bradyphasia; increased pauses before answering) (3).

Suicidal behavior (completed suicides and suicide attempts or threats) can occur at all times during the major depressive episode and it is known that the rate of suicide is higher in patients with depression compared with the general population. The factors associated with an increased risk for completed suicide are: male sex, being single or living alone, having prominent feelings of hopelessness, and the most relevant, a past history of suicide attempts or threats (3,9).

Depression may appear at any age but its age-of-onset is usually later than the age-of-onset for bipolar disorder (the prevalence is higher during the period between 15 and 45 years) (11); early-onset depression has a stronger association with family history and genetic factors than late-onset depression.

The average length of a single depressive episode is about 6 months but it increases with subsequent episodes as well as its severity does. The duration of the episode influences the probability of recovery; other factors associated with lower recovery rate are the passage of time, psychotic features, prominent anxiety, personality disorders, an underlying illness and symptom severity.

There are some individuals that rarely experience remission (2 or more months with no symptoms, or only one or two symptoms to no more than a mild degree); it has been calculated that approximately 10-25% of patients will present a chronic depression (defined as non-remitting episode of at least 2 years of duration).

The majority of patients have a recurrent course of depressive disorder; the risk of recurrence is higher: in individuals whose preceding episode was severe; in younger persons; in individuals who have experienced multiple episodes; in individuals with

persistent depressive symptoms during remission; in persons who had an early age-of-onset; if there is substance misuse; in persons with personality disorder; and in individuals with lack of social support. The first interval between episodes is longer than subsequent intervals, and a later age-of-onset of depression is associated with shorter first intervals (3,9).

* *3.1.5. Diagnosis*

The clinical interview is essential in the diagnosis of depression; the evaluation of this disorder should contain: characterization of the episode (duration, number and intensity of the symptoms and comorbidity), psychosocial evaluation (social support and interpersonal relationships), dysfunction and/or disability degree associated, previous treatment response and suicidal risk (11).

It is important to differentiate the instruments used to diagnose the disorder such as ICD-10 or DSM-5, and the instruments used to assess the depressive symptomatology or to monitor the treatment (HRSD, PHQ-9, BDI, MADRS, etc.).

OPERATIVE DIAGNOSTIC CRITERIA

Nowadays, the systems most commonly used in the diagnostic and classification of depression disorders are ICD-10 (International Classification of Diseases, 10th version) created by the WHO (World Health Organization) in 1992 (*Annex 1*); and DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th version) created by the APA (American Psychiatric Association) in 2013 (the criteria for Major depressive episode and Major depressive disorder, which is the prototype of depressive disorders, can be found in *Annex 2*).

STANDARDIZED SCREENING AND DIAGNOSTIC TOOLS

The existent number of instruments used to evaluate depression and its symptomatology is extremely high; below are exposed the most important ones.

- *EURO-D scale* (18)

  EURO-D is a scale used to assess the presence of depression symptoms; it was developed in 1999 by a collaboration of 14 research groups from 11 European countries (EURODEP Concerted Action Programme) in order to harmonize and compare the data obtained in each of these research groups which had used different late-depression measures (GMS, SHORT-CARE, CES-D, ZSDS or CPRS).

  It consist in a 12-item scale that asks respondents to rate the levels at which they had experienced, in the preceding month: feelings of depression, pessimism, wishing death, guilt, sleeping disturbances, loss of interest, irritability, loss of appetite, fatigue, reduction in concentration, loss of enjoyment, and tearfulness. Each item is scored 0 (symptom not present) or 1 (symptom present) therefore the maximum score which can be obtained is 12.

* *Reliability* --> The internal consistency was assessed by calculating the inter-item correlations (with a mean range of 0.12-0.38), the item-total correlations (with a range of 0.06 - 0.42) and the standardized alpha value (with a range of 0.58-0.80). The inter-item and item-total correlations and the standardized alpha value were higher for the CES-D EURO-D than for the GMS EURO-D.
* *Validity* --> Agreement with continues was assessed by Spearman non-parametric correlations, and for dichotomous measures by the area under the receiver operating characteristic curve (area under ROC curve). The Spearman correlation where the CES-D had been used had a range of 0.70-0.93, where the ZUNG had been used was 0.84 and where the SHORT-CARE had been used was 0.79. The area under ROC curve was 0.83 where EURO-D was compared with DSM-III clinical diagnoses of major depression, dysthymia and atypical depression; 0.93 when compared with CIDI major depression; 0.93 when compared with SHORT-CARE pervasive depression; a range of 0.85-0.98 when compared with CES-D ≥16; and a range of 0.79-0.95 when compared with GMS-AGENCAT depression [DN3+ or DP3+]).

  The optimal cut-off point on the EURO-D scale for prediction of GMS depression and SHORT-CARE pervasive depression was generally 3/4 with a sensitivity range of 70-83%, a specificity range of 49-95% and a PPV of 32-76%. For the CES-D centers, a score of 2.5 or above seemed better which was associated with a sensitivity of 94%, a specificity of 90% and a PPV of 64% in the LASA study.

  It was also assessed whether a common factor structure existed across all the centers by carrying out a principal-components analysis of the EURO-D scale items for each centre.

The uses for the EURO-D in the EURODEP collaboration are: 1) comparison of EURO-D item prevalence between centers; 2) comparison of EURO-D scale distribution between centers; and 3) comparison of effect sizes for associations between risk factors and EURO-D score between centers.

- *Hamilton Rating Scale for Depression (HAM-D or HRSD)* (19,20)

The HRSD, developed by Max Hamilton in 1960, is a clinician-rated protocol used in adults diagnosed with a depressive disorder in order to assess the severity of the depressive symptoms and to measure changes over time; it is one of the most widely used instruments to quantify data gathered from clinical interviews.

It consists of a 21-item scale completed through a clinical interview; each item presents a symptom of depression and is rated according to its severity as experienced by the patient during the past few days or week.

The HRSD is scored by summing the ratings for each item and the total score range from 0 to 50; higher scores indicate greater severity of depressive symptoms.

Interpretation: scores between 0 and 6 indicate that there is no depression, scores between 7 and 17 indicate mild depression, scores between 18 and 24 indicate moderate depression, and scores over 24 indicate severe depression;
Since its origin, different variations of this scale have been produced; one of those is the 17-item version which has become the most used scale for controlled clinical trials in depression.
There are different approaches to scoring depending on the version used so, when reporting results in studies using the HRSD, it is important to explain which version of the scale and which method to scoring are used.

* *Reliability* --> Most inter-rater reliability coefficients for HRSD total scores have been ≥ 0.84 (for the original 21-item scale) and test-retest reliability using the Structured Interview Guide has been reported to be 0.81.
* *Validity* --> Its validity has been established by comparing HRSD scores to scores of other scales; for example, comparisons with the BDI yielded correlations ranging from 0.21 to 0.82 (with a median of 0.58).

- *Beck Depression Inventory - second edition (BDI-II)* (19,20)

The BDI is the gold standard of self-rating scales; it was designed to measure the severity of depressive symptoms experienced at the time when the test was taken and it was initially developed to assess the efficacy of psychoanalytical psychotherapy in depressed subjects. The original one, developed by A.T. Beck, Ward, Mendelson, Mock, and Erbaugh (1961); later on, it was modified to BDI-IA in 1979 and, after the publication of the DSM-IV, to BDI-second edition (BDI-II) in which the time frame for ratings was extended from 1 to 2 weeks.
The BDI-II, is used in adults and adolescents aged 13 years and older. This instrument has 21 items and each one represents a symptom characteristic of depression; 19 of the items include a 4-point scale representing ascending levels of severity and the remaining 2 (changes in sleeping patterns, changes in appetite) allow the respondent to indicate increases or decreases in them.
The scoring is done by summing the ratings for the 21 in a way that higher scores indicate higher levels of depressive symptoms (the maximum score is 63). The scores can be interpreted as minimal depression (0-13), mild depression (14-19), moderate depression (20-28), and severe depression (29-63). However, to give the definitive diagnosis other sources of information should be used.

* *Reliability* --> Coefficient α estimates (internal consistency) were found to be 0.92 and 0.93 and test-retest reliability was estimated to be 0.93.
* *Validity* --> BDI-II was found to correlate 0.93 with the version BDI-IA which shows its construct validity and 0.71 with HRSD.

- *Montgomery-Asberg Depression Rating Scale (MADRS)* (19,20)

The MADRS, developed by S. A. Montogmery and M. Asberg in 1979, is a clinician-rated scale used to assess depression symptoms in adults receiving antidepressant medication in order to detect changes following the treatment. It consist of 10 items representing depressive symptoms that are sensitive to change; these items are rated on a 7-point scale with descriptions of the symptoms (this scale is more focused toward psychological aspects of depression rather than to somatic aspects).

The MADRS may be used in examining score changes both in individual items scores or in summed scores and its interpretation should be that a score greater than 30 or 35 indicates severe depression and if it is 10 or below indicates remission.

* *Reliability* --> The MADRS inter-rater reliability ranged from 0.89 to 0.97 (one goal of this scale was to obtain an instrument that could be used by psychiatrists as well as other professionals with minimal psychiatric training); its internal consistency is considered very high due to its 0.95 correlation between all items.
* *Validity* --> Correlation of MADRS with other scales has been high: between 0.80 and 0.90 with HAM-D and 0.81 with IDS-C.

- *Center for Epidemiological Studies Depression Scale (CES-D)* (20)

The CES-D, developed by L. S. Radloff in 1977, is a self-report scale created to be used in epidemiological studies of depression in the general population in order to measure the level of depression symptoms at the moment of the interview (although it has a high research applicability its clinical utility is limited). This scale is neither useful to assess the symptoms severity, nor to diagnose depression.

This scale consist of 20 items and each of them provides a statement representing a common symptoms of depression, followed by a 4-point response scale ranging from "rarely or none of the time" (less than 1 day) to "most all of the time" (5-7 days).

This instrument is scored by summing the ratings of all the items. Scores range from 0 to 60 and higher scores indicate higher frequency of depressive symptoms experienced during the past week. It has been designated a cutoff score of 16 to differentiate depressed from non-depressed patients.

* *Reliability* --> Coefficient alpha estimates (internal consistency) were found to be 0.85 for general population and 0.90 for the a patient sample. Test-retest correlations were studied in two groups; in the first one, the correlations ranged from 0.51 to 0.67 and in the second one, the correlations ranged between 0.32 and 0.54.
* *Validity* --> Correlation with the HRSD was 0.44 and it increased to 0.69 after 4 weeks of treatment.

- *Inventory of Depressive Symptomatology (IDS)* (19–21)

The IDS, developed by John Rush and colleagues (1986), is used in adult inpatients and outpatients with Major Depressive Disorder (MDD) in order to measure the severity of depressive symptoms, discriminate between depressed and euthymic states as a screening instrument, and monitor treatment.

This inventory is available in self-report (IDS-SR) and clinician-rated (IDS-C) forms; it contain 30 items which measure ascending levels of frequency, duration, and severity of symptoms along a 4-point response scale (the period of time assessed in each item are the past 7 days).

Both scales, IDS-C and IDS-SR, are scored in the same manner; the maximum score possible is 90 and higher scores indicate higher severity of symptoms.

The cutoff scores used to describe symptom severity for the IDS-C are: normal (≤13), mild (14-22), moderate (23-30), moderate to severe (31-38) and severe (≥39); for the IDS-SR, the cutoff scores are normal (≤15), mild (16-24), moderate (25-32), moderate to severe (33-40) and severe (≥41).

There is a clinical-administered version named Quick Inventory of Depressive Symptomatology (QIDS) with its own self-report version (QIDS-SR); both scales have 16 items from the IDS-30 which assess the nine symptom domains included in the DSM-IV criteria for MDD. The maximum score possible is 27. A score of 5 or lower would be classified as remission; scores between 6 and 10 would indicate mild depressive symptoms; scores between 11 and 15, moderate depression; scores between 16 and 20, severe depression; and scores of ≥21, very severe depression.

* *Reliability* --> Cronbach's α was used to measure internal consistency of 30-item versions of the IDS. Estimates were 0.94 in general population; among patients with current MDD the estimates were 0.67 for IDS-C and 0.77 for IDS-SR. Inter-rater reliability for IDS-C was found to be 0.96.
* *Validity* --> Concurrent validity was estimated 0.62 (IDS-C) and 0.54 (IDS-SR) with clinical severity as described by the DSM-III-R fifth digit. The discriminant validity of the IDS-C and IDS-SR was demonstrated by their ability to significantly differentiate groups of depressed and euthymic individuals; specificity was found to be 0.95 (IDS-C) and 0.94 (IDS-SR) and sensitivity was found to be 0.997 for both.

- *Brief Patient Health Questionnaire (PHQ-9)* (21)

The PHQ-9 is a self-report scale developed in 1999 from the Primary Care Evaluation of Mental Disorders (PRIME-MD) and based on the DSM-IV criteria for MDD; it was used to detect depression in primary care and non-psychiatric settings and also to monitor the treatment.

It consist in 9 items that evaluate the presence of depression symptoms and one additional question that assess functional impairment by measuring the impact of the symptoms in patients' relationships, work, and home life; the 9 items are rated

from 0 to 3 based on frequency over the last 2 weeks. Interpretation: mild depressive symptoms (score of 5-9), moderate (score of 10-14), moderately severe (score of 15-19), and severe depression (score of ≥20); moreover, it is said that patients with total scores ≥ 15 should be treated with antidepressants.

There is another possible scoring system used for diagnostic purpose which takes into account the number of symptoms present and its duration; depending on the results it suggests major depression, minor depression or other depression.

- *Reliability* --> The internal reliability of the PHQ-9 had a Cronbach's α of 0.89 in the PHQ Primary Care Study and 0.86 in the PHQ Ob-Gyn Study; and test-retest reliability was also good (correlation between the PHQ-9 completed by the patient in the clinic and the one administered telephonically by mental health professionals within 48 hours was 0.84) (22).
- *Validity* --> ROC analysis showed that the PHQ-9 discriminates well between persons with and without major depression (the area under the curve in diagnosing major depression was 0.95). A strong association was found between increasing PHQ-9 depression severity scores and worsening function on the 20-tiem Short Form Health Survey (SF-20) scales used. The correlation between PHQ-9 severity levels and other measures of construct validity were: 0.39 with disability days, 0.24 with physician visits, and 0.55 with symptom-related difficulty (22).

* *3.1.6. Treatment*

The stepped-care model is used for the treatment of various disorders; the two main features are: 1) the treatment done should be the least intensive among all the possibilities but one that provides significant health gain; 2) the results of the treatment have to be monitored and if the patient does not improve clinically a treatment one step more intensive should be done ("stepping-up") (9).

The stepped-care model of depression according to NICE clinical guideline is as explained below (23):

Focus of the intervention	Nature of the intervention
STEP 1: All known and suspected presentations of depression.	Assessment, support, psychoeducation, active monitoring and referral for further assessment and interventions.
STEP 2: Persistent subthreshold depressive symptoms; mild to moderate depression.	Low-intensity psychosocial interventions, psychological interventions, medication and referral for further assessment and interventions.
STEP 3: Persistent subthreshold depressive symptoms or mild to moderate depression with	Medication, high-intensity psychological interventions, combined treatments, collaborative care (only for depression where

inadequate response to initial interventions; moderate and severe depression.	the person also has a chronic physical health problem and associated functional impairment) and referral for further assessment and interventions.
STEP 4: Severe and complex depression (depression that shows an inadequate response to multiple treatments, is complicated by psychotic symptoms, and/or is associated with significant psychiatric comorbidity or psychosocial factors); risk to life; severe self-neglect.	Medication, high-intensity psychological interventions, electroconvulsive therapy (ECT), crisis service, combined treatments, multiprofessional and inpatient care.

STEP 1 (Recognition, assessment and initial management)

It is important to advise the persons with depression and their familiars or carer to be vigilant for mood changes, negativity and hopelessness and suicidal ideation, especially when starting or changing treatment and at times when the individual is more stressed. In order to develop an appropriate management plan, risk of suicide should be assessed for all the individuals suspected or diagnosed of having depression as well as other physical illness, medications, possible psychosocial precipitants of the current episode and predisposing and perpetuating factors (9).

STEP 2 (Persistent subthreshold depressive symptoms or mild to moderate depression)

If depression is accompanied by symptoms of anxiety the first problem to be treated should be depression unless the person has a diagnosis of anxiety disorder. Another possible presentation of depression is sleep disturbances; in this case, advice on sleep hygiene should be offered.

For individuals who may recover with no formal intervention, those with mild depression who do not want an intervention or those with subthreshold depressive symptoms who request an intervention, it has to be arranged a further assessment within 2 weeks as well as discuss any concerns that the person may have and provide information about depression.

For people with persistent subthreshold depressive symptoms or mild to moderate depression, self-programmes based on the principles of cognitive behavioural therapy (CBT) or a structured group physical activity programme should be offered; if these low-intensity psychosocial interventions are declined, consider group-based CBT.

Usually, CBT for depression is short-term and it pretends to change the negative thoughts of the patient; apart from the current episode, this therapy is important to prevent relapses (9).

The antidepressants are not used because the risk-benefit ratio is poor in this patients but should be considered for people with a past history of moderate or severe depression, initial presentation of subthreshold depressive symptoms that have been present for at least 2 years, or subthreshold depressive symptoms or mild depression that persist after other interventions.

STEP 3 (Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions, and moderate and severe depression)

The interventions to be provided in this Step are: antidepressants, high-intensity psychological interventions [normally CBT, interpersonal therapy (IPT) which addresses current interpersonal problems associated with the onset of the disorder (9), behavioural activation or behavioural couples therapy if necessary]. If the patient declines these interventions, consider counseling or short-term psychodynamic psychotherapy. For people with moderate or severe depression a combination of antidepressant medication and CBT or IPT is provided.

The first antidepressant choice should be a selective serotonin reuptake inhibitor (SSRI) and when prescribed it has to be taken into account their association with an increased risk of bleeding. As an example of medicaments that can be used for depression, a part of SSRI, the table below shows antidepressants approved by the US Food and Drug Administration (FDA) and its proposed mechanism of action (14):

	Drugs	Proposed mechanism of action
Selective serotonin reuptake inghibitors	*Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline*	Selectively inhibits the reuptake of serotonin
Tricyclic antidepressants	*Amitriptyline, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine*	Nonselectively inhibits the reuptake of monoamines, including serotonin, dopamine, and norepinephrine
Norepinephrine-dopamine reuptake inhibitor	*Bupropion*	Inhibits the reuptake of norepinephrine and dopamine
Serotonin modulator	*Nefazodone, trazodone*	Primarily antagonises 5-HT2 receptors
Serotonin-norepinephrine reuptake inhibitors	*Desvenlafaxine, duloxetine, venlafaxine*	Inhibits the reuptake of serotonin and norepinephrine
Noradrenergic and specific serotonergic modulatro	*Mirtazapine*	Primarily antagonises α-2 and 5-HT2C receptors
Serotonin reuptake inhibitor and 5-HT1A-receptor partial agonist	*Vilazodone*	Potently and selectively inhibits serotonin reuptake and acts as a partial agonist at the 5-HT1A receptor
MAO inhibitors	*Isocarboxazid, phenylzine, tranylcypromine*	Nonselectively inhibits enzimes (MAO-A and MAO-B) involved in the breakdown of monoamines, including serotonin, dopamine, and norepinephrine
	Selegiline	MAO-B selective inhibitor

The medication should be continued for at least 4-6 weeks before analyzing its efficacy (9) and if the symptoms have not responded to initial treatment is important to check if the treatment has been inadequately delivered or adhered to and then, if it is the case, consider reintroducing it correctly. Increasing the dose, combining medications or switching to alternative antidepressant are other possibilities (23).
When changing from one antidepressant medication to another there are three ways of doing it: 1) with a direct switch from one drug to another (normally if the change is between SSRIs); 2) by cross tapering (the dose of the current antidepressant is reduced slowly while the new antidepressant dose is introduced slowly); 3) to phase out the first antidepressant completely before introducing the new drug (important when changing to a MAOI or vice versa). There is a possibility of discontinuation reaction symptoms if the treatment with an antidepressant needs to be stopped, therefore the dose has to be reduced gradually (9).

The treatment with antidepressants should be continued for at least 6 month after achieving remission to reduce the risk of relapse; then the need for continued treatment should be considered for people who have a history of two or more depressive episodes, those with higher risk for relapse (presence of residual symptoms, multiple previous episodes, or a history of severe or prolonged episodes or of inadequate response) or if the consequences of relapse are likely to be severe (9,23).

STEP 4 (Complex and severe depression)
Persons with complex and severe depression should be referred to specialist mental health services and medication should be prescribed by a psychiatrist. If there is a significant risk of suicide, self-harm or self-neglect, the inpatient treatment has to be considered. The treatment for this type of depression includes medication as well as high-intensity psychological interventions.

There are different options for treatment-resistant depression (a failure to respond to two different antidepressants for a sufficient period of time and at an adequate dose): augmentation with lithium, using venlafaxine, augmenting antidepressant treatment with another antidepressant but with an increment of the risk to develop side effects, or using phenelzine
A personwho presents a depression with psychotic symptoms has to be treated with an antipsychotic in addition to increasing the antidepressant therapy; however, there is a higher possibility of developing side effects due to interactions between the two. (9)

Electroconvulsive therapy (ECT) is used as an acute treatment of severe depression that is life-threatening and a rapid response is required, or when other treatments have failed, particularly when psychotic or severe endogenous features are present. Before

using this treatment, its risk associated with anesthesia and the possible cognitive impairment should be considered (9,23).

* *3.1.7. Consequences and Comorbidity*

The consequences of depression are variable depending on the symptoms and its severity; some of them are (5): increased risk of failure to complete secondary school, especially in high-income countries; increased risk of divorce if there is a pre-marital history of mental disorders, major depressive disorder being the most important; job loss; marital dissatisfaction and marital violence (nevertheless, the association between history of major depressive disorder before the marriage and marital violence disappears after controlling disruptive behavioral disorders and substance use disorders so depression would be a risk marker rather than a causal risk factor); negative parenting behaviors; a higher number of days out of role and disability at the individual level along with musculoskeletal disorders; lower personal earnings and household income although it is unclear whether depression is a cause, consequence or both; and high decrement in perceived health. It has also been found that depression has a higher mortality which has been related with the association between depression and other physical disorders and a higher suicide risk.

Regarding comorbidities, major depressive disorder is associated with different chronic physical disorders like arthritis, asthma, cancer, diabetes, hypertension, chronic respiratory disorders, various chronic pain conditions and cardiovascular disease. Moreover, it frequently co-occurs with other mental disorders such as substance related disorders, panic disorder, obsessive-compulsive disorder, anorexia nervosa, bulimia nervosa, and borderline personality disorder (3).

3.2. Socioeconomic position (SEP)

* *3.2.1. Concept*

Socioeconomic position (SEP) refers to the social and economic factors that influence what positions individuals or groups hold within the structure of a society and it is a commonly used concept in health research. Other terms associated to it, and often used interchangeably despite their different theoretical bases and interpretations, are "social class", "social stratification" or "socioeconomic status (SES)" (24).

The term Socioeconomic position encompasses both social class (social relations of ownership and control over productive assets) and SES (ordering of persons according to some valued socioeconomic attribute such as income, education or occupation) (25).

* *3.2.2. Indicators*

When choosing an indicator of socioeconomic position it is important to use the one that fits better to the objective of the study. If the main purpose of the study is descriptive, almost any measure of SEP can be used because each one is able to capture and describe health inequalities if these exist; but if the main purpose is to explain the causal mechanisms through which SEP generates health differences, for example, the indicator of socioeconomic should be chosen thoroughly. Another possible purpose of measuring SEP is to statistically adjust for socioeconomic circumstances when another exposure is the main focus of interest (in order to control SEP as a confounder); in this case will be useful to capture several aspects of SEP and therefore composite indicators are usually used (26).

INDIVIDUAL-LEVEL INDICATORS

- *Education*

  This indicator captures the knowledge-related assets of an individual and measures the transition from childhood SEP, in which the parents have an important role, to adulthood SEP. Education is related with other indicators; for example, it affects the individual's future employment and income (26). It can be measured as a continuous variable (years of completed education), or as a categorical variable (measuring the levels achieved) (24).

  * *Strengths* --> It is relatively easy to measure in self-administered questionnaire; has a high response rate; it can be obtained from everybody independently of age or working circumstances (24).
  * *Limitations* --> The meaning of educational level varies for different birth cohorts (the result from studies that use education as an indicator and include participants from a number from different birth cohorts may be biased). A limitation of educational levels exist if individuals have obtained their education outside the country of residence; another limitation, also present when measuring years of education, is that they may not contain information about the quality of the educational experience (24).

- *Income*

Income is the indicator that most directly measures the material resources; it has a cumulative effect over the life course and is the SEP indicator that can change most on a short-term basis. There are different ways of measuring it: a) As a relative indicator establishing *levels of poverty*; b) *Individual income*; and c) *Household income* (when calculating it, additional information on family size or the number of people dependent on the reported income should be elicited in order to be able to compare income of different households) (24).

* *Strengths* --> It is the best single indicator of material living standards.
* *Limitations* --> People may be reluctant to provide information necessary to measure income (it has greater non-response rates, therefore more sophisticated methods have been developed in order to obtain the data necessary). Gross income is frequently measured although it would be better collecting information on disposable income and prices in order to calculate what a disposable income is really worth. Income may be a less reliable indicator to measure the true SEP for young people and older adults (24,26).

- *Wealth*

Wealth also gives information of material resources and it is a continuous measure that combines total assets and income (income as well as financial and physical assets such as the value of housing, cars, investments, inheritance or pension, are taken into count) (27).

* *Strengths* --> Income in combination with total assets is a better measure of someone's socioeconomic circumstances than income alone (income captures the resources that are available at particular periods of time, whereas wealth measures the accumulation of these resources); the importance of wealth compared with income may change over the life course (for example, wealth is more important in older age) or in population subgroups (26,27).
* *Limitations* --> Similar to those explained for income.

- *Occupation-based indicators* (24)

Occupation can reflect a person's place in society related to their social standing, income and intellect and it can characterise working relations between employers and employees.

There are many ways to measure occupation, and each one of them measure particular aspects of SEP; the most frequently used is current or longest held occupation of a person, for adults. Parental occupation can be used as an indicator of childhood SEP.

* *Strengths* --> It has a high availability. In health studies, this indicator can also be used to capture the exposure to certain toxic or physical working conditions.

* *Limitations* --> Some groups such as retired people, people whose work is inside the home, the unemployed, students, and people working in unpaid, informal or illegal jobs, are commonly excluded; furthermore, there are other groups more difficult to classify or less willing to give the information. Occupation may have different meaning for different birth cohorts and in different geographical settings.

- *Other indicators*

There are other indicators, but they are not used so often:

* Indicators used to classify those people excluded of the occupation indicator (*unemployment*, *job insecurity* or *type of employment*)(27).
* Housing characteristics such as *housing tenure*, *housing conditions* (for example overcrowding) and *household amenities*. This type of indicators are easy to collect and may also provide information about specific mechanisms linking SEP to particular health outcomes; their main limitation is that they may be specific to the temporal and geographical context where they were developed and difficult to compare across studies (24).
* Different composite indicators, usually measured as a score that adds up the presence or absence of several SEP indicators, have been developed (*Hollingshead index of social position, Duncan index, Warner's index of status characteristics*, etc.) and some measure individual SEP and other area-level SEP. Although these indicators can be used when SEP is measured as a confounding factor, they should not be used when the objective of the study is determining specific mechanisms of the relationship between socioeconomic inequalities and other variables such as a particular health outcome (26,27).
* When direct measures of SEP are not available, proxy indicators can be used. These indicators are not strictly indicators of SEP but they can be correlated with it and in some cases they may provide information about the mechanism that explains the association of SEP and other variables. Examples are: *number of siblings*, *infant mortality*, *maternal mortality*, *death of father or mother*, etc (26,27).

AREA-LEVEL INDICATORS

Area-level indicators are used when measuring the SEP of a geographical area and they are obtained by aggregating individual-level or small area data from census or other administrative databases. These indicators can be used to characterize areas on a continuum from deprived to affluent (***deprivation indices***) or as a proxy for individual-level SEP indicators when these are not available.

One of the deprivation indices most frequently used is *The Townsend deprivation index* which uses four variables: unemployment, the proportion of household with no car, the proportion of households that are not owner occupied, and the proportion of

households with overcrowding (>1 person per room); its score is a summation of the scores for each variable and a greater score indicates higher levels of material deprivation.

Area-level measures of SEP are specifically needed when the goal is to investigate if socioeconomic aspects of the place where a person lives affect that person's health (26,27).

* *Strengths* --> Using this type of indicators makes easier the statistical analysis and the presentation of results .
* *Limitations* --> They are difficult to construct and validate; furthermore, these area-level indices tend to mask variation and have limited external validity or utility across time and space and may measure certain aspects of neighbourhoods better than others (28).

* *3.2.3. Socioeconomic position and health*

It is known that socioeconomic conditions influence health outcomes; although most of the studies associate low socioeconomic circumstances to poor health, the truth is that there is some heterogeneity: in some cases health outcomes are equally distributed across all socioeconomic groups and in other cases, greater risk of certain diseases is experienced by the more affluent groups (26). Moreover, there is evidence that the association of socioeconomic circumstances and health occurs at every level of the SES hierarchy, not simply below the threshold of poverty (it is said that a SES-health gradient exists) (29).

Socioeconomic conditions are related to mortality, morbidity and health behaviours:

- All the studies have found an increased risk of mortality in poorer or more deprived neighbourhoods (28).
- Socioeconomic conditions of the neighbourhood has been associated with psychiatric disorders (30), birth weight, self-rated health, long term disability or illness, cardiovascular diseases, respiratory diseases, and alterations of the body mass index (28).
- Socioeconomic position has also been associated with certain health behaviors such as smoking, consuming alcohol, dietary intake, physical activity, and domestic violence (28); health behaviors have not only been studied as consequences of certain socioeconomic conditions but also as a possible mechanism for SEP and health outcomes (29).

Several theories about the mechanisms involved in the relationship between SES and health have been developed (29):

- The association between SES and health has been related to a mutual relationship with certain genetically based factors. However, genetic predispositions are likely to become important only when environmental and behavioral factors impinge on them.
- The *drift hypothesis* suggests that the association reflects the influence of illness on socioeconomic conditions, rather than of socioeconomic conditions on illness.

Nonetheless, if illness was the main factor influencing SES, then no association would be expected for family members when SES is determined by income or occupation of the head of the household, or for retired individuals for whom income is no longer dependent on health.

- Availability to healthcare services also explain in part, but not completely, the association between SES and health outcomes.
- Another explanation is that socioeconomic position affects biological functions which, in turn, influence health status; different variables have been used to study the mechanisms of SES-health gradient:
    * Health behaviours

      Smoking rates are directly related with morbidity and mortality, particularly form cardiovascular disease and cancer, and inversely related with socioeconomic position. Low SES is also associated with both obesity and lack of physical activity which are related with poor health outcomes. On the other hand, alcohol consumption shows the opposite pattern to smoking and other risk behaviors (different studies have found a positive correlation of alcohol consumption with socioeconomic position) but the relationship between alcohol consumption and health outcomes is not uniform cross diseases.

      Although health behaviours are related to both socioeconomic position and health outcomes they are not the only cause of the association between socioeconomic conditions and health outcomes (when these behaviors are statistically controlled, the association is reduced but not eliminated).
    * Psychological characteristics

      Low SEP has been related to hostility as well as depression and depressive symptoms and these, in turn, are linked to health outcomes such as coronary heart disease.
    * Psychological stress

      Associations between SES and health may be caused, in part, from differential exposure to and experience of greater stress (stress can be caused by life events that require adaptation such as divorce or job loss, and it can occur when persons perceive that demands exceed their abilities to cope) which has been related with higher risk of heart attacks, gastrointestinal disorders or susceptibility to infectious agents, among others.

      It has been found that higher placement in the SES hierarchy can reduce stress and its somatic correlates. This can be explained because high SES diminishes the likelihood that individuals encounter negative events and because the persons with higher SEP have more social and psychological resources to cope with stressful life events than those with lower SEP.
    * Effects of social ordering

      One's relative position in the SES hierarchy, apart from the material implications of one's position, may affect risk of disease; for example, among developed

countries, individual-income is not as strongly related to life expectancy as income distribution (people with the same characteristics who live in countries where income is equally distributed to the majority of the population has a longer life expectancy than those who live in countries where income is not equally distributed).

3.3. Depression and Socioeconomic deprivation

Low socioeconomic status (SES) is associated with psychiatric morbidity; this association is related to a higher prevalence of psychiatric risk factors, such as poorer coping styles, ongoing life events, stress exposure and weaker social support, in lower SES groups (30).

The country-level relationship between socioeconomic inequalities and adverse mental health outcomes has been studied using measures such income inequality, which measures the distribution of incomes across a society, or socioeconomic deprivation, which is used to compare socioeconomic disadvantages between different areas. If the association between socioeconomic inequalities and mental health is studied at a subnational/regional level, using socioeconomic deprivation, rather than income inequality, is better because in these studies within-area inequalities are less important than the comparison to wider society (the degree of within-area inequality becomes smaller and the differences between different areas become larger) (31).

Depression is one of the psychiatric disorders related to SES: low SES has been associated to a higher prevalence of depression and also to a higher risk of episode onset and persistence of depression, particularly the later one; however, the association between SES and depression persist throughout the entire social stratum (the socioeconomic gradient of depression). Furthermore, it has also been found that not only low SES increases risk of depression but depression, in its turn, also affects the position in the SES hierarchy (30).

There are two theories that explain the link between SES and depression. One is *the stress theory*, which suggest that personal resources, such as coping style or self-esteem, buffer the impact of stress on depression; this explains why people in higher SES position, who have more of these resources, have a lower prevalence of depression. The other is *the strain theory*, which gives importance to community features such as values, social welfare, social cohesion, infrastructure, and public health policy; this theory would explain the differences between countries in socioeconomic health inequalities (30).

When studying the relationship between depression and socioeconomic deprivation some confounding factors should be kept in mind. One of those is gender (women have a higher prevalence of depression and lower SES than men) and another one is age (age has a U-shaped relation with depression and a reverse U-shaped association with

income); although not always considered in psychiatric epidemiology, physical disease could be another confounding factor (physical diseases such as cancer and cardiovascular disorders have been related to both psychiatric disorders and SES) (30).

4. STUDY JUSTIFICATION

Depression is one of the most prevalent and disabling diseases worldwide. In order to prevent its development, it is important to know the different associated risk factors and one of those is socioeconomic deprivation.

The major part of the studies only assess the relationship between socioeconomic deprivation (using variables such as income, occupation or education) but few compare the degree of this association among different countries. The aim of the present study is to know if there are differences in the degree of the association between clinically significant depressive symptomatology and the socioeconomic deprivation among different countries. To do the research data has been obtained from the 5th wave of the SHARE (Survey of Health, Ageing and Retirement in Europe) achieving a big sample of 48,319 adults which gives statistical power to the study.

Moreover the instrument used to measure the presence of socioeconomic deprivation is a multidimensional socioeconomic of socioeconomic deprivation that takes into account other factors that cannot be assessed using variables such income, occupation or education alone.

5. RESEARCH QUESTION

Is the association between socioeconomic deprivation and depressive symptomatology the same for all the European countries in persons aged 50 and over?

6. HYPOTHESIS

6.1. Principal hypothesis

- *The degree of association between socioeconomic deprivation and clinically significant depressive symptomatology will be higher in European countries with a lower prevalence of social deprivation.*

  One of the hypothesis developed to explain the mechanism linking income inequality (variable that, like socioeconomic deprivation, is used to measure socioeconomic inequalities) to mental health outcomes is "the status anxiety hypothesis" which exposes that the perception of lower social status leads to poorer health (31). It is though that in places where the difference between the people in a higher socioeconomic position and the people in a lower socioeconomic position is bigger, the individuals with socioeconomic deprivation tend to make comparisons of themselves to those without socioeconomic deprivation and it results in higher prevalence rates of depression (12).

6.2. Secondary hypotheses

- *The prevalence of clinically significant depressive symptomatology will be higher in women and individuals with advanced age.*

The association between women and higher prevalence rates for depression has been reported by the majority of studies of depression and its epidemiology (5,7,10,12), therefore, it is likely that this study will obtain the same results.

Different studies have found that although the prevalence of depression initially increases with age, when this relationship is explored controlling for other variables such as chronic diseases, limitations in activities of daily living, or education and economic constraints, the association vanishes (10,32). According to these findings it would be expected to find higher prevalence rates of depression as age increases in simple analysis but not when controlling for other variables that are risks factors for depression and more prevalent in the elderly.

- *Individuals with clinically significant depressive symptomatology will have poorer socio-demographic and health characteristics.*

  Different factors such as being divorced/separated or widowed, unemployment, history of previous depressive episodes, chronic physical disorders, other psychiatric disorders, low-income, or being of a lower socioeconomic position have been associated with higher rates of depressive symptomatology/depression (5,9,12). Similar results are expected to be found in the present study.

- *Individuals with socioeconomic deprivation will have poorer socio-demographic and health characteristics.*

  Persons with socioeconomic deprivation are the ones at the bottom of socioeconomic position and its association with poorer socio-demographic characteristics such as divorce or job loss, and health characteristics such as higher rates of mortality and morbidity, health risk behaviors, have been reported (29). Moreover levels of education and occupation are two of the variables most frequently used to measure socioeconomic position (24,26) so it is likely that individuals with socioeconomic deprivation will have higher rates of lower levels of these two variables.

7. OBJECTIVES

7.1. Main objective

To assess the relationship between socioeconomic deprivation and the prevalence of clinically significant depressive symptomatology among different European countries in adults aged 50 and over.

7.2. Secondary objectives

- To determine the global prevalence of clinically significant depressive symptomatology by sex and different ages groups in European countries.

- To compare socio-demographic and health characteristics between individuals with and without clinically significant depressive symptomatology.

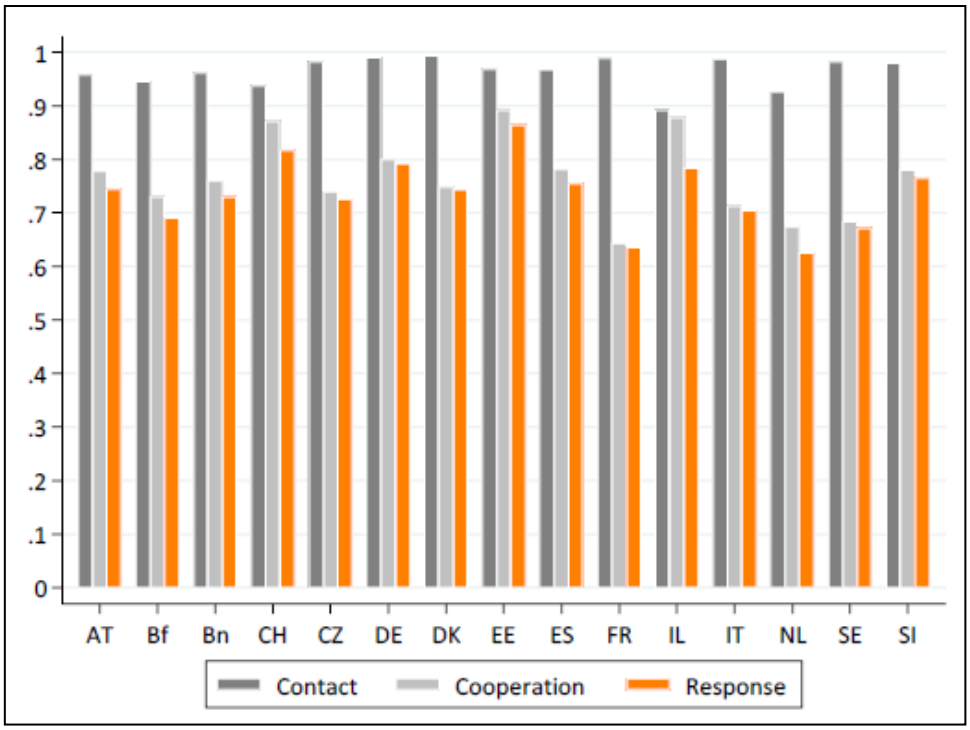
- To compare socio-demographic and health characteristics between individuals with and without socioeconomic deprivation.

8. METHODOLOGY

8.1. Study design

This study is observational and transversal and the data used, collected in 2013, is obtained from the 5th wave of the Survey of Health, Ageing and Retirement in Europe (SHARE, release 1.0.0 from March 31st 2015) which is a European cross-national and longitudinal research project collecting data among people aged 50 years and older (33,34). The overall participation rate was higher than 60%. The figure 1 shows the contact, cooperation and response rate of wave 5 stratified by country.

Figure 1.Contact, cooperation and response rate (SHARE wave 5) (%)



8.2. Study population

The target population are persons aged 50 years and over at the time of sampling who have their regular domicile in one of the 15 participant countries of the SHARE; the data is obtained from these countries: 14 European (Austria, Belgium, Czech Republic, Denmark, Estonia, France, Germany, Italy, Netherlands, Slovenia, Spain, Sweden, Switzerland, Luxemburg) and 1 non-European (Israel).

- *Inclusion criteria*
  - Persons born in 1962 or earlier (people who were 50 years or older at the moment of the survey).
  - Persons who are a spouse/partner of a person born in 1962 or earlier.
  - People who were residents in nursing homes and other institutions for elderly although this population group may not be well represented in all countries due to the lack of suitable sampling frames.
- *Exclusion criteria*
  - People who were either incarcerated, hospitalized, or out of the country during the fieldwork period.
  - Persons who are unable to speak one of the official languages of the country.
  - Person who has moved to an unknown address.

8.3. Sampling

In order to facilitate inference to the population of interest, SHARE is based upon probability samples with full population coverage. This was the key principle of the SHARE sampling design in Wave 5. The availability of a probability sample ensures that every unit in the target population has a chance greater than zero of being selected into the sample. The sampling frames for each country were based on the National or Municipal Population Registers.

8.4. Variables

* *8.4.1. Independent variable*

- *Socioeconomic deprivation*

  It has been measured with a multidimensional index of socioeconomic deprivation developed specially for the 5th wave of the SHARE. The deprivation index results from the weighted summation of the achievements with respect to the whole set of dimensions considered. Once de results of this summation were obtained they were classified into two groups (*people at risk of severe socioeconomic deprivation* and *people without risk of severe socioeconomic deprivation*) taking into account the 75th percentile as the cut-off point.

  The following questions were used to develop the socioeconomic deprivation index:

  - In the last twelve months, have you ever found yourself more than two months behind with your rent? *1. Yes, 5. No*
  - Do you regularly repay your mortgages or loans? 1. *Yes, 5. No* (asked only to home-owners who have mortgage or loans on their property)
  - In the last twelve months, have you ever found yourself more than two months behind with these repayments? *1. Yes, 5. No* (asked only to home-owners who regularly repay mortgage or loans on their property)

* Could your household afford to pay an unexpected expense of {AffordExpenseAmount} without borrowing any money? *1. Yes, 5. No*
* This area is kept very clean. (Would you say you strongly agree, agree, disagree or strongly disagree?) *1. Strongly agree, 2. Agree, 3. Disagree, 4. Strongly disagree*
* Vandalism or crime is a big problem in this area. (Would you say you strongly agree, agree, disagree or strongly disagree?) *1. Strongly agree, 2. Agree, 3. Disagree, 4. Strongly disagree*
* (In the last twelve months, to help you keep your living costs down, have you...) Put up with feeling cold to save heating costs? *1. Yes, 5. No*
* (In the last twelve months, to help you keep your living costs down, have you...) Continued wearing shoes that were worn out because you could not afford replacement? *1. Yes, 5. No*
* Please think of your financial situation over the last twelve months. In the last twelve months, to help you keep your living costs down, have you... Continued wearing clothing that was worn out because you could not afford replacement? *1. Yes, 5. No*
* Would you say that you do not eat meat, fish or chicken more often because...*1. you cannot afford to eat it more often, 2. for other reasons* (asked only to those who eat meat, fish or poultry at most twice a week)
* Would you say that you do not eat fruits or vegetables more often because... *1. you cannot afford to eat it more often, 2. for other reasons* (asked only to those who eat a serving of fruits or vegetables at most twice a week)
* How easy is it to get to the nearest pharmacy? (Would you say it is very easy, easy, difficult or very difficult?) *1. Very easy, 2. Easy, 3. Difficult, 4. Very difficult*
* (In the last twelve months, to help you keep your living costs down, have you...) Gone without or not replaced glasses you needed because you could not afford new ones? *1. Yes, 5. No*
* (In the last twelve months, to help you keep your living costs down, have you...) Postponed visits to the dentist? *1. Yes, 5. No*
* How easy is it to get to your general practitioner or the nearest health centre? (Would you say it is very easy, easy, difficult or very difficult?) *1. Very easy, 2. Easy, 3. Difficult,4. Very difficult*
* How easy is it to get to the nearest bank or cash point? (Would you say it is very easy, easy, difficult or very difficult?) *1. Very easy, 2. Easy,3. Difficult, 4.* Very difficult
* Could your household afford to go for a week long holiday away from home at least once a year? *1. Yes, 5. No*

* *8.4.2. Dependent variable*

- *Clinically significant depressive symptomatology*

The presence of clinically significant depressive symptomatology has been assessed using the EURO-D scale which was developed by a collaboration of different European research groups in order to be able to compare the data of late-depression that each research group had obtained using different instrument.

This scale is a 12-item (depression, pessimism, wishing death, guilt, sleep, interest, irritability, appetite, fatigue, concentration, enjoyment and tearfulness) and the timeframe of the symptoms refers to the month preceding the interview. The score of EURO-D ranges from 0 to 12, with higher scores indicate higher levels of depression.

In order to separate the individuals with clinically significant depressive symptomatology and those without, the score of 3 has been defined as the cut-off point; the group "*people with depressive symptomatology*" is constituted with people scoring higher than 3 in the EURO-D scale and the group "*people without depressive symptomatology*" is constituted with those who score 3 or lower.

* *8.4.3. Covariates*

- *Gender*

Gender (*man / woman*) was recorded for each participant from observation.

- *Age*

Age was obtained from the birth date and was grouped in three groups (*from 50 to 64 years old; from 65 to 74 years old*; *and 75 years old or more*) when analyzing it.

- *Country*

The country used was the one where the survey was held. Of all countries, 14 are European (*Austria*, *Germany*, *Sweden*, *Netherlands*, *Spain*, *Italy*, *France*, *Denmark*, *Switzerland*, *Belgium*, *Czech Republic*, *Luxembourg*, *Slovenia* and *Estonia*), and 1 is not European (*Israel)*.

- *Marital status*

Marital status was assessed with the question "What is your marital status?" and six possible responses were given: 1) Married and living together with spouse, 2) Registered partnership, 3) Married, living separated from spouse, 4) Never married, 5) Divorced, and 6) Widowed.

The answers were clustered in four groups (*married or registered partnership*; *separated or divorced*; *single*; and *widower*) when doing the statistical analysis.

- *Education*

Education was collected using the *International Standard Classification of Eductation-97 (ISCED-97)* codes by the UNESCO, and we further clustered the codes in three groups:

1. *Low education group*, which included participants with no education or ISCED-97 codes 1 and 2 (illiterate participants or those with primary and lower secondary education).
2. *Medium education group*, which included participants wit ISCED-97 codes 3 and 4 (secondary and post-secondary non-tertiary education.
3. *High education group*, which included participants with ISCED-97 codes 5 and 6 (first and second stages of tertiary education).

- *Employment*

Employment was clustered in four groups: *employed or self-employed*, *retired*, *unemployed*, *permanently sick or disabled*, and *homemaker*.

- *Medication for anxiety or depression*

To asses if the person *was taking anxiolytics or antidepressants* or *was not taking them*, the interviewer showed him/her a card with several drugs for different disorders and the respondent had to indicate if he/she had taken some of them; one of the possible medications the person could have t was "Drugs for anxiety or depression".

- *Body Mass Index (BMI)*

The BMI was calculated from the height and weight reported by the participants. The participants were then classified according to the WHO BMI International Classification: *normal* (18.50-24.99 Kg/m^2), *underweight* (<18.50 Kg/m^2), *overweight* (≥25.00 Kg/m^2) and *obese* (≥30.00 Kg/m^2).

- *Number of chronic diseases*

The number of self-reported chronic diseases was recorded, and further classified into two groups: *less than 2 chronic diseases,* and *2 or more chronic diseases*.

- *Presence of Affective/Emotional Disorders*

To determine if the respondent *had affective/emotional disorders* or *did not have affective/emotional disorders*, the person had to indicate if he/she had any of the disorders written on a card; one of them was "Other affective or emotional disorders, including anxiety, nervous or psychiatric problems".

- *General health status*

Self-perceived general health was assessed with the question "Would you say your health is excellent, very good, good, fair, or poor?.

8.5. Measure instrument

To collect the data, the SHARE study uses an interview with an average duration of 90 minutes, conducted at the respondent's home. Questions cover a wide range of topics, including health and health related variables, economic variables, and social support variables. Data are freely available to the research community (www.share-project.org).

8.6. Statistical analysis

A descriptive and univariate analysis of the study variables was conducted; distributional assumptions of normality were analyzed with the Shapiro-Wilk test.
Bivariate analyses were conducted to assess the prevalence of depressive symptomatology according to the characteristics of the participant, as well as to determine the prevalence of people at risk of severe socioeconomic deprivation by gender, age groups and among different countries. Chi-square was used for the categorical variables.

A general multivariate logistic regression was performed to analyze the variables involved in the association between depression and socioeconomic deprivation. All the models were controlled by gender, age, marital status, employment, education level, number of chronic diseases, country, taking anxiolytics or antidepressants, BMI, presence of affective/emotional disorder and general health status. A country specific multivariate logistic regression analysis was performed in order to determine the degree of association between socioeconomic deprivation and clinically significant depressive symptomatology for each country.

Results are expressed as absolute numbers and percentages, means, standard deviations, odd ratios, and 95% confidence intervals (CI) and some represented with bar charts and. Statistical tests were considered to be significant with a two-tailed p value <0.05. The processing and analysis of the data were performed using the statistical package SPSS v20.0 for Windows (SPSS, Inc., Chicago, IL).

8.7. Statistical power

The available sample size guarantees an appropriate statistical power for the statistical analyses required to achieve the study objectives. For example, if the sample size is of 40,000 participants, for a multivariate linear regression analysis with a maximum of fifteen predictors and a 0.05 alpha risk, the statistical power is greater than 95%.

9. ETHICAL ASPECTS

The 5th wave of SHARE was reviewed and approved by the Ethics Council of the Max-Planck-Society for the Advancement of Science which attested that the overall research project and its procedures, the measures to assure confidentiality and data privacy, and the information given to the participants agree with international ethical standards.

This study has been conducted according to the last Declaration of Helsinki (October, 2013) of the World Medical Association which postulates ethical principles for medical research involving human subjects, including research on identifiable human material and data. It also complies the local "Ley Orgánica 15/1999, de 13 de Diciembre, de Protección de Datos de Carácter Personal" which aims to protect the correct processing of personal data, public freedoms and the fundamental rights of individuals, especially their personal and family privacy.

10. RESULTS

10.1. Sample characteristics

The total of adults participating in the 5th wave of the SHARE were 61,970; of this persons, those who were ≤49 years old and those who did not provide the necessary information to measure all the variables, were excluded. The final sample with which the statistical analysis was done was of 48,319 adults.

The characteristics of the 48,319 adults are presented in Table 1 and Table 2. Among the participants, 54.7% were females and 45.3% were males. The average age at interview was 66.51 (SD=9.55), being 50 and 100 years, approximately, the minimum and maximum values, respectively.

Table 1. Social and demographic characteristics of the sample from the Survey of Health, Ageing and Retirement in Europe (n=48319).

Gender, n (%)	
Males	21910 (45.3)
Females	26409 (54.7)
Age groups, n (%)	
50-64	21959 (45.4)
65-74	15819 (32.7)
75+	10541 (21.8)
Education, n (%)	
Low level (1+2)	16648 (34.5)
Medium level (3+4)	19652 (40.7)
High level of (5+6)	12019 (24.9)
Employment, n (%)	
Employed/Self-employed	13738 (28.4)
Retired	28213 (58.4)
Unemployed	1295 (2.7)
Permanently sick/Disabled	1597 (3.3)
Homemaker	3476 (7.2)
Marital status, n (%)	
Married/Registered partnership	34339 (71.1)
Separated/Divorced	5170 (10.7)
Single	2747 (5.7)
Widower	6063 (12.5)

Table 1. Health characteristics of the sample from the Survey of Health, Ageing and Retirement in Europe (n=48319).

Medication for anxiety/depression, n (%)	
Takes anxiolytics or antidepressants	2985 (6.2)
BMI, n (%)	
Normal	17916 (37.1)
Underweight	573 (1.2)
Overweight	19724 (40.8)
Obese	10106 (20.9)
Number of chronic diseases, n (%)	
<2 chronic diseases	25578 (52.9)
≥2 chronic diseases	22741 (47.1)
Affective/Emotional disorders, n (%)	
Has or has had affective/emotional disorders	2611 (5.4)
General health status, n (%)	
Excellent	4236 (8.8)
Very good	8819 (18.3)
Good	17764 (36.8)
Fair	12886 (26.7)
Poor	4614 (9.5)

BMI, Body Mass Index

10.2. Depressive symptomatology and socioeconomic deprivation among European countries.

The global prevalence of clinically significant depressive symptomatology is 24.3% (95% CI, 23.9-24.7) and the prevalence of people at risk of severe socioeconomic deprivation is 9.8% (95% CI, 9.6-10.1).

Figure 2 and Figure 3 show the prevalence rates of depressive symptomatology and the proportion of people at risk of severe socioeconomic deprivation among countries, respectively.

Figure 1. Prevalence rates of clinically significant depressive symptomatology (EURO-D >3) in different countries (n=48319).

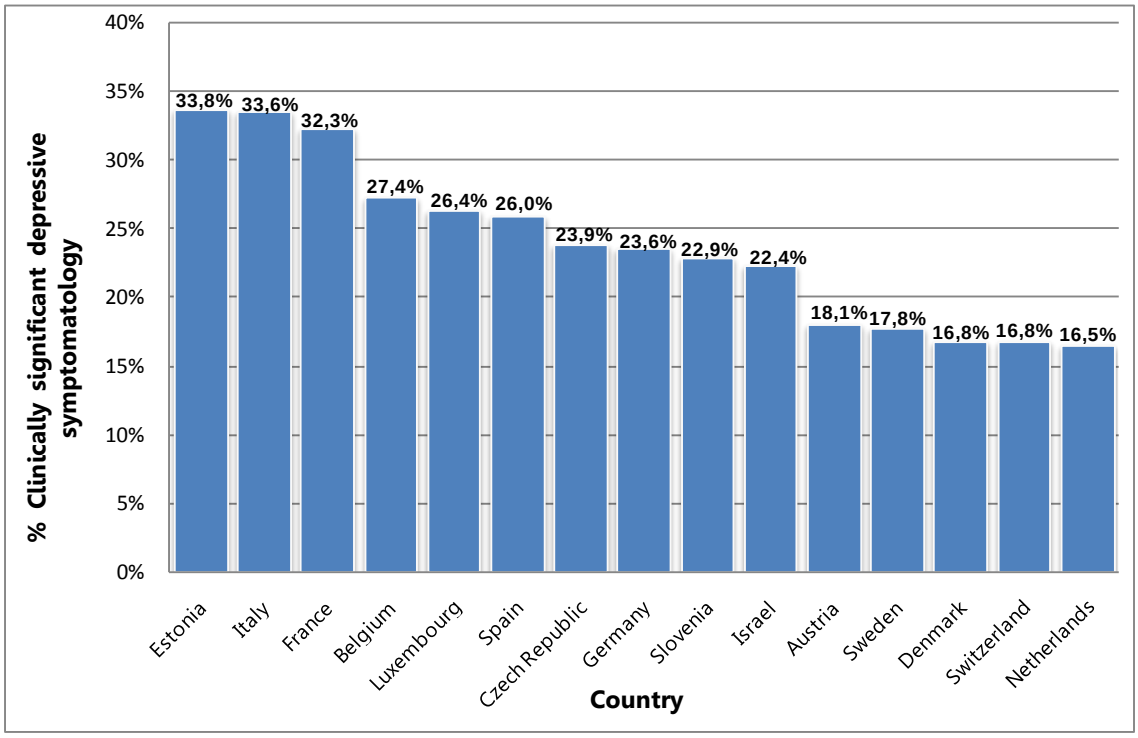


Figure 2. Proportion of people who are at risk of severe socioeconomic deprivation in different countries (n=48319).

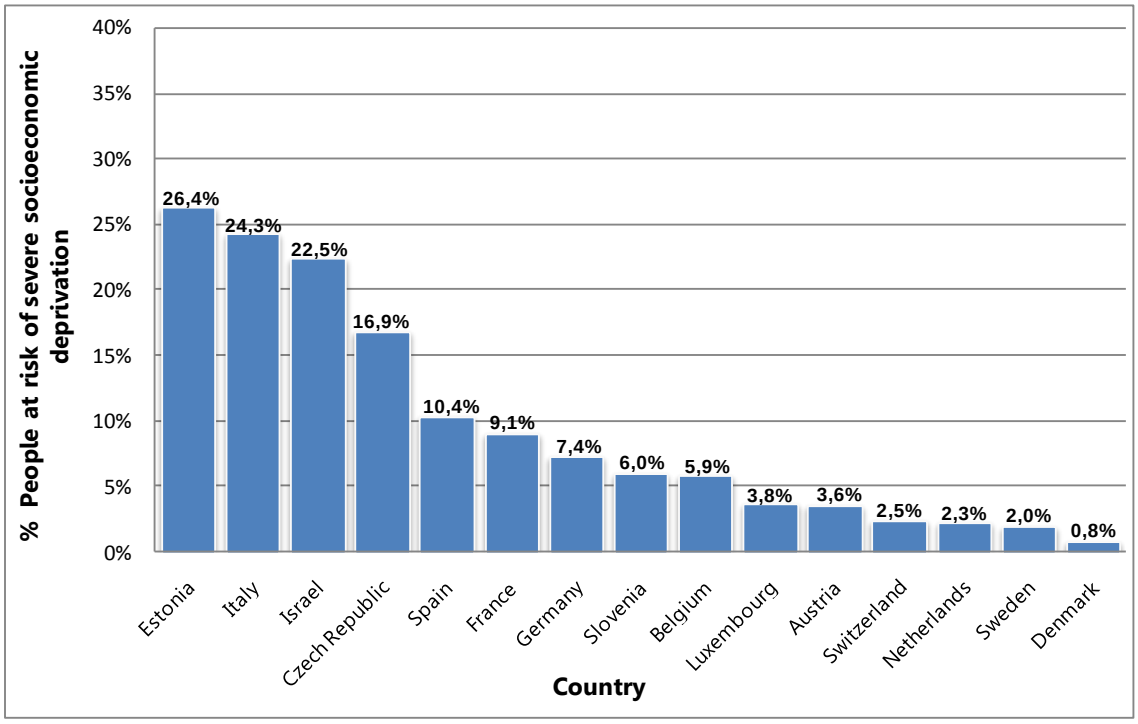


Table 3 provides results of multilevel logistic regression model in which the association between the presence of depressive symptomatology and the country where a person lives can be seen: when Spain was set as the reference, the prevalence of depressive symptomatology was statistically higher in Italy, France and Belgium; and it was statistically lower in Austria, Netherlands, Switzerland and Israel.

Table 2. Multiple logistic regression model for prevalence of clinically significant depressive symptomatology (EURO-D >3) related to different countries being Spain the reference (n=48319).

	OR	*95% CI*
Country		
Spain	1	--
Austria	**0.78**	**0.68 - 0.90**
Germany	0.96	0.83 - 1.09
Sweden	0.90	0.78 - 1.04
Netherlands	**0.76**	**0.66 - 0.88**
Italy	**1.39**	**1.22 - 1.59**
France	**1.59**	**1.39 - 1.82**
Denmark	0.88	0.75 - 1.02
Switzerland	**0.71**	**0.60 - 0.83**
Belgium	**1.31**	**1.15 - 1.50**
Israel	**0.73**	**0.60 - 0.88**
Czech Republic	0.92	0.80 - 1.06
Luxembourg	1.16	0.98 - 1.38
Slovenia	0.98	0.84 - 1.14
Estonia	0.94	0.83 - 1.08

10.3. Depressive symptomatology and socioeconomic deprivation according to gender and age.

The prevalence of depressive symptomatology as well as the risk of severe socioeconomic deprivation is statistically significant higher in females (30.0% [95% CI, 29.5-30.6] and 10.2% [95% CI, 9.9-10.6], respectively) than males (17.4% [95% CI, 16.9-17.9] and 9.3% [95% CI, 9.0-9.7], respectively).

The same association between depressive symptomatology and gender can be seen in Table 4 after controlling for other variables: females have a nearly twofold higher prevalence of depressive symptomatology than males.

Regarding the relationship between age and depressive symptomatology, the highest prevalence of depressive symptomatology is among the people aged ≥75 (30.7% [95% CI, 29.8-31.6) and prevalence rates in age groups between 50-64 and 65-74 are similar (23.0% [95% CI, 22.4-23.5] and 21.9% [95% CI, 21.3-22.6], respectively).

After controlling for other variables (Table 4), when setting the group of people aged between 50-64 years as a reference, the group of people aged between 65-74 years have a lower prevalence of depressive symptomatology and those who are aged 75 years and over have a higher prevalence.

The proportion of individuals at risk of severe socioeconomic deprivation is also higher in the group of people aged 75 years or more (11.9% [95% CI, 11.3-12.5]); the

prevalence between the groups of people aged between 50-64 and 65-74 is alike (9.3% [95% CI, 8.9-9.7] and 9.2% [95% CI, 8.7-9.7], respectively).

Table 3. Multiple logistic regression model for prevalence of clinically significant depressive symptomatology (EURO-D >3) related to gender and different ages groups (n=48319).

	OR	*95% CI*
Gender		
Males	1	--
Females	1.98	1.88 - 2.08
Age groups		
50-64	1	--
65-74	0.91	0.84 - 0.97
75+	1.13	1.04 - 1.22

10.4. Global socio-demographic and health characteristics of individuals with and without depressive symptomatology.

Table 5 and Table 6 show socio-demographic and health characteristics, respectively, of individuals with clinically significant depressive symptomatology compared to those without clinically significant depressive symptomatology.

Table 4. Socio-demographic characteristics of people with clinically significant depressive symptomatology [EURO-D >3] (n=11749) and those without clinically significant depressive symptomatology (n=36570).

	Without depressive symptomatology	*With depressive symptomatology*
Education, n (%) [95% CI]		
Low level of education (1+2)	11553 (**31.6**) [31.1-21.1]	5095 (**43.4**) [42.5-44.3]
Medium level of education (3+4)	15194 (**41.5**) [41.0-42.1]	4458 (**37.9**) [37.0-38.8]
High level of education (5+6)	9823 (**26.9**) [26.4-27.3]	2196 (**18.7**) [18.0-19.4]
Employment, n (%) [95% CI]		
Employed / Self-employed	11261 (**30.8**) [30.3-31.3]	2477 (**21.1**) [20.5-21.8]
Retired	21318 (**58.3**) [57.8-58.8]	6895 (**58.7**) [57.8-59.6]
Unemployed	881 (**2.4**) [2.3-2.6]	414 (**3.5**) [3.2-3.9]
Permanently sick / Disabled	763 (**2.1**) [1.9-2.2]	834 (**7.1**) [6.6-7.6]
Homemaker	2347 (**6.4**) [6.2-6.7]	1129 (**9.6**) [9.1-10.2]
Marital status, n (%) [95% CI]		
Married / Registered partnership	26868 (**73.5**) [73.0-73.9]	7471 (**63.6**) [62.7-64.5]
Separated / Divorced	3683 (**10.1**) [9.8-10.4]	1487 (**12.7**) [12.1-13.3]
Single	2050 (**5.6**) [5.4-5.8]	697 (**5.9**) [5.5-6.4]
Widower	3969 (**10.9**) [10.5-11.2]	2094 (**17.8**) [17.1-18.5]
Severe socioeconomic deprivation, n (%) [95% CI]		
At risk of severe deprivation (1)	2132 (**5.8**) [5.6-6.1]	2613 (**22.2**) [21.5-23.0]

Table 5. Health characteristics of people with clinically significant depressive symptomatology [EURO-D >3] (n=11749) and those without clinically significant depressive symptomatology (n=36570).

	Without depressive symptomatology	*With depressive symptomatology*
Medication for anxiety/depression, n (%) [95% CI]		
Takes anxiolytics or antidepressants	1516 (**4.1**) [3.9-4.4]	1469 (**12.5**) [11.9-13.1]
BMI, n (%) - [95% CI]		
Normal	13787 (**37.7**) [37.2-38.2]	4129 (**35.1**) [34.3-36.0]
Underweight	361 (**1.0**) [0.9-1.1]	212 (**1.8**) [1.6-2.1]
Overweight	15263 (**41.7**) [41.2-42.2]	4461 (**38.0**) [37.1-38.9]
Obese	7159 (**19.6**) [19.2-20.0]	2947 (**25.1**) [24.3-25.9]
Number of chronic diseases, n (%) [95% CI]		
≥2 chronic diseases	15096 (**41.3**) [40.8-41.8]	7645 (**65.1**) [64.2-65.9]
Affective/Emotional disorders, n (%) [95% CI]		
Has or has had affective/emotional disorders	1226 (**3.4**) [3.2-3.5]	1385 (**11.8**) [11.2-12.4]
General health status, n (%) [95% CI]		
Excellent	3779 (**10.3**) [10.0-10.7]	457 (**3.9**) [3.5-4.3]
Very good	7600 (**20.8**) [20.4-21.2]	1219 (**10.4**) [9.8-10.9]
Good	14327 (**39.2**) [38.7-39.7]	3437 (**29.3**) [28.4-30.1]
Fair	8532 (**23.3**) [22.9-23.8]	4354 (**37.1**) [36.2-37.9]
Poor	2332 (**6.4**) [6.1-6.6]	2282 (**19.4**) [18.7-20.2]

BMI, Body Mass Index

From the tables above one can observe that people with depressive symptomatology are prone to have poorer socio-demographic and health characteristics such as higher number of chronic diseases; worse self-rated general health status; being unemployed or permanently sick / disabled; higher risk of severe socioeconomic depression; lower levels of education; and being divorced/separated or widowed. The results also show that people with depressive symptomatology have a higher prevalence of underweight and obesity; on the other hand, the prevalence of overweight is lower. Similar patterns can be observed in Table 7 and Table 8, after controlling for other variables.

The association between the presence of depressive symptomatology and socioeconomic deprivation is also represented in Table 7: people at risk of severe deprivation have a threefold higher prevalence of depressive symptomatology than people who are not at risk threefold.

Table 6. Multiple logistic regression model for prevalence of clinically significant depressive symptomatology (EURO-D = >3) related to socio-demographic characteristics (n=48319).

	OR	*95% CI*
Education		
Low level of education (1+2)	1.17	1.10 - 1.25
Medium level of education (3+4)	1.05	0.99 - 1.12
High level of education (5+6)	1	--
Employment		
Employed / Self-employed	1	--
Retired	0.92	0.85 - 0.99
Unemployed	1.29	1.13 - 1.49
Permanently sick / Disabled	1.79	1.58 - 2.02
Homemaker	1.00	0.91 - 1.11
Marital status		
Married / Registered partnership	1	--
Separated / Divorced	1.27	1.18 - 1.36
Single	1.09	0.98 - 1.20
Widower	1.29	1.21 - 1.39
Severe socioeconomic deprivation		
At risk of severe deprivation (1)	3.20	2.98 - 3.44

Table 7. Multiple logistic regression model for prevalence of clinically significant depressive symptomatology (EURO-D = >3) related to health characteristics (n=48319).

	OR	*95% CI*
Medication for anxiety or depression		
Do not take anxiolytics or antidepressants	1	--
Takes anxiolytics or antidepressants	1.57	1.43 - 1.73
BMI		
Normal	1	--
Underweight	1.32	1.08 - 1.60
Overweight	0.94	0.89 - 0.99
Obese	0.97	0.91 - 1.03
Number of chronic diseases		
<2 chronic diseases	1	--
≥2 chronic diseases	1.84	1.75 - 1.93
Affective/Emotional disorders		
Never has had affective/emotional disorders	1	--
Has or has had affective/emotional disorders	1.71	1.55 - 1.88
General health status		
Excellent	1	--
Very good	1.19	1.05 - 1.33
Good	1.56	1.40 - 1.75
Fair	2.76	2.46 - 3.08
Poor	4.37	3.86 - 4.95
Severe socioeconomic deprivation		
Not at risk of severe deprivation (0)	1	--
At risk of severe deprivation (1)	3.20	2.98 - 3.44

BMI, Body Mass Index

10.5. Global socio-demographic and health characteristics of individuals with and without socioeconomic deprivation.

Table 9 and Table 10 show socio-demographic and health characteristics, respectively, of persons at risk of sever socioeconomic deprivation compared to those who are not at risk. The results obtained are similar to those for people with or without clinically significant depressive symptomatology presented in Table 7 and Table 8.

Table 8. Socio-demographic characteristics of people at risk of sever socioeconomic deprivation (n=4745) and those who are not at risk (n=43574).

	Not at risk of deprivation	*At risk of deprivation*
Education, n (%) [95% CI]		
Low level of education (1+2)	14099 (**32.4**) [31.9-32.8]	2549 (**53.7**) [52.3-55.1]
Medium level of education (3+4)	17968 (**41.2**) [40.8-41.7]	1684 (**34.5**) [34.1-36.9]
High level of education (5+6)	11507 (**26.4**) [26.0-26.8]	512 (**10.8**) [9.9-11.7]
Employment, n (%) [95% CI]		
Employed / Self-employed	12981 (**29.8**) [29.4-30.2]	757 (**16.0**) [14.9-17.0]
Retired	25395 (**58.3**) [57.8-58.7]	2818 (**59.4**) [58.0-60.8]
Unemployed	1002 (**2.3**) [2.2-24]	293 (**6.2**) [5.5-6.9]
Permanently sick / Disabled	1156 (**2.7**) [2.5-2.8]	441 (**9.3**) [8.5-10.2]
Homemaker	3040 (**7.0**) [6.7-7.2]	436 (**9.2**) [8.4-10.0]
Marital status, n (%) [95% CI]		
Married / Registered partnership	31265 (**71.8**) [71.3-72.2]	3074 (**64.8**) [63.4-66.1]
Separated / Divorced	4537 (**10.4**) [10.1-10.7]	633 (**13.3**) [12.4-14.3]
Single	2436 (**5.6**) [5.4-5.8]	311 (**6.6**) [5.9-7.3]
Widower	5336 (**12.2**) [11.9-12.6]	727 (**15.3**) [14.3-16.4]

Table 9. Health characteristics of people at risk of sever socioeconomic deprivation (n=4745) and those who are not at risk (n=43574).

	Not at risk of deprivation	*At risk of deprivation*
Medication for anxiety/depression, n (%) [95% CI]		
Takes anxiolytics or antidepressants	2500 (**5.7**) [5.5-6.0]	485 (**10.2**) [9.4-11.1]
BMI, n (%) - [95% CI]		
Normal	16493 (**37.9**) [37.4-38.3]	1423 (**30.0**) [28.7-31.3]
Underweight	504 (**1.2**) [1.1-1.3]	69 (**1.5**) [1.1-1.8]
Overweight	17888 (**41.1**) [40.6-41.5]	1836 (**38.7**) [37.3-40.1]
Obese	8689 (**19.9**) [19.6-20.3]	1417 (**29.9**) [28.6-31.2]
Number of chronic diseases, n (%) [95% CI]		
≥2 chronic diseases	19668 (**45.1**) [44.7-45.6]	3073 (**64.8**) [63.4-66.1]
Affective/Emotional disorders, n (%) [95% CI]		
Has or has had affective/emotional disorders	2137 (**4.9**) [4.7-5.1]	474 (**10.0**) [9.2-10.9]
General health status, n (%) [95% CI]		
Excellent	4041 (**9.3**) [9.0-9.6]	195 (**4.1**) [3.6-4.7]
Very good	8307 (**19.1**) [18.7-19.4]	512 (**10.9**) [9.9-11.7]
Good	16529 (**37.9**) [37.5-38.4]	1235 (**26.0**) [24.8-27.3]
Fair	11173 (**25.6**) [25.2-26.1]	1713 (**36.1**) [34.7-37.5]
Poor	3524 (**8.1**) [7.8-8.3]	1090 (**23.0**) [21.8-24.2]
Depressive symptomatology[1], n (%) [95% CI]		
With depressive symptomatology (>3)	9136 (**21.0**) [20.6-21.4]	2613 (**55.1**) [53.6-56.5]

[1] Derived from EURO-D scale; BMI, Body Mass Index

10.6. Degree of the association between socioeconomic deprivation and depressive symptomatology across the different European countries.

Figure 4 presents, stratified by countries, the prevalence of depressive symptomatology in people at risk of severe socioeconomic deprivation and in people who are not at risk. The relationship between socioeconomic deprivation and clinically significant depressive symptomatology for each one of the countries of study is represented in Figure 5, which has been originated from a multilevel logistic regression model stratified by countries.

Figure 3. Proportion of people with clinically significant depressive symptomatology stratified by people at risk (n=4745) and people not at risk (n=43574) of severe socioeconomic deprivation in different countries *(NED-Netherlands; BEL-Belgium; DEN-Denmark; AUT-Austria; LUX-Luxembourg; GER-Germany; FRA-France; SWE-Sweden; ITA-Italy; SLO-Slovenia; EST-Estonia; ESP-Spain; SUI-Switzerland; ISR-Israel; CZE-Czech Republic).*

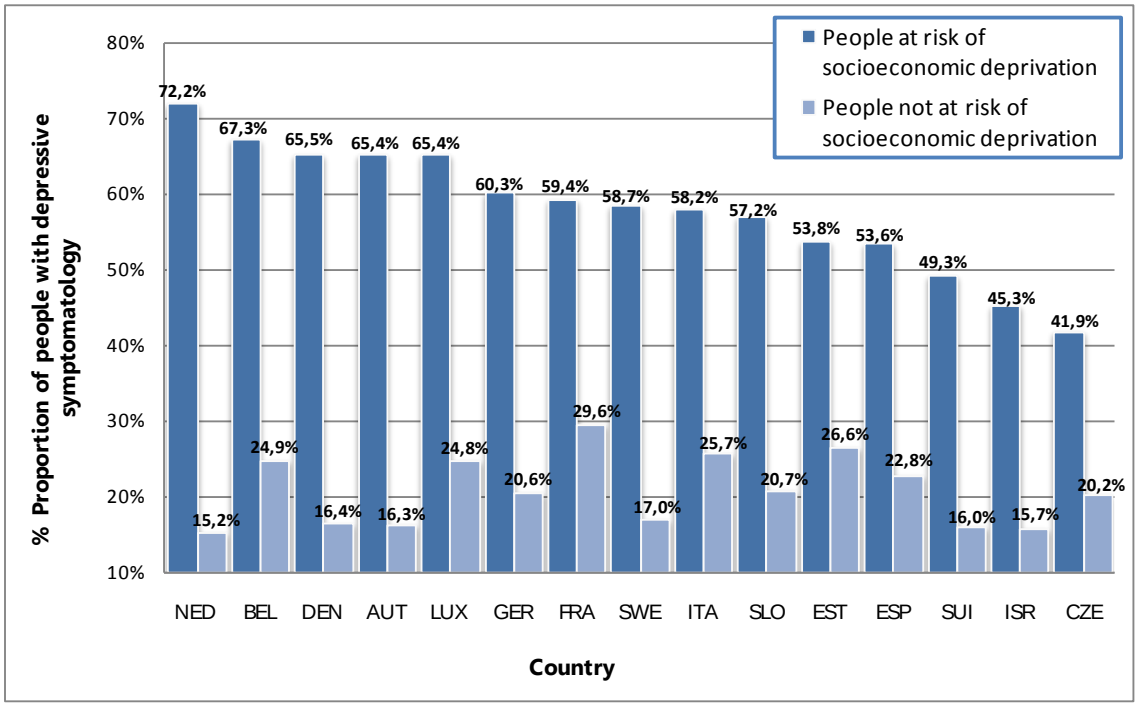
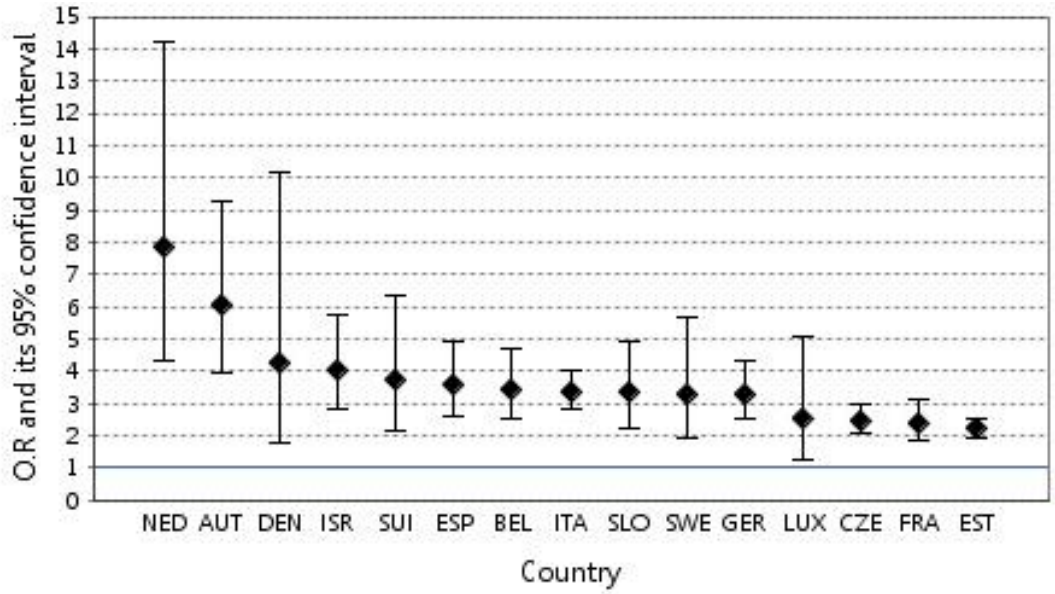


Figure 4. Association between socioeconomic deprivation and clinically significant depressive symptomatology in each country studied *(NED-Netherlands; BEL-Belgium; DEN-Denmark; AUT-Austria; LUX-Luxembourg; GER-Germany; FRA-France; SWE-Sweden; ITA-Italy; SLO-Slovenia; EST-Estonia; ESP-Spain; SUI-Switzerland; ISR-Israel; CZE-Czech Republic).*



11. DISCUSSION

11.1. Global prevalence rates of depressive symptomatology and socioeconomic deprivation.

The present study, using data from 14 European countries and 1 non-European country, has estimated a 24.3% global prevalence of clinically significant depression in adults aged 50 years or more, which means that almost a quarter of the European population has depressive symptoms that affect significantly its quality of life. However, it is difficult to compare this result with other global prevalence rates of depressive symptomatology due to its wide variability between studies.

When examining the association between socioeconomic deprivation and depressive symptomatology, several studies use variables such income, education or occupation to measure the socioeconomic position, but these variables individually cannot completely explain this association because many other factors act in it. The preset study, on the other hand, has used a multidimensional socioeconomic deprivation index specifically developed for the 5th wave of the SHARE in which more factors related to the relationship between socioeconomic deprivation and depressive symptomatology are considered. It is important to clarify that this study is descriptive and that searching for mechanisms that could explain the association is not an objective, therefore the independent variable, the multidimensional socioeconomic deprivation index, is well used.

The multivariate analysis done in this study has shown a strong association between depressive symptomatology and socioeconomic deprivation (OR 3.20). This association has been studied and accepted in several studies (12,25,30,31,35) and different mechanisms to explain it have been given: 1) societies with higher levels of socioeconomic inequality tend to have a greater number of people who do not have access to health resources and consequently worse health outcomes (including depression); 2) stressful social comparisons tends to rise when the differences between the rich and poor widens; 3) high socioeconomic inequalities cause that politics and legislations serve the interest of the wealthy more than those who are at the low SEP group making the situation worse (12).

11.2. Depressive symptomatology and socioeconomic deprivation according to gender and age.

According to gender

Both the prevalence of socioeconomic deprivation and the prevalence of clinically significant depressive symptomatology is higher in females than males even after controlling for other variables such as age, number of chronic diseases, self-rated general health, history of other anxiety/depressive disorders, education, or occupation,

among others. The multiple logistic regression model that has been carried out in this study, shows that females have an approximately twofold higher probability than males of having clinically significant depressive symptomatology. This findings are consistent with results exposed in other studies (5,7,12,35)

According to age

As was expected, higher prevalence rates of clinically significant depressive symptomatology for the oldest age group (≥75years) have been obtained but, contrary to the literature (10,32), this association remained after controlling for other variables, related to depressive symptomatology and more prevalent among older people, such as number of chronic diseases, self-reported general health, or educational level. Perhaps the relevant confounding variables are those which have not been measured in the present article but were measured in the articles reporting contrary results: financial problems, problems with normal daily activities and cognitive difficulties.

11.3. Global socio-demographic and health characteristics of individuals with and without depressive symptomatology and individuals with and without socioeconomic deprivation.

With and without clinically significant depressive symptomatology

As seen in the literature (5,9,12), people with clinically significant depressive symptomatology have higher prevalence rates of poor socio-demographic and health characteristics even when controlling for the other variables measured.

With and without socioeconomic deprivation

People with socioeconomic deprivation, like people with depressive symptomatology, have higher prevalence rates of poor socio-demographic and health characteristics. These findings also confirm what has been observed through the literature revision (29,30).

Other variables used frequently to measure the socioeconomic position are level of education, gross individual or household income, and type of occupation (24,26); therefore it is no surprise that people with socioeconomic deprivation have higher prevalence rates of low-level education and worse occupation. In the present study, individual or household income has not been directly assessed, but if they had been measured, it is likely that similar results would have been obtained.

11.4. Association between socioeconomic deprivation and depressive symptomatology among European countries.

As seen in Figure 1 and Figure 2, the countries with higher prevalence rates of clinically significant depressive symptomatology (Estonia, Italy and France) also have a high proportion of people with severe socioeconomic deprivation; on the other hand, the

countries with lower prevalence rates of clinically significant depressive symptomatology (Netherlands, Switzerland, Denmark, Sweden and Austria) are also the countries with a lower proportion of people with severe socioeconomic deprivation. These findings would be related to the theory that a socioeconomic status-health gradient exists; this means that the association between socioeconomic deprivation and depressive symptomatology is not only at the bottom of the socioeconomic position but across all of the socioeconomic position levels (29). The results are consistent with the ones obtained in a study that also used data of the SHARE but from the 1st wave (36).

The main objective of this study was *"to assess the relationship between socioeconomic deprivation and the prevalence of clinically significant depressive symptomatology among different European countries in adults aged 50 and over".* The results obtained indicate that the main hypothesis is correct, or at least that it cannot be discarded; in those countries where the prevalence of socioeconomic deprivation is lower, the general association with significant depressive symptomatology is stronger compared to those countries with higher prevalence. Furthermore, countries with less socioeconomic deprivation exhibit a wider difference between the proportion of people with socioeconomic deprivation that has depressive symptomatology and the proportion of people without socioeconomic deprivation that has depressive symptomatology. These findings could be explained with "the status anxiety hypothesis" which exposes that the perception of lower social status (the people with socioeconomic deprivation tend to compare themselves with those in higher socioeconomic position; this comparison worsens when differences between people not socioeconomic deprived and people socioeconomic deprived are wider) leads to poorer health (12,31).

Figure 3 demonstrates that, almost in every country, more than half of the individuals with socioeconomic deprivation have clinically significant depressive symptomatology, while in the group of individuals without socioeconomic deprivation, the persons with depressive symptomatology account for less than 30%.

11.5. Limitations of the present study

This study has three main limitations:

- It is a cross-sectional study and therefore no causal associations between clinically significant depressive symptomatology and socioeconomic deprivation can be made.
- The EURO-D scale has been used in order to classify the individuals in those who present clinically significant depressive symptomatology and those who do not present clinically significant depressive symptomatology. Although this scale has a high reliability and validity, it cannot be used to diagnose major depression or other depressive disorders and therefore only depressive symptomatology could be assessed in this study. In order to give clinical significance to the independent

variable, a score of 3 in the EURO-D scale was established as the cut-off point; this cut-off point has been validated in other studies.

- The global response rate was higher than 60% and rates between countries were similar for the major part of them; however, a non-response bias could have occurred if the respondents were different than those who did not answer.

12. CONCLUSIONS

This study demonstrates that an association between depressive symptomatology and socioeconomic deprivation exist and also that the degree of this association changes between countries depending, in part, of the proportion of individuals who have socioeconomic deprivation in each country.

Although being a cross-sectional study, the results presented should be used as an argument in favor of prospective studies in which the causal relationship between socioeconomic deprivation and depression could be confirmed; prospective studies to investigate the other factors associated with depression in those countries with high prevalence of depression and socioeconomic deprivation should also be made. With these information, new social and equality policies could be developed to prevent depression, one of the most common and disabling diseases worldwide.

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14. INDEX OF TABLES AND FIGURES

15. ANNEXES

15.1. Annex 1.

ICD-10 criteria for Depressive episode [F32] (37)
The core symptoms are: 1. Depressed mood 2. Loss of interest and enjoyment 3. Reduced energy leading to increased fatigability and diminished activity. Other common symptoms are: a) Reduced concentration and attention. b) Reduced self-esteem and self-confidence. c) Ideas of guilt and unworthiness (even in a mild type of episode). d) Bleak and pessimistic views of the future. e) Ideas or acts of self-harm or suicide. f) Disturbed sleep. g) Diminished appetite. The categories of mild, moderate and severe depressive episodes should be used only for a first depressive episode. Further depressive episodes should be classified under one of the subdivisions of recurrent depressive disorder. The number, type and severity of symptoms present are necessary to differentiate between mild, moderate, and severe depressive episodes. *F32.0 - Mild depressive episode* At least two of the core symptoms (1-3), plus at least two of the other symptoms (a-g) exposed above should usually be present for a definite diagnosis and none of these symptoms should be present to an intense degree. Minimum duration of the episode is about 2 weeks. The individual is usually distressed by the symptoms and has some difficulties in work and social activities, but will probably not cease to function completely. It can be specified if it is: - "Without somatic syndrome" [F32.00] --> few or none of the somatic symptoms present. - "With somatic syndrome" [F32.01] --> four or more of the somatic symptoms are also present or there are two or three somatic symptoms but they are unusually severe; examples of somatic symptoms are: psychomotor retardation, loss of appetite and weight, and sleep disturbance. *F32.1 - Moderate depressive episode* At least two of the core symptoms (1-3) should be present, plus at least three (and

preferably four) of the other symptoms (a-g) exposed above should be present. Several symptoms are likely to be present to a marked degree, but this is not essential if a particularly wide variety of symptoms is present overall. Minimum duration of the episode is about 2 weeks.
The individual will usually have considerable difficulty in continuing with social, work or domestic activities.
It can be specified if it is "Without somatic syndrome" [F32.10] or "With somatic syndrome" [F32.11].

F32.2 - Severe depressive episode without psychotic symptoms
This category should be used for single episodes of severe depression without psychotic symptoms.
The person usually shows considerable distress or agitation, unless retardation is a marked feature. Loss of self-esteem or feelings of uselessness or guilt are likely to be prominent, and suicide is a distinct danger in particularly severe cases. It is presumed here that the somatic syndrome will almost always be present in a severe depressive episode.
All three of the core symptoms (1-3) should be present, plus at least four other symptoms (a-g), some of which should be of severe intensity. However, if important symptoms such as agitation or retardation are marked, the patient may be unwilling or unable to describe many symptoms in detail. An overall grading of severe episode may still be justified in such instances. The depressive episode should usually last at least 2 weeks, but if the symptoms are particularly severe and of very rapid onset, it may be justified to make this diagnosis after less than 2 weeks.
It is very unlikely that the sufferer will be able to continue with social, work, or domestic activities, except to a very limited extent.

This category should be used only for single episodes of severe depression without psychotic symptoms; for further episodes, a subcategory of recurrent depressive disorder (F33.=) should be used.

F32.3 - Severe depressive episode with psychotic symptoms
A severe depressive episode which meets the criteria for F32.2 above and in which delusion (usually involve ideas of sin, poverty, or imminent disasters, responsibility for which may be assumed by the patient), hallucinations (usually of defamatory or accusatory voices or of rotting filth or decomposing flesh), or severe psychomotor retardation that can may progress to stupor.
If required, delusions or hallucinations may be may be specified as mood-congruent or mood-incongruent.

F32.8 - Other depressive episodes

Episodes should be included here which do not fit the descriptions given for depressive episodes described above, but for which the overall diagnostic impression indicates that they are depressive in nature.

Examples include fluctuating mixtures of depressive symptoms (particularly the somatic variety) with non-diagnostic symptoms such as tension, worry, and distress, and mixtures of somatic depressive symptoms with persistent pain or fatigue not due to organic causes (as sometimes seen in general hospital services).

Includes atypical depression.

F32.9 - Depressive episode, unspecified

Includes: depression NOS (Not Otherwise Specified) and depressive disorder NOS.

15.2. Annex 2.

DSM-5 criteria for Major Depressive Disorder (3)

The individual has to meet all criteria to be diagnosed of having Major Depressive Disorder (t*he criteria A-C represent a* ***major depressive episode****).*

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
   Note: Do not include symptoms that are clearly attributable to another medical condition.
   1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (Note: in children and adolescents, can be irritable mood).
   2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
   3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: in children, consider failure to make expected weight gain).
   4. Insomnia or hypersomnia nearly every day.
   5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
   6. Fatigue or loss of energy nearly every day.
   7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
   8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
   9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
B. The symptoms cause clinically significant distress or impairment in social, occupational, or other areas of functioning.
C. The episode is not attributable to the physiological effects of a substance or to another medical condition.
D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
E. There has never been a manic episode or a hypomanic episode.
   Note: This exclusion does not apply if all of the manic-like or hypomanic-like

episodes are substance-induced or are attributable to the physiological effects of another medical condition.

It has to be specified if the episode corresponds to a single episode or a recurrent episode; to be considered recurrent, there must be an interval of at least 2 consecutive months between separate episodes in which criteria are not met for a major depressive episode.

Severity and Course specifiers

* Mild --> Few, if any, symptoms in excess of those required to make the diagnosis are present, the intensity of the symptoms is distressing but manageable; the symptoms result in minor impairment in social or occupational functioning.
* Moderate --> The number of symptoms, intensity of symptoms, and/or functional impairment are between those specified for "mild" and "severe".
* Severe --> The number of symptoms is substantially in excess of that required to make the diagnosis, the intensity of the symptoms is seriously distressing and unmanageable; the symptoms markedly interfere with social and occupational functioning.

- With psychotic features.

Current severity and psychotic feature are only indicated if full criteria are currently met for a major depressive episode.

- In partial remission.
- In full remission.

Remission specifiers are only indicated if the full criteria are not currently met for a major depressive episode.

Other specifiers

- With anxious distress
- With mixed features
- With melancholic features
- With atypical features
- With mood-congruent psychotic features
- With mood-incongruent psychotic features
- With catatonia
- With peripartum onset
- With seasonal pattern (recurrent episode only)