From Centre for Family and Community Medicine,
Department of Neurobiology, Care Sciences and Society,
Karolinska Institutet, Stockholm, Sweden

DEPRESSION IN PRIMARY CARE

Detection, Description and Mortality

Ranja Strömberg de Sousa Soares

Stockholm 2013

'Låt munnen tala om det som hjärtat är fyllt av'

Let your mouth speak of that with which your heart is filled

ABSTRACT

Aims

The aims of these studies were to explore the prevalence and severity of depression among unscheduled drop-in patients in primary care and to identify possible cues to depression in the consultation. Further aims were to analyse the association between depression and psychosocial stressors and lifestyle factors from a gender perspective and to evaluate the usefulness of the Gotland Male Depression Scale (GS) in screening for depression among men. A final aim was to analyse the long-term mortality rate (MR) and the standardised mortality rate (SMR) among the patients who had been diagnosed as having a major depressive disorder (MDD).

Background

Depression is a common diagnosis in primary care, but had been reported to remain undetected in half of the consultations, especially among men despite the fact that men had higher rates of suicide. Detecting and diagnosing patients with depression in primary care is essential since depression reduces quality of life, functioning level, work ability and possibly also life expectancy.

Patients and Methods

Patients visiting two primary care physicians' drop-in clinics were screened using the Beck Depression Inventory (BDI) with a cut-off value of ≥ 10 and the men were screened also with the GS with a cut-off value of ≥ 13. A two-step screening method was used among patients aged 18–75 years visiting two primary care physicians' drop-in clinics in opportunistic and targeted screenings. Patients with screening scores above the cut-off values were interviewed by the physicians at a repeat visit by applying the DSM-IV criteria for major depressive disorder (MDD). Severity of depression was measured with the Montgomery-Åsberg Depression Rating Scale (MADRS).
The study population consisted of 404 patients (men n=235, women n=169) categorised as depressed (n=124) or non-depressed (n= 280).
Their socio-demographic data, lifestyle and psychosocial stressors were obtained from a questionnaire. Symptoms mentioned at the screening visit were examined from the medical charts and categorised as somatic or mental.
Twelve years after inclusion, the causes of death for the depressed patients were obtained from the National Cause of Death Register. Mortality data regarding the non-depressed patients were obtained from the Swedish National Register and data from the Life Tables Statistics Sweden were used to calculate standardised mortality rates (SMRs).

The screenings among men with GS and BDI were compared, as were the outcomes from the opportunistic and targeted screenings. Differences between depressed and non-depressed men and women regarding socio-demographic and clinical data were analysed. The odds ratios (ORs) with 95% confidence intervals (95% CI) for being depressed were calculated for the psychosocial stressors and lifestyle factors. Multiple logistic regression modelling was used to obtain the main effect models separately for men and women for the risk factors for depression.

Differences in the MRs between the depressed and the non-depressed patients were calculated as well as their SMRs. As a reference for comparison the SMRs in the Swedish population in the same age and in the same time period were calculated.

Cox regression was applied to calculate the hazard ratios (HRs) for the mortality rate during the 12-year follow-up period for the depressed and the non-depressed patients in relation to the explanatory variables.

Main results

The prevalence of depression was 25% among women and 11% among men. The severity of depression was mild or moderate and severe depression was very rare. Mentioning a mental symptom was a cue to detect depression among women but not consistently among men. The proportions as depressed patients were higher from the targeted screenings than from the opportunistic screenings. Screening with GS did not detect more depressed men than BDI.

Smoking was associated with depression only among men. Three psychosocial stressors were equally associated with depression among the men and the women: being dissatisfied with family situation, being very stressed and perceiving poor physical health, and the ORs in the main effect models varied from 3.1 (95% CI 1.4–6.6) up to 22.4 (95% CI 5.8–86.8). Dissatisfaction with one's working situation was also associated with depression: in men OR 13.2 (95% CI 4.7–37.5) and in women: OR 32.5 (95% CI 4.1–254.7). The MR among the depressed men was significantly higher than among the non-depressed. The SMRs among depressed men and women did not differ from those in the general Swedish population.

Conclusions

The prevalence and severity of depression was comparable to that in other primary care settings. Depressed women had often mentioned mental symptoms. Questions about family and working situation, feeling very stressed and feelings about one's physical health could be used as risk indicators for depression in clinical practice for both men and women. Moreover, the long-term follow-up underlines the importance of finding patients with depression and thoroughly examine them also regarding their somatic health.

CONTENTS

LIST OF PUBLICATIONS

This thesis is based on the following original articles, which will be referred to in the text by their Roman numbers.

I   Ranja Strömberg, Estera Wernering, Anna Åberg-Wistedt, Anna-Karin Furhoff, Sven-Erik Johansson and Lars G. Backlund. Screening and diagnosing depression in women visiting GP's drop in clinic in Primary Health Care. BMC Family Practice 2008; 9:21–7.

II   Ranja Strömberg, Lars G. Backlund and Monica Löfvander. A comparison between the Beck's Depression Inventory and the Gotland Male Depression Scale in detecting depression among men visiting a drop-in clinic in primary care. Nordic Journal of Psychiatry 2009; 63:1–7.

III   Ranja Strömberg, Lars G. Backlund and Monica Löfvander. Psychosocial stressors and depression at a Swedish primary health care centre: A gender perspective study. BMC Family Practice 2011; 12:120–8.

IV   Ranja Strömberg, Lars G. Backlund, Sven-Erik Johansson and Monica Löfvander. Mortality in a cohort of depressed and non-depressed patients at a primary care centre in Stockholm, Sweden: A 12-year follow-up study. Under revision.

ABBREVIATIONS

BDI	Beck's Depression Inventory
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
GAD	Generalised anxiety disorder
GS	The Gotland Male Depression Scale
MADRS	Montgomery-Åsberg Depression Rating Scale
MDD	Major depressive disorder
MR	Mortality rate
NPV	Negative predictive value
PCC	Primary Care Centre
PPV	Positive predictive value
SES	Socioeconomic status
SMR	Standardised mortality rate
SSRI	Selective serotonin reuptake inhibitor
STG	Standard glasses of alcohol

INTRODUCTION

Why study depression?

Depression in the medical context is a mental disorder with a depressed state of mind that affects the individual's quality of life and social functioning (1). It entails considerable costs to society due to reduced working capacity and high health care costs (2).

The prevalence of depression in primary care settings has been found to be high and comparable to the prevalence of diabetes (3-6).

The diagnosis of depression has been reported to be overlooked in primary care in about half of the patients (4, 7-9) and screening procedures have been discussed as a method to improve the detection of depression in primary care (10, 11).

New drugs for the pharmacological treatment of depression, the serotonin reuptake inhibitors (SSRIs), had been available for prescription since the early 1990s and were reported to have fewer and milder side effects than earlier pharmacological therapies. Despite the fact that prescriptions for SSRIs doubled in Sweden between 1991 and 1996 (12), studies have shown that many depressed patients in primary care were not treated according to the guidelines at that time (13, 14).

It was considered an important issue for clinical practice and research to improve the methods for detecting depression in primary care. Together with my colleague I started these studies in 1997 at a health centre in central Stockholm, Sweden. We wanted to investigate the prevalence and severity of undiagnosed cases of depression in this primary care setting, also with a focus on men, as depression among men might be more frequently overlooked than among women (15).

Personal reflections

I had been working as a primary care physician for about ten years when the reorganisation called 'Kvartersakuten' (small primary care centres in a neighbourhood), was implemented in 1991, in the centre of Stockholm. The number of primary care physicians was doubled and each primary care physician, in cooperation with a district nurse, became responsible for about 2000–2500 inhabitants living in specified quarters, so as to establish continuity of care. In order to increase the patients' access to their primary care physicians, 'drop-in hours' were introduced. This organisational model had proved to be cost-effective with increased primary care physician visits and reduced visits to the hospitals' emergency departments and to private specialists (16, 17). The waiting room for the 'drop-in hour' was full of patients every morning and our experience was that many women were frequent attendees.

BACKGROUND

Organisation of primary care

General tasks

A law concerning primary care physicians was implemented in 1994 and defined the responsibility for primary care in Sweden so as to comprise all primary health care needs for the inhabitants (18). All inhabitants should be assigned, actively or passively, to specialists in family practice and each physician should have between 1000 and 3000 listed patients and cooperate with district nurses.

Psychosocial care

At the time when we started the studies in 1997, two social counsellors were employed and worked in one of the primary care centres (PCCs). They were skilled in social counselling and had psychotherapeutic training to varying degrees and handled many problems, e.g. in family relations and crisis reactions, and primary care physicians referred patients to them. The charge for these consultations was low. At this time therapy by a psychologist was too expensive for the majority of the patients, as this care was not reimbursed by the county council. When the new systems for financial compensation for PCCs were implemented the social counsellor positions at the centres were closed. This was regrettable, since counselling by social workers in primary care in Scotland had been found to be cost-effective and, among women with mild depressions, more effective than pharmacological treatment and treatment by psychotherapists (19).

Today a primary care physician is usually responsible for about 1800–2600 listed patients and cooperates in PCCs with other physicians, district nurses and other personnel categories. About half of the primary care physicians in Stockholm work in privately operated PCCs. The financial compensation to the PCCs is today based on the number of listed patients and the number of consultations.

The length of a scheduled consultation is often about 20 minutes, which is longer than in many other European countries, but in Sweden patients have fewer consultations with their primary care physicians. The unscheduled consultations at the drop-in hours are shorter, about 10 minutes.

Depression – Definitions

What is depression?

In everyday conversation the term 'depressed' might be used to mean temporary feelings of low mood, connected with disappointments and shortcomings, but in the medical context, depression is a mental disorder with defined diagnostic criteria.

Definitions of depression in three diagnostic systems

Three diagnostic systems for diagnosing mental disorders were in use at the time of our studies and are still in use today:

1. The International Statistical Classification of Diseases and Health Related Problems, (ICD-10) was developed by the World Health Organisation (WHO) (20). It is used worldwide and classifies all diseases and other health problems and has specific diagnostic codes for diseases. A 'depressive episode' is defined as a combination of symptoms, which are grouped in A, B and C criteria. The core symptoms are low mood, low energy and low activity, and at least 1–2 of these must be combined with a specified number of other symptoms from the C category to make the diagnosis, and the B category defines the exclusion criteria. Separate codes for a mild (F32.0), moderate (F32.1) or severe (F32.2) depressive episode are available and based on the number of symptoms and the level of impairment. In mild depression, normal daily activities can be performed; in moderate depression, normal daily activities are difficult to get through. In severe depression, the patient is gravely impaired and has suicidal thoughts. Severe depression with psychotic symptoms has a separate code (F32.3). Recurrent depressive disorder (F33.0) is the diagnosis used when depressive episodes occur repeatedly. Seasonal depressive disorder is a label used for recurrent depressive disorders during a specific season, often in the autumn or spring.

Depressive episodes alternating with elated mood are termed bipolar affective disorder (F31), with many further specifications.

2. The classification register for use in Swedish primary care, 'Klassifikation av sjukdomar och hälsoproblem 1997 – Primärvård, (KSH97 – P)' is a shortened version of ICD-10 (21). Diagnoses available for depressed mood are: 'Depressive episode' (F32), 'Recurrent depressive disorder' (F33), 'Neurotic depression' (in Swedish, 'Förstämningssyndrom') (F39-P) and 'Bipolar affective disorder' (F31). Several versions of the KSH97 – P were and are in use in primary care, but none of these have separate codes for mild, moderate or severe depression.

Other possible diagnoses used to classify depressive symptoms are 'Reaction to stress, Crisis reaction' (F43.9P) and the symptom describing diagnosis 'Symptoms of burnout' (Z73).

3. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) was issued by the American Psychiatric Association (22). It defines the diagnostic criteria for mental disorders including major depressive disorder (MDD). Five symptoms, of which one of two mandatory symptoms, depressed mood or loss of interest or pleasure, have to be combined with at least four additional symptoms (Appendix).

In this thesis the diagnosis of depression was based on the criteria for MDD in DSM-IV.

Other diagnoses with low mood relevant in primary care

Minor Depression
According to DSM-IV, two up to four symptoms must be present for the diagnosis Minor Depression compared to five symptoms in MDD. In research, the term 'Minor Depression' has had several definitions (23). Minor depression may occur independently of MDD or as a stage of MDD and is also associated with functional impairment (24, 25).

Burnout

Mental diagnoses as a reason for long-term sick leave had increased greatly during the last years of the 1990s (26). Work-related stress was also often noted in the sick-listing certifications (27). Long-lasting exposures to stress could produce symptoms of burnout with the core symptoms of lack of energy and rapidly increasing symptoms of memory and concentration problems (28). In 2003 the National Board of Health and Welfare in Sweden published diagnostic criteria for the diagnosis 'Depression with burnout syndrome' or, alternatively, 'Burnout depression' (27). The diagnostic code for 'Depressive Episode' (F32) should be used if criteria for MDD are fulfilled. In less severe cases the diagnoses 'Burnout syndrome' or 'Maladaptive reaction to stress' can be used (F43.8A).

Severity of depression

In clinical practice, it is important to follow the effects of treatment with assessments of the severity and the risk of suicide. The ICD-10 and DSM-IV include definitions of mild, moderate and severe depression. More precise assessments were developed to evaluate the effects of pharmacological treatment of depression in clinical practice and research, i.e. the Hamilton Depression Rating Scale (HDRS) (29) and the Montgomery-Åsberg Depression Rating Scale (MADRS) (30). The MADRS has been shown to be more sensitive to change when depressed patients were treated with antidepressants.

Montgomery-Åsberg Depression Rating scale

The ten items in the MADRS (total score 0–60, each item six steps, 0–6) cover the diagnostic criteria of depression in DSM-IV, except for motor retardation. The severity can be classified on the basis of the summed score as: no clinical depression (<7), mild depression (7–19), moderate depression (20–34) or severe depression (35–60) (31).

Suicide and major depressive disorder

In Sweden the number of suicides was 1783 in 1995. During the last few decades the number of suicides in Sweden and in Finland has decreased, which might be an effect of the increased prescription of SSRIs and other anti-depressive pharmacological treatments (32-34). However, the frequency of suicides had decreased before the increase in the new anti-depressive treatments (35) and many countries in Europe have not noted any decrease in suicide rates despite increasing prescriptions of SSRIs (36).

The majority of suicides are related to MDD (37, 38). Suicidal ideation has also been found to be common among depressed patients in primary care in Finland (39). In Swedish psychiatric care the risk of suicide was found to be very high among depressed patients (40). The risk of suicide has been shown to increase with the severity of depression (41).

In a Danish study it was shown that the majority of patients who had committed suicide had been in contact with health care providers some weeks before the suicide (42).

Depressed patients in psychiatric and in primary care

Psychiatric care

The regional treatment guidelines advised that the following patients with depression should be referred to psychiatric care: those with severe depression and suicidal ideation, those with psychotic symptoms, those with bipolar disorders and those with depression after childbirth (43).

Primary care

The majority of the depressed patients were and still are treated by their primary care physicians. In primary care, depression is one of the most common diagnoses (44). The prevalence of persons on SSRI treatment has steadily increased in Sweden, and is now about 7% and, in elderly patients, about 20% (45). Primary care physicians see un-selected patients, often with several diseases. Thus, the clinical pictures of depression in psychiatric care and primary care are different.

Prevalence, duration and recurrence

The prevalence of depression in primary care has been estimated in European studies to range between 10% and 24%, depending on the study population and methods used (46-48). The detection rates have been found to be higher in cases of severe depression (49, 50), as well as in continuous care (51, 52).

The prevalence among women has been reported cross-culturally to be twice that of men (15, 53-55). The reasons for this higher prevalence have not been fully understood (56, 57), but the excess among women was reduced by about 50% when adjusted for socio-financial factors (54).
Notably, population studies have shown that not all depressed patients seek help for their problems (58).

Duration and recurrence

Population studies from the Netherlands on the duration of MDD have reported that half of the patients had recovered within three months, but 20% still had depression after two years (59). The recurrence rates of MDD in primary care have been reported to range between 30% and 40% (60). Because of the duration and recurrence rate, the burden of MDD is evident (61).

Clinical picture in primary care

Depression is a syndrome diagnosis with at least 14 combinations of the symptoms from the MDD criteria. According to several studies, the majority of depressed patients in primary care consultations had presented somatic symptoms, such as pain in the head, back, chest or stomach, musculoskeletal pain, loss of appetite, constipation and fatigue and, in about two thirds of cases, combined with other psychiatric diagnoses (62, 63).

Patients with depression have rated their quality of life as low as that of patients who have had a severe stroke (64). Depressed patients have been shown to be frequent attendees at all health care levels because of feelings of illness and worries (65-69).

Quality of life and social functioning

Regardless of its severity (1, 5), depression has negative effects on the individual's quality of life (64), social functioning and working life (24, 70, 71). Particularly, early onset of depression in women has been found to highly affect their educational attainment and thus involves a large loss of human capital (72).

Comorbidity

Depressed patients in primary care often have comorbid somatic diseases. Diabetes is a prevalent disease in primary care, and a meta-analysis found that patients with diabetes had a doubled risk of depression compared with patients without diabetes (73). Depression was found to be associated with an increased risk of heart disease among men and women and increased mortality from heart disease among men (74).

Comorbidity with other psychiatric disorders

A WHO study on primary care patients from 15 countries showed that about two thirds of depressed patients had additional mental disorders such as anxiety disorders, alcohol dependency or personality disorders (63).

Alcohol: Population studies in the USA had shown that persons affected by alcohol abuse or dependence had more than a twofold increased risk of anxiety and depressive disorders (75). Other later studies have reported a dose-response relationship between alcohol and depression (76, 77). A combination of harmful or hazardous alcohol use combined with depression has been shown to increase the risk of suicide, especially among men (78). Patients with depression, anxiety and high alcohol consumption have also been shown to be frequent primary health care users (69).

In Sweden the recommendation for safe limits of alcohol use was for men not to exceed 14 standard glasses (stg) (1 stg = 12 g pure alcohol) per week and for women not to exceed 9 stg per week.

Anxiolytic treatment: Depressed patients have increased levels of anxiety. Earlier, in the 1970s and 1980s, anxiolytic treatment with benzodiazepines was in widespread use and some patients developed a dependency (79). Today the rate of benzodiazepine descriptions is lower, but in a survey in Belgium and Luxemburg half of the patients with generalised anxiety disorder (GAD) and MDD were treated with benzodiazepines (80).

Illegal use of drugs: Use of cannabis has been shown to increase the risk of depressive symptoms and suicidal ideations (81) and also predicted later depression in teenage girls (82).

Mortality

Depressed patients treated as in-patients in psychiatric care have been shown to have increased standardised mortality rates compared to the general population (40). There were at the time no studies on mortality in primary care, but one Dutch study reported no higher mortality rate among depressed patients than among non-depressed patients (83).

Significance of depression in society

Societal costs for depression doubled between 1997 and 2005 due to losses of working capacity and sick-listing (2). The costs for sick leave increased rapidly from 1997 and

peaked in 2003 mainly because of increased numbers of cases with psychiatric diagnoses (84), especially among women (85) with burnout depression/burnout syndrome who were employed in the public services (86). The number of sickness benefit days, the number of days/ individual (16–64 years)/year who received sickness insurance. It was at an all-time high level in 2002 reaching among women 52 days, and among men 35 days according to the Swedish National Audit Office.

Risk factors for depression

The prevalence of depression in women peaks at the age of 25–45 years pointing out a vulnerable period in women's lives (87) and single mothers as an especially vulnerable group (88).

Depression and socioeconomic status (SES) are associated and low SES signified a higher risk of being depressed (89). Other risk factors have been recognised, such as negative life events, poor physical health, poor interpersonal relationships, poor socioeconomic conditions and alcohol problems (90).

The influence of heredity has been reported to be important only in severe depression (91).

Migration has an enormous effect on nearly all aspects of the individuals' lives, and immigrant status often involves an increased risk of mental disorders and suicides (92-94).

Good prognostic factors for the outcome of depression were found to be initially mild depression, high educational level, being employed and stable life situation (95).

Gender differences

Female *gender* can be viewed as a risk factor for depression because of the higher prevalence (55).

Threatening *life events* involve a risk of developing depression, and women were found vulnerable to events involving children, housing and reproductive problems and men to financial problems (96).

Gender-related risk factors for depression have been investigated in the population study conducted in Lundby, Sweden where differences were identified in personality traits such as being nervous/tense, which was a risk factor in both men and women (97).

One gender difference regarding *lifestyle* was noticed in US primary care regarding hazardous drinking, which was present among 19% of men and 8% of women with depressive symptoms (98). In recent years Swedish women have developed more harmful alcohol habits, especially young women (99).

Men have a higher rate of *suicide* than women (100, 101). Notably, the number of suicides decreased solely among women as a result of an educational programme in primary care regarding treatment of depression (102). It was therefore suggested that depressed men might communicate other *symptoms when depressed* and thus might not have been recognised by health care personnel (37). *A male depressive syndrome* has been postulated by psychiatrists to include symptoms such as attacks of anger, use of alcohol in order to calm down, extensive working and jogging, heredity of depression or suicidal behaviour or alcohol abuse, or gambling (103-105).

Once the male depression syndrome had been discussed, the Gotland Male Depression Rating Scale (GS) was developed to be especially appropriate for screening men (106).

Guidelines for treatment in primary care

Guidelines for managing depression were found in textbooks in psychiatry and family medicine at the time the study was being planned. They were also found in 'Läkemedelsboken', a book with updated overviews of common diagnoses and their treatments distributed to all physicians in Sweden (107). The importance of establishing a good therapeutic alliance with depressed patients was pointed out, as well as using patient-centred consultations, discussions of pharmacological treatment and considering a psychotherapist contact.

Also, physicians from local Drug Therapeutic Committees visited the PCCs in Sweden regularly and informed about appropriate diagnoses and therapies. Regional Guidelines for Depressive Disorders are presented electronically in the County of Stockholm at www.viss.nu since 2007.

Detecting depression in primary care

Many studies in the 1990s reported missed diagnoses of depression in primary care, but the severity of the missed cases was not discussed (46, 108-111). Later studies have shown higher detection rates for severe depressions (50) and in continuous care (112).

An English study found that primary care physicians had set a diagnosis of depression in the medical records only when it was severe (113). Higher rates of diagnosed depression have been demonstrated among women and persons with a higher level of education (7). Physicians' attitudes to setting a diagnosis in the medical record have been studied in the USA. It was found that in about one third of the patients with MDD other diagnoses were set in the medical record, and one reason for the physicians' hesitation was that the diagnosis might involve harm to the patients, i.e. loss of some insurance benefits (114).

Comorbidity with somatic diseases has been shown to be a barrier to detect depression, as management of the somatic topics tends to take up the whole of the consultation (115). A literature review has reported that a longer consultation time was associated with a more accurate diagnosis of psychological problems (116).

Screening instruments
Many screening instruments with high validity are available for screening for depression (117). However, none of the instruments is diagnostic.

The four most frequently used self-rated screening instruments in primary care are the Hospital Anxiety and Depression Scale (HADS) (118), the Prime-MD (119), the Patient Health Questionnaire (PHQ 9) (120) and the Montgomery-Åsberg Depression Rating Scale, self-rated version (MADRS-S) (121, 122). The overall sensitivity was reported to be 84% (95% CI: 79% to 89%) and the specificity to be 72% (95% CI: 67% to 77%) (123).

The Swedish Council on Health Technology Assessment (SBU) has recently stated that the sensitivity of a screening instrument for depression should reach 80% to be acceptable, and SBU found that the Beck Depression Inventory, second version (BDI–

II), had high enough sensitivity, in contrast to PHQ-9 and HADS, which did not reach the required level of sensitivity to be evaluated as useful for screening of depression (124).

Another method, where the doctor asks only two questions face-to-face, showed a sensitivity of 97% (95% CI: 83% to 99%) and a specificity of 67% (95% CI: 62% to 72%) (125). Also, one single question: 'Have you felt depressed or sad much of the time the past year?' was found to have a sensitivity similar to longer questionnaires (126).

Beck's Depression Inventory
Beck's Depression Inventory (BDI) was constructed by Aaron T. Beck and based on clinical observations of depressed patients (127). It was revised in 1978. Beck stressed the cognitive genesis of depression and noted that negative thoughts were central in depressed patients. Of the 21 items (score steps 0–3, total score 0–63), 13 cover emotions, four contain behavioural dimensions and four cover somatic symptoms. The recommended cut-off score for screening for depression among medical patients was BDI ≥ 10 (128). The BDI score provides guiding information about the severity of depression, where less than 10 indicates no or minimal depression, 10–18 mild to moderate depression, 19–29 moderate to severe depression and scores of more than 30 severe depression (129).

The diagnostic validity has been studied in different settings, including primary care (129-131). In population studies using the cut-off score of ≥ 10, the sensitivity was 84.6% and the specificity 86.4% (128). In a community sample using the cut-off score of ≥ 13 with an interview by a psychiatrist as the gold standard, the sensitivity was 100% and the specificity was 99%, the positive predictive value was 72% and the negative predictive value was 100% (132). Recently, the revised BDI, BDI II, was regarded as one of the best-validated instruments for screening adult patients for depression with a sufficiently documented sensitivity, with a cut-off score of 14 (133).

The Gotland Male Depression Scale
The Gotland Male Depression Scale (GS) was presented in 1997 at the National Convention of Physicians (Läkarstämman) in Sweden. It is a self-rated screening questionnaire with items covering specifically the symptoms described in male depression syndrome in addition to items regarding depressed mood (106). At an alcohol outpatient clinic the correlation between GS and Major Depression Inventory was 0.77 (134). The correlation between GS and WHO-5 among young men enrolling for military service was reported to be –0.56 (135, 136). However, the GS has not been validated among patients in primary care.

Opportunistic and targeted screening

Opportunistic screening
Opportunistic screening signifies that unselected patients are screened for a disease whenever they contact health care. Opportunistic screening for depression in primary care, without any organisational enhancements, had no effects on the diagnostic rates or outcome of depression and therefore has not been recommended in the Cochrane Report (137).

Targeted screening

Targeted screening signifies that screening is restricted to individuals who have a known increased risk of the disease or symptoms of the disease. Targeted screening as a method for finding cases of depression has been mentioned in the Cochrane Report (137) and has been studied in Denmark (138), the USA (139) and the Netherlands (140).

Two-step screening method

A two-step screening method was mentioned in the Cochrane Report as a method that increases the detection rate of depression (137). This method means that patients are first screened with a screening instrument and, in the second step, only those with screening scores above the cut-off limit are interviewed according to the diagnostic criteria.

KNOWLEDGE GAPS

At the start of the project, we identified the following main knowledge gaps:

- Few studies had reported on the prevalence and severity of depression among unselected patients attending drop-in clinics in settings with good socio-demographic conditions.

- Few studies had reported on depression in men and women attending primary care centres with regard to clinical cues for detection and the usefulness of different screening scales.

- Gender differences regarding depression and the association with psychosocial stressors and lifestyle factors, including alcohol consumption, were sparsely reported.

- The long-term mortality was not known regarding patients in primary care who were once diagnosed as having had depression.

AIMS

OVERALL AIMS

To improve the methods for detecting patients with depression in primary care, with special reference to gender differences.

To identify clinical and social characteristics which could be used as clinical cues to identify patients in need of further diagnostic assessment regarding depression.

To explore the mortality rate in depressed patients diagnosed in primary care in a 12-year follow-up perspective.

SPECIFIC AIMS

Study I

1. To estimate the prevalence and severity of depression among unselected women visiting the participating physicians' drop-in clinics.

2. To explore possible differences in socio-demographic and clinical characteristics between depressed and non-depressed women.

3. To evaluate the usefulness of the two-step screening method among women in clinical practice.

Study II

1. To estimate the prevalence and severity of depression among men visiting the participating physicians' drop-in clinics.

2. To compare the usefulness of the Gotland Male Depression Scale with that of the Beck Depression Inventory for detecting depression among men.

3. To compare the results obtained from opportunistic screening with the results from targeted screening and to evaluate the two-step screening method among men.

Study III

1. To explore possible associations between depression, socio-demographic conditions, psychosocial stressors and lifestyles in depressed and non-depressed men and women.

Study IV

1. To explore the all-cause mortality rates during a 12-year follow-up period among depressed and non-depressed men and women and possible associations with socio-demographic, psychosocial and lifestyle factors.

2. To explore the all-cause mortality in this cohort in comparison with all-cause mortality in the general Swedish population.

3. To explore the proportion of unnatural causes of death among the depressed patients.

HYPOTHESES

Study I

We expected to identify a number of women with undiagnosed depression among the women visiting drop-in clinics and to find some differences in socio-demographic and clinical characteristics between depressed and non-depressed women.

Study II

We expected to find more depressed men by using the screening scales GS and BDI jointly than by using the BDI alone, and that opportunistic screening would be less effective than targeted screening for finding men with depression.

Study III

We expected to find differences in psychosocial stressors and lifestyle factors between men and women.

Study IV

We expected that the depressed patients would have higher mortality rates during the follow-up period compared to the non-depressed patients, also when adjustment was made for age and other risk factors, and in comparison to the general population in Sweden. Furthermore, we expected that unnatural causes of death might be prevalent among the depressed patients.

PATIENTS AND METHODS

Design

Studies I, II and III had cross-sectional designs.
Study IV had a prospective design.

Setting

The studies were conducted at a Primary Care Centre (PCC) in Kungsholmen, in central Stockholm, Sweden. This PCC provided health services for approximately 10,000 persons living in the area, and listed with a 'personal physician' among the five specialists in family medicine at the centre. All physicians at the PCC had been working at the centre for many years.

Each physician had approximately 16–20 consultations daily and two thirds of the patients were women. Half of the consultations were unscheduled 10-minute visits during the drop-in hour, which was usually extended to two hours. All physicians at the PCC had their drop-in hours simultaneously.

Power estimation

We aimed to sample a minimum of 30 depressed men and 30 depressed women. The estimated prevalence of depression was 10% in men and 20% in women. Furthermore, we estimated a dropout rate of 10%. We applied for and received approval from the Ethics Committee to screen 500 patients altogether.

Sampling procedure

The sampling of men and women started in October 1997. The target group was men and women aged 18–75 years, who were patients at the drop-in clinic of the two participating female physicians. Sampling of women continued to the end of December 1998 and sampling of men continued until January 2001.

Both opportunistic and targeted screening was used.

Opportunistic screening

Study population
In the opportunistic screening, unselected patients aged 18–75 years visiting the two physicians' drop-in clinics were invited at random days by a study nurse to participate in the study. Upon consent, they were asked to fill in the Beck Depression Inventory (BDI) and a social condition questionnaire (SC) before the consultation with the physician and to return them to the nurse.

Patients who could not answer the questionnaires in the study unaided, e.g. due to dementia or language barrier, were excluded.

From the start of 1998 the Gotland Male Depression Scale (GS) was distributed to both men and women together with the BDI and SC.

The flowchart (Figure 1.) shows the sampling results from the opportunistic screenings of the women and the men. Out of the invited 155 women, 92% agreed to participate. Finally, 135 (87%) completed the BDI correctly, thus female participants numbered 135.

Out of the 254 invited men, 88% agreed to participate and completed the BDI correctly, thus male participants numbered 223.

Invited patients in opportunistic screening
Women n = 155
Men   n = 254
Total   N = 409

Declined/incomplete questionnaires
Women n = 20 (13%)
Men   n = 31 (12%)
Total   **N** = 51

Study population/participants
Women n = 135 (87%)
Men   n = 223 (88%)
Total   N = 325

BDI < 10 (No depression)
Women n = 76 (56%)*
Men   n = 177 (79%)

BDI > = 10 (Possible depression)
Women n = 59 (44%)
Men   n = 46 (21%)

Dropouts/abstained
Women n = 9 (15%)
Men   n = 12 (26%)

Clinical interview/DSM-IV&MADRS
Women n = 50 (85%)
Men   n = 34 (74%)

No depression/No psychiatric diagnosis
Women n = 4
Men   n = 6

Depression
Women n = 35   35/135 (26%)
Men   n = 23   23/223 (10%)
Total   N = 55 (17%)

Psychiatric patients
Women n = 3
Men   n = 0

Crisis reactions
Women n = 8
Men   n = 5

Figure 1. Flowchart of the opportunistic screening of men and women visiting the PCC drop-in clinic screened with BDI. MDD diagnosed according to DSM-IV criteria by the physicians and severity of MDD assessed with MADRS.

Targeted Screening

Study population

Use of targeted screening signifies that only patients with known risk factors or symptoms of disease or disorder are screened. The participating physicians used targeted screening on the days when the study nurse was not working.

Patients (aged 18–75 years) who seemed to have low mood, wept or presented such symptoms as tiredness, anxiety, stress, sleepiness or concentration problems were invited to participate in this study. They received the questionnaires after the visit and returned them by post.

The flowcharts in Fig. 2 and Fig. 3 show the study populations from the targeted screenings of men and women.
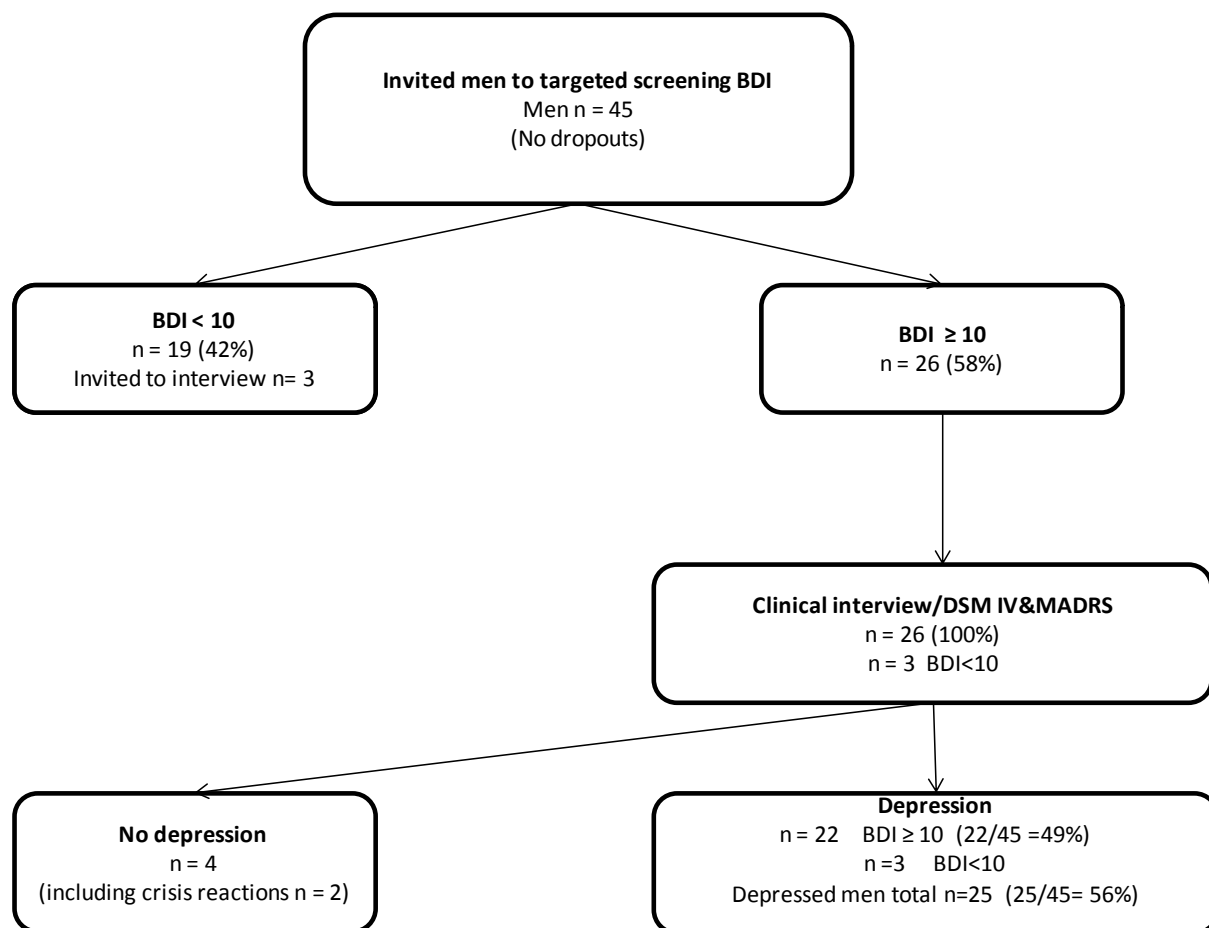

Figure 2. Flowchart of the targeted screening with BDI of men who visited the PCC drop-in clinic. MDD diagnosed according to DSM-IV criteria by the physicians and severity assessed with MADRS.
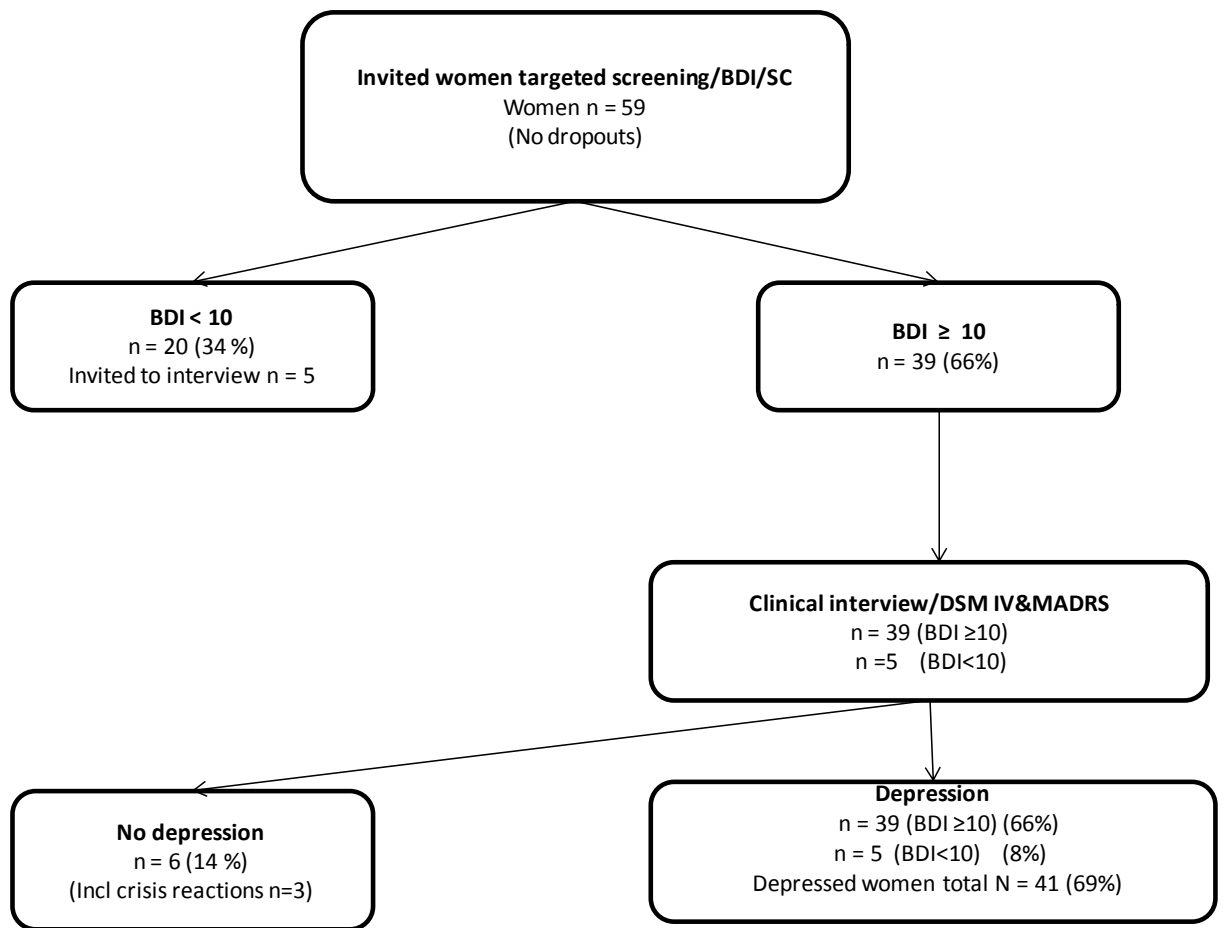
```
                    ┌─────────────────────────────────────┐
                    │  Invited women targeted screening/BDI/SC │
                    │            Women n = 59             │
                    │          (No dropouts)              │
                    └─────────────────────────────────────┘
                         /                         \
          ┌──────────────────────┐      ┌──────────────────────┐
          │       BDI < 10       │      │       BDI ≥ 10       │
          │      n = 20 (34 %)   │      │      n = 39 (66%)    │
          │ Invited to interview n = 5 │ └──────────────────────┘
          └──────────────────────┘                   │
                                      ┌─────────────────────────────┐
                                      │  Clinical interview/DSM IV&MADRS │
                                      │        n = 39 (BDI ≥10)      │
                                      │        n = 5   (BDI<10)      │
                                      └─────────────────────────────┘
          ┌──────────────────────┐      ┌─────────────────────────────┐
          │    No depression     │      │          Depression         │
          │      n = 6 (14 %)    │      │  n = 39 (BDI ≥10) (66%)      │
          │ (Incl crisis reactions n=3) │ │  n = 5  (BDI<10)   (8%)     │
          └──────────────────────┘      │ Depressed women total N = 41 (69%) │
                                        └─────────────────────────────┘
```

Figure 3. Flowchart of the targeted screening with BDI of women who visited the PCC drop-in clinic. MDD diagnosed according to DSM-IV criteria and severity assessed with MADRS.

Thus, in summary, there were 104 participants from the targeted screening, 45 men and 59 women. Three men and 5 women with BDI < 10 were interviewed because of clinical suspicion of depression and are added in the squares 'clinical interview'.

Questionnaires, measurements and data sources

Beck's Depression Inventory (BDI)
BDI was regarded as one of the best validated instruments for screening adult patients for depression, with a high enough documented sensitivity and with a cut-off score of 14 (133). The BDI revised version with 21 items, was used in its self-rating form, where each item is rated 0, 1, 2 or 3 and the total score ranges from 0 to 63 The recommended cut-off score of ≥ 10 for medical patients was used (128). It takes 5–10 minutes to complete the BDI.

The Gotland Male Depression Scale
The GS contains 13 items with scale steps of 0, 1, 2, 3 and a total score range of 0–39. Besides questions about depressed mood, the GS also includes items supposed to predominate in depressed men, i.e. anger attacks, overactive working or sport activities, heredity for suicidal behaviour and harmful alcohol consumption.

In the original questionnaire, two questions, 9 and 13, contain more than one statement. Therefore, these questions were divided into 9a and 9b and 13a, 13b and 13c and our questionnaire contains 16 questions. We adjusted the answers in questions 9 and 13 so that the total score did not increase. For example, when a person had scored 2 on both 9a and 9b, we adjusted this to a sum of 3 (not 4). In this way, we were able to use the cut-off scores suggested by the constructor of the GS.

The recommendation from the authors to interpret the total score on the GS was:

0–13   No indications of depression
14–26   Possible depression, consideration of pharmacological treatment
27–39   Indicates presence of depression, pharmacological treatment indicated

Social Characteristics Questionnaire
The Social Characteristics (SC) Questionnaire was constructed by the researchers to obtain information on:

1. Socio-demographic data: Age, marital status, number of children, education, employment, sick leave and health care contacts during the year before inclusion in the study.

2. Psychosocial stressors and life circumstances: Financial situation, satisfaction with one's work, family or housing situation, perceived level of stress and perceived physical health. Five fixed alternatives were given. These were dichotomised in order to identify a high level of discomfort. (Example: 'How do you rate your physical health?' the answers 'poor' and 'quite poor' were dichotomised as poor and 'excellent' and 'very good' and 'good' as good.

3. Lifestyle questions about smoking and alcohol consumption were included. We asked about daily smoking (Yes or No).

The question about alcohol was formulated as: 'How much alcohol do you consume during an average week?' A picture was attached showing several common drinks representing one standard glass (stg) of alcohol (e.g. one glass, 15 cl, of wine equals one stg alcohol) (141). The patients noted the sum of each sort of consumed stg.

A consumption of ≥ 15 stg by men and ≥ 10 stg by women was dichotomised as above the safe limit, and < 15 stg by men and < 10 stg by women as a safe limit.

4. In addition, the SC questionnaire included questions about weight and height, and problems with pain and pain intensity recorded on a visual analogue scale. Two questions with open text answers were included: 'Do you have any somatic diseases or handicaps?' and 'Has anything serious happened to somebody in your family or among your close friends? '

Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

Depression was diagnosed in a face-to-face interview with the physician according to the criteria for major depressive disorder (MDD) in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) (142).

Montgomery-Åsberg Depression Rating Scale

The severity of depression was measured using the Montgomery-Åsberg Depression Rating Scale (MADRS) containing 10 items with scale steps 0–6 and a total range of 0–60 (30). The first two questions in the MADRS are observer-related. The other items are also rated by the observer in discussion with the patient. The following recommended cut-off scores for assessing severity were used, with the score range of 0–6 interpreted as absence of depressive symptoms and score ranges of 7–19 as mild depression, 20–34 as moderate depression and 35–60 as severe depression (31).

Chart notations

The chart notations were examined by two of the authors for symptoms mentioned at the index visit. Symptoms of anxiety, distress and being worn out, and feelings of low mood, sleeping problems or fatigue were categorised as mental symptoms, other symptoms as somatic.

The National Cause of Death Register

From the National Cause of Death Register, a database comprising all death certificates in Sweden, managed by the National Board of Health and Welfare was used to obtain the causes of deaths regarding the depressed patients. Commitment from the Ethical Board was obtained. The death certificates are classified as secret.

The Swedish National Population Register

The Swedish National Population Register is an open database comprising all persons registered as living in Sweden (143). All deaths are noted in there along with the date of death. Commitment from the Ethical Board was obtained to require the dates of deaths for the patients who did not have any psychiatric disease.

Statistics Sweden

Statistics Sweden is an annual publication that includes information on life expectancy in Sweden in the Life Tables regarding all ages (144).

Procedures after the screening

Evaluation of the questionnaires
The questionnaires were evaluated by the physicians after the index visit.

Three categories of participants were invited by letter to a repeat visit by their physician for a clinical interview concerning depression within two weeks:

1. Participants who scored BDI ≥ 10.
2. Men who scored GS ≥ 13.
3. Participants reporting a consumption of alcohol above the safe limits of standard glasses of alcohol/week (women, ≥ 10 standard glasses; men ≥ 15 standard glasses).

The invitation to the repeat visit was sent three times if needed.

Diagnosing depression and assessment of severity
At the repeat visit the DSM criteria were applied to diagnose a possible depression, and when found, MADRS was applied to assess its severity. Diagnosis and treatment were discussed, as were the patient's answers to the questionnaires as well as other health problems. Moreover, if alcohol consumption was above the safe limits, treatment was started according to guidelines.

STUDY POPULATIONS

Study I

The study population consisted of women recruited by opportunistic screening when they visited the drop-in clinic who had completed the BDI (Fig. 1). The number of participants was 135 women with a mean age of 46.2 years (95% CI: 43.4–48.9).

Study II

The study population consisted of men recruited by opportunistic or targeted screening who had completed the BDI and the GS. The number of participants was 223 men, 190 from opportunistic screening and 33 from targeted screening. Their mean age was 42.7 years (95% CI: 40.8–44.7).

Study III

The study population consisted of both the men and the women from both the opportunistic and the targeted screenings with BDI. The total study group consisted of 404 participants, i.e. the opportunistically screened 266 men and 135 women, and the targeted screened 45 men and 59 women. The participants were 48 depressed men (opportunistic screening n=23, targeted screening n=25) and 76 depressed women (opportunistic screening n=35, targeted screening n=41) and the reference groups of 187 men and 93 women. The reference group was made up of both the patients with

BDI < 10 and those with BDI $\geq$ 10 who had no psychiatric diagnosis. There were no statistically significant differences in age between the groups of depressed and non-depressed men and women.

Study IV

The study population was the same as in Study III.

DROPOUTS

Women
The women who had declined participation in the opportunistic screening (n=12; 8%) did not differ significantly in age from the participants. The women who failed (n=8; 6%) to complete the forms correctly were significantly older than the participants, with a mean age of 63.1 years.

The women who did not turn up for the clinical interview were significantly younger than those who were interviewed, with a mean age of 27.8 years.

There were no dropouts in the targeted screening.

Men
The men who declined participation had a mean age of 54.8 years, not differing in age from those who participated. The men who did not come to the interview (n=12, 26%) had a mean age of 41.7 years, not differing from those who were interviewed.

ETHICAL ISSUES

Approval was obtained from the Ethics Committee of Huddinge Hospital on 1 September 1997 to screen 500 patients (Dnr: 232/97). Permission to use the GS together with the BDI was given by the chairman of the Ethics Committee of Huddinge Hospital on 27 July 1998. Permission to conduct study IV was given by the Ethical Review Board in Stockholm (Dnr: 2011/566-31/1). The ethical principles of the Helsinki Declaration were adhered to. All participants were given oral and written information about the study underlining that they could withdraw at any moment from the study without any consequences concerning care, and were informed that the data would be handed confidentially and that individual data could not be identified.

METHODS

Study I

Women visiting the two participating physicians' drop-in clinics were screened using an opportunistic screening with the BDI with a cut-off score of BDI $\geq$ 10 and answered the SC.

The women with BDI $\geq$ 10 were invited by their physicians to a repeat visit and interviewed regarding MDD according to DSM-IV criteria. If MDD was diagnosed, its severity was assessed using the MADRS. The treatment was planned in cooperation with the patient according to best practice principles. Physical examinations and necessary blood tests were performed. Care for other medical disorders was continued. Women who had reported their weekly alcohol consumption to be $\geq$ 10 stg were invited to counselling.

The women with BDI < 10 constituted the control group.

The prevalence of depression was calculated as well as the distribution of the severity of the depressions. The two-step screening method was evaluated based on participation rates and the prevalence of depression.

The symptoms mentioned at the index visit were obtained from the medical charts and grouped as mental or somatic symptoms and the differences in their distribution were analysed. Possible differences in the distribution of socio-demographic characteristics between the identified diagnostic groups and controls who had a BDI of <10 were analysed.

In order not to miss depression among women with < 10 the physician also invited women to interview if they had mentioned symptoms suggestive of depression at the index visit. The outcome is reported separately and they were analysed in Study I as belonging to controls.

Study II

Men visiting the participating physicians' drop in clinics were screened with opportunistic and targeted screening. Besides the BDI, GS was also used as a screening instrument.

Socio-demographic data including alcohol consumption were received from the SC.

The men with BDI $\geq$ 10 or GS $\geq$ 13 were invited by their physicians to a repeat visit for diagnostics concerning MDD according to DSM-IV. If MDD was diagnosed, the severity was assessed using the MADRS.

In addition, the men who had reported alcohol consumption above the recommended safe limit of $\geq$ 15 stg were invited to a repeat visit. The treatment was planned in cooperation with the patient according to best practice principles. Physical examinations and necessary blood tests were performed. Care for other medical disorders was continued.

The screening with the BDI was compared to the screening with GS regarding detection of MDD.

The prevalence of depression in opportunistic screening was calculated. The outcomes in the proportion of depressed men from the opportunistic and targeted screenings were compared.

The two-step screening method was evaluated based on participation rates and the prevalence of depression.

Study III

The study population included all the men and the women screened by opportunistic or targeted screening.

The depressed men were compared to the non-depressed men and the depressed women to the non-depressed women regarding the distribution of socio-demographic characteristics, psychosocial stressors and lifestyle choices. Patients defined as non-depressed were those with a screening score BDI < 10 together with those who were identified in the interview as having no mental diagnoses.

Logistic regression was used to calculate the association between depression and the possible risk factors in crude models and in main effect models separately for men and women, in order to identify the best risk factor models associated with depression. The risk factor models for men and women were compared with each other.

Study IV

The study population is the same as in study III. The dates of deaths and causes of deaths during the time period from inclusion of the participants in the study until 25 September 2011 were obtained from the National Cause of Death Register. For the non-depressed patients the dates of deaths were obtained from the Swedish National Registration. Dates of deaths and causes of deaths were thereafter recorded using unidentified data.

All-cause mortality data from the Life Tables from Statistics Sweden, based on the entire Swedish population were obtained for the same time period and the same age as the participants in the study and were used to calculate the standardised mortality rates (SMRs).

The SMRs were calculated separately for men and for women in the study population and compared to the SMRs calculated for men and women the Swedish population in the in the same ages, during the same time period in (SMR=1). Socio-demographic data and lifestyle variables were obtained from the SC. The mortality rates between depressed and non-depressed patients are compared. Cox regression, sex and age- adjusted was applied to estimate the Hazard ratios (HRs) for mortality in relation to the explanatory variables. Survival curves were created for depressed and non-depressed patients. Suicide, accident, intoxication and alcohol-related liver disease were classified as unnatural causes of death.

STATISTICS

Statistical calculations were performed using STATA statistical software version 8 in Studies I–II and version 11 in Study IV (145).

Study I

Pearson's chi-square test or Fisher's exact test was used to analyse categorical data and significant differences in proportions. Two-sided significance tests were used and the level of the significance was set at 5%. Differences between groups regarding continuous variables were shown as means with 95% confidence intervals (95% CI). Ordinal data were described with medians and ranges. Pearson's correlation coefficient was calculated to describe the correlation between age and the MADRS score.

Study II

Significant differences between proportions regarding categorical data and continuous data were analysed using the same statistical methods as in Study I. Ordinal data were described with medians and ranges. Spearman's rank correlation coefficient was calculated to describe the relationship between GS and BDI.

Study III

Differences between proportions regarding categorical data and continuous data were analysed using the same statistical methods as in Studies I–II. Ordinal data were described with medians and ranges. Age-adjusted logistic regression for being depressed was used to estimate odds ratios (ORs) with 95% CIs for the explanatory variables. Multivariable logistic regression analyses were performed with manual stepwise inclusion of the actual variables. Model improvement was tested by applying the likelihood ratio test where $p < 0.05$ indicated model improvement. Finally, the Hosmer-Lemeshow test was applied to assess the goodness of fit of the model (GoF). It was considered satisfactory if the p-value was > 0.05.

Receiver operating characteristic curves (ROC curves) for the age-adjusted main effect models were created and also visualised for men in Fig. 4. An ROC curve is a graph showing the relation between the sensitivity and specificity, where sensitivity is plotted against 1-specificity. The numerical value below the graph shows the area under the curve. A model estimating an area under the ROC curve of 0.5 has no predictive value at all. A value above 0.8 is considered to represent a good discrimination. The area under the ROC curve shows the model's capacity to discriminate between those subjects who experience the outcome and those who do not. The positive and negative predictive values of the main effect models were analysed separately for men and women.

Study IV

Significant differences between proportions regarding categorical data and continuous data were analysed using the same statistical methods as in Studies I–III. The mortality

(percentage) and the mortality rate per 10,000 person-years were calculated for the depressed and non-depressed men and women.

SMRs were calculated to compare the mortality rate of the depressed and non-depressed men and women with that of the entire Swedish population of men and women (SMR = 1 = reference) aged 18–75, based on Life Tables for 2001–2010 from Statistics Sweden (146). First, the expected number of deaths for each 1-year age group was calculated. Second, the expected number of deaths for each 1-year age group was summed up for depressed and non-depressed men and women. Finally, SMR was calculated as the ratio between the observed number of deaths (O) and the expected number of deaths (E), thus SMR= O/E.

Cox regression, adjusted for sex and age, was applied to estimate the hazard ratios (HRs) for mortality in relation to the explanatory variables: depression, socio-demographic data, psychosocial factors, perceived physical health, smoking and alcohol use. Possible confounders/effect modifiers (socio-demographic data, psychosocial factors, smoking and alcohol use) were tested.

A final main effect model, also adjusted for sex and age, was developed to identify the most powerful factors.

A test of proportionality for the main effect model was performed and this assumption was satisfied.

Interactions between depression and any of the included variables in the main effect model were tested. None was found.

Survival curves were created to illustrate the mortality rate among depressed versus non-depressed patients.

RESULTS

Study I

Of the 135 participants 59 women, (44%) had a BDI score ≥ 10 (Fig. 1) and had a mean age of 45.3 years, not significantly differing from the 76 with BDI < 10. Fifty women (85%; mean age 48.5 years) performed the diagnostic interview. Those nine women (15%) who abstained from the interview were significantly younger (mean age 27.8) than the interviewed women.

Among the women who accepted participation (n=143) and had BDI ≥ 10 the prevalence of depression was 24.5% (35/143). Out of the 35 identified women with depression ten women had already ongoing treatment with SSRI, whereas in 25 women the depression was not previously detected.

The severity of depression according to MADRS was mild in 43% and moderate in 53%. One woman had a severe depression. The MADRS score ranged from 7–35, with a mean value of 20, and the interquartile range (IQR) was 16-24.

The only statistically significant difference in socio-demographic characteristics between the depressed women and the controls was that a higher proportion among depressed women had been sick-listed 14 days or longer compared to the controls (32% versus 11%) during the year before inclusion in the study (p=0.036).

The depressed women mentioned at the index visit only mental symptoms significantly more often (22% versus 3%) than the controls ((p<0.0001). They mentioned mental symptoms combined with somatic symptoms significantly more often (69% versus 15%) than the controls (p<0.0001). One third of the depressed women mentioned only somatic symptoms.

We found that the two-step method, when performed by the physicians, worked well for identifying depressed women, especially as the dropout rate was low in the second step compared to other studies (147, 148).

Our hypothesis regarding detection of depressed women visiting the drop-in clinics was supported. Differences in socio-demographic and clinical characteristics were identified in the length of sick-listing period and in mentioning mental symptoms.

Study II

The prevalence of depression among the men in the opportunistic screening was 11%. Two thirds (63%) had a mild depression and about one third (35%) had a moderate depression, while one man had a severe depression.

GS and BDI correlated well (r=0.80). Compared to the BDI, the screening with the GS overlooked five depressed men with mild depression.

In addition, one of six among the participants reported an alcohol use of ≥ 15 standard glasses per week, but no statistically significant difference was found between depressed and non-depressed men.

In targeted screening the proportion of diagnosed depression (20/33 = 60.6%) was six times higher than in the opportunistic screening (14/190 = 10.5% = 11%).

Our hypotheses were partly confirmed. We did not detect more cases of depression by screening with GS compared to screening with BDI; however, we found that

opportunistic screening was less effective than targeted screening in detecting men with depression.

Study III

Here, the participants were the men and women from both the opportunistic and the targeted screenings.

In *socio-demographic characteristics* the only statistically significant difference was that the depressed men were unemployed to a higher extent than the non-depressed men.

A strong association was found between depression and the *psychosocial stressors* in both men and women, with no gender difference. The three strongest psychosocial stressors associated with depression in the logistic regression models were in decreasing order: 'being dissatisfied with one's family situation', 'feeling very stressed' and 'perceiving poor physical health'. The ORs in the main effect models varied between 3.1 (95% CI: 1.4–6.6) and 22.4 (95 % CI: 5.8–86.8). The ROC values of the main effect model were 0.88 in men and 0.83 in women. The ROC curve among men is visualised in Fig. 4. The negative predictive values of the models in men were 90.7% and in women 76.5%.

Also, dissatisfaction with one's working situation had high ORs for being depressed, in men 13.2 (95% CI: 4.7–37.5) and women 32.5 (95% CI: 4.1–254.7).

A gender difference was found regarding one of the *lifestyle* questions, as smoking was significantly more common in depressed men than in non-depressed men. For alcohol consumption no statistically significant difference was found between depressed and non-depressed men or between depressed and non-depressed women.

Our hypothesis was only partly confirmed as the most powerful stressors were identical in men and women.
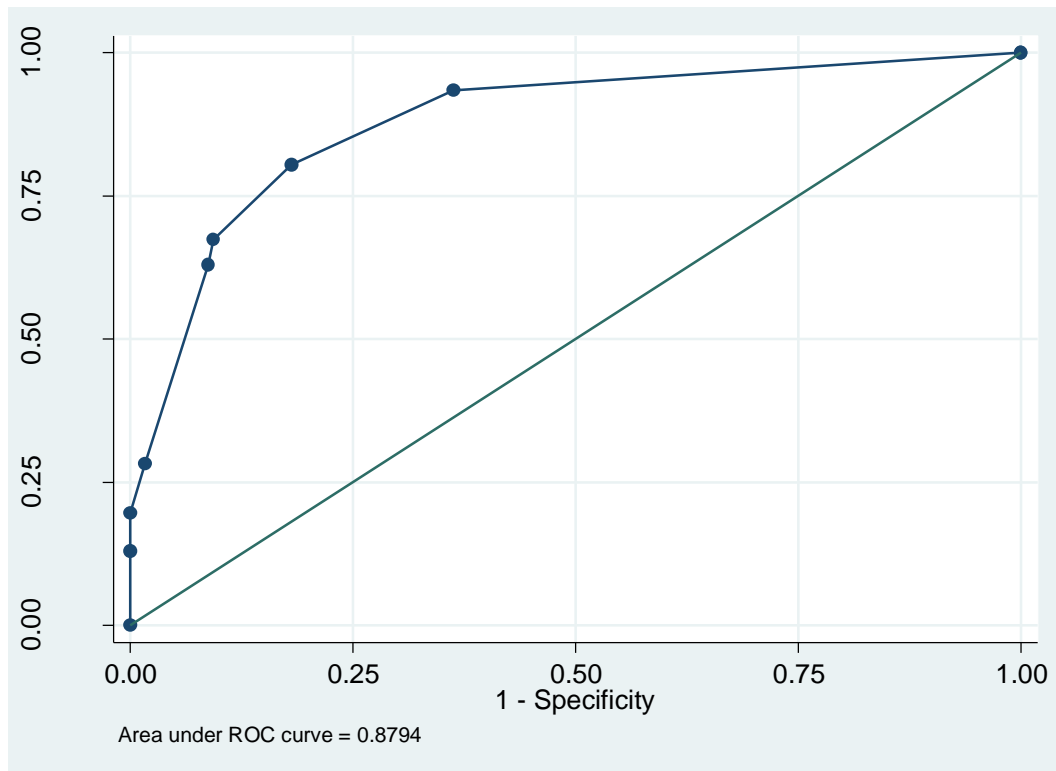
Figure 4. Receiver operating characteristics (ROC) curve visualising the probability among men of being depressed when having (or not having) the psychosocial stressors included in the logistic regression main effect model (dissatisfied with family situation, perceiving very stressed and perceiving one's physical health as poor).

Study IV

The study population here was the same as in study III.

The patients with mild or moderate depression at inclusion had an almost threefold mortality rate compared to the non-depressed patients during the 12-year follow-up period. This difference in mortality rate was significant only among men.

The threefold higher risk of dying remained after adjustment for all other explanatory variables.

The standardised mortality ratios did not significantly differ from those in the Swedish general population.

Nearly one-quarter died of unnatural causes when alcohol-related liver disease was also included.

Thus, our hypotheses were only partly confirmed; the depressed men had a higher mortality rate than their non-depressed counterparts, but there were no significant differences in the depressed men's and women's raised SMRs when compared by gender to the general population in Sweden. Also, nearly one quarter died of unnatural causes when alcohol-related liver disease was also included.
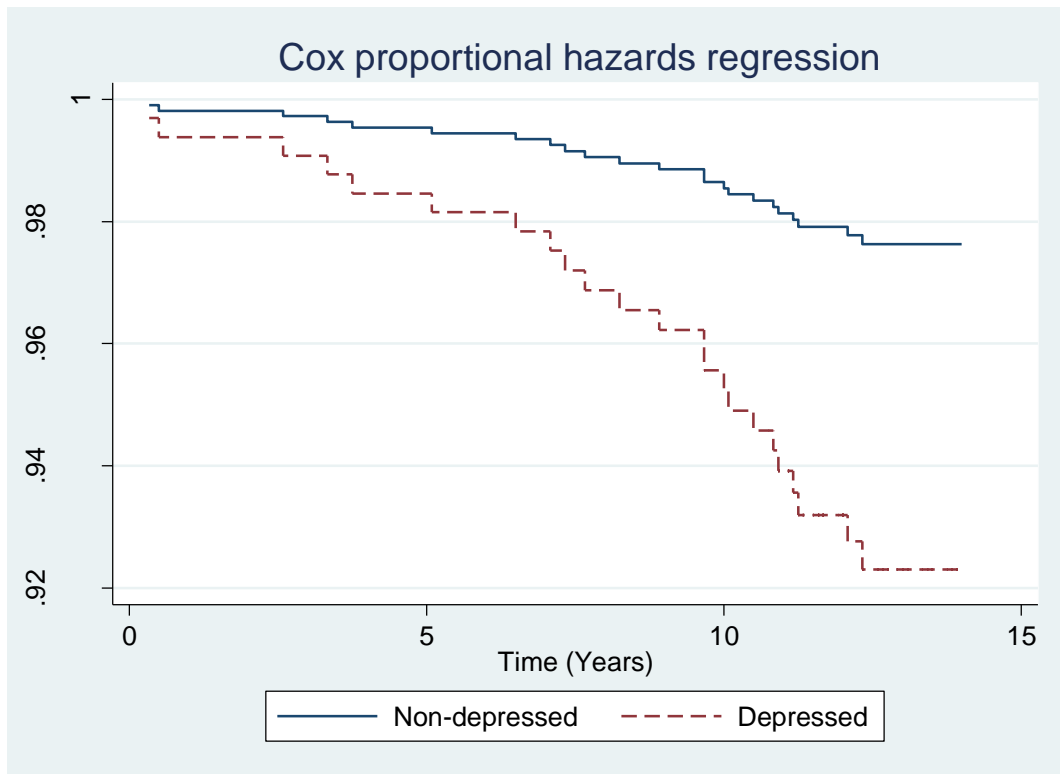
Figure 5. Survival curves from the age and sex-adjusted Cox regression main effect model showing survival among depressed and non-depressed patients during a 12 year follow-up. The upper curve = non-depressed patients. The lower curve = depressed patients.

ADDITIONAL RESULTS

Symptoms mentioned by opportunistically screened men

The women's symptoms mentioned at the index visit were reported in Study I. Here we report the symptoms mentioned by opportunistically screened men, which were obtained in the same way as among the women. Low mood, anxiety, feelings of stress, sleeping problems or concentration problems, ruminating and fatigue were categorised as mental symptoms.

Table 1. Symptoms mentioned among opportunistically screened men and women diagnosed with depression and non-depressed controls with BDI < 10.

	Depressed men		Depressed women		Non-depressed men		Non-depressed women	
N	23		32		177		76	
Symptoms	n	%	n	%	n	%	n	%
Somatic only	16	70	10	31	145	82	65	85
Mixed	3	13	15	47	25	14	9	12
Mental only	4	17	7	22	7	4	2	3

Mental symptoms, as a single symptom or combined with somatic symptoms, did not differ significantly between the depressed men and the non-depressed men.

However, the depressed women mentioned statistically more frequent mental symptoms compared with depressed men (p=0.005, chi2).

The most commonly mentioned mental symptoms among men were: sleeping problems, low mood, anxiety, feeling of stress and fatigue. Among the targeted screened men the most common mental symptoms mentioned were: sleeping problems and feeling stressed.

Like among women the depressed men were sick-listed more than 14 days more frequently than the non-depressed men (38% versus 15%, p=0.001).

Half of the opportunistically screened men had been sick-listed more than 14 days the year before the index visit compared to 17% among the controls (p=0.001).

Among women in Study I the difference between depressed and controls was also significant (p=0.036).

The total range of the MADRS scores among all the depressed men was 7–37, median 19 and IQR 14–22, which may be compared with the values among women with a total range of 7–35, median 20 and IQR 16–24.

DISCUSSION

General comments

Summary of the aims

These studies aimed to elucidate major depression in a primary care setting with mostly good socio-demographic conditions with regard to the prevalence and severity of depression among men and women, and further to find possible clinical cues for detection, to shed light on gender-related psychosocial stressors and lifestyle factors, and lastly to explore long-term mortality among depressed men and women.

Summary of results

Major depressive disorder, mild or moderate, was detected in every fourth woman visiting this unscheduled drop-in clinic meant for quick consultations. Severe cases of depression were rare. Every tenth man was detected as having mostly mild depression, and these depressed men had reported fewer mental complaints than the depressed women.

Detection of depression among patients was done using BDI in a two-step screening procedure by screening unselected patients and, in addition, by a screening targeted to those patients who mentioned mental symptoms; and in the second diagnostic step evaluate against the DSM-IV criteria for major depressive disorder, also including assessment of the severity with MADRS.

Screening men with the Gotland Male Depression Scale did not increase detection of depression among men. The same three psychosocial risk factors – being dissatisfied with one's family situation, feeling very stressed and perceiving one's physical health as poor – were equally associated with depression among men and women. Finally, the mortality rate was higher among the depressed men visiting drop-in clinics than among the non-depressed but their standardised mortality rates did not differ statistically from that of the general population in Sweden.

Evaluation of methods and results with regard to the time period

Patients with burnout depression were categorised as depressed if they satisfied the criteria for MDD. The sampling of patients was performed during the years when sick-listing increased rapidly in Sweden because of burnout syndrome. The criteria for these diagnoses were specified in 2003 and described to include specific symptoms of emotional exhaustion, rapid onset of cognitive dysfunction and rumination about working situation which separated them from depressed patients usually seen in psychiatric care (27). Notably, dissatisfaction with the work situation was common among the depressed men and women, and some of them might have been diagnosed today as burnout depression.

Moreover, in the early 1990s there was a financial crisis affecting many public service institutions with many women employees, and women working in public sector that had been shown to be at risk of the 'burnout syndrome' (86). Such consequences might have influenced the prevalence found here.

Recently, a Swedish research group has identified biochemical markers for psychosocial stress in blood tests among women with burnout depression, and in the future it might be possible to identify these markers among women who are under prolonged psychosocial stress (149).

Methods

This project had a practice design, often labelled as action research, which is a research method derived from social research where the aim is to improve practice handling. It involves the actor and the person/patient/client (150). At that time many projects in primary care were organised using a similar research design (151, 152), and also later (153, 154). Its strength is its proximity to clinical practice, thus creating a sound pragmatic validity, while its limitations are due to its often single practice design and thus a reduced ability to generalise the results.

Screening procedures

The two-step screening method used here worked well with a low dropout rate in the second step when the patients' own primary care physician had invited them to a repeat visit. By comparison, a higher dropout rate was shown in other studies where invitations to the repeat visits were made by a research team (147, 148). This showed confidence in the primary care physician and underlines the importance of continuity of care.

Opportunistic screening

There were several problems in using an opportunistic screening method.

Here, a low cut-off score for the BDI was used in order to reach high sensitivity, but nearly one half of all women and one-fifth of the men had to be invited to the diagnostic interview. Today a higher cut-off score of ≥ 14 of BDI II is recommended by SBU (124). Using that cut-off value would have reduced the number of repeat visits, but some patients with mild depression would then have been missed.

Using the GS did not catch more cases of depression among men.

The BDI and GS with the cut-off scores used here were, as expected, not specific for depression; instead patients with other mental problems were detected but also these patients needed help, which is an important aspect to consider for primary care physicians.

Some patients attend their primary care physicians often. It is not realistic to screen them at every visit, as we observed early in the project. A later review concluded that opportunistic screening for depression is not cost-effective in primary care (137).

Targeted screening

In order to reach the required number of patients, targeted screening was used among patients who had mentioned any mental problems, as only opportunistic screening of men would have taken very long time.

Here, a patient-centred consultation was used by both the research doctors. In Denmark, the accuracy of the physicians' 'clinical suspicion' of depression in patients has been shown to yield high ROC values; the method has been demonstrated to be more efficient than the screening programme recommended by the Danish National Board of Health (138). A patient-centred consultation model has been shown to have

lower sensitivity than the MADRS-S and PRIME-MD, resulting in fewer diagnostic interviews being required (155).

Discussion of the results

Prevalence and severity

A meta-analysis of studies regarding diagnosed depression using data from 50,000 primary care patients in 41 countries reported a prevalence of 20% (11% up to 23%), thus a prevalence in line with these results (156). However, the measured prevalence of depression depends largely on societal factors in the setting, the patients' behaviours, and the health care organisation. The idea of the drop-in clinic was that it was the patients' own decision to consult the physician with no barriers and without any restrictions or declaring their symptoms in advance.

Here, the majority of the patients with depression were new cases. The prevalence was comparable to that found among multi-ethnic patients in Jordbro, a suburb of Stockholm (9), but higher than in a small town north-east of Stockholm (157). Among elderly patients in Gothenburg 15% had depressive symptoms according MADRS-S (158).

Severe depressions in primary care patients were proven to be very rare also in studies from Sweden among immigrants with long-term disability and pain (159) and in Finland (6). However a higher prevalence of severe depression was identified in a Danish primary care study when ICD-10 criteria were used (160).

Psychosocial stress and lifestyle

Depression was previously categorised as endogenous or reactive but for a period the preceding factors for depression were scarcely debated. Reactive depression was seen as depressions following stressful events or losses. There is a renewed focus on societal determinants of depression (161).

In our study, men and women had the same psychosocial stressors associated with depression, which facilitates using them as clinical cues, but above all as rule-out criteria for depression. Consequently, it seems that the stress linked to 'double responsibilities' of working life and family responsibilities among women (151) might also affect men today. This is also reflected in the general conceptions and the rules of the social security system in Sweden which stimulate fathers to take part in child care from the beginning. Whether relational stressors are important predicting factors in other settings as well, and in other countries, should be an interesting subject for future studies.

In this setting, only a few men were unemployed, or smoked, yet they were more frequent among the depressed men. In general, alcohol use above the safe recommended limit was high among the men. Contrary to other research, there was thus no statistical evidence of association between excessive drinking and depression (76, 77).

Patients with a burnout depression were included here among the depressed patients. It has since been shown that these patients often need multimodal treatment and their recovery takes a long time (162, 163).

Mortality

Mortality rates among primary care patients with depression in Sweden have not been presented before. This cohort of depressed and non-depressed patients was followed up regarding mortality for 12 years. More depressed patients had died compared to the non-depressed. This difference was probably due to the fact that the healthy non-depressed both men and women had very low SMRs, especially evident among the non-depressed men, thus these figures must be interpreted with precaution.

Unnatural causes of death were found as well, but the interpretation is restricted since data on causes of death among the non-depressed patients were not analysed. This too should be subject for future studies.

Patients with depression in primary care often have comorbid somatic and psychiatric diseases (6, 9); and depression has been found to be common among women with cardiovascular disease (164). In a Swedish population study, depression was identified as a risk factor for developing cardiac disease, in both men and women aged 25–50 years (165). An elevated risk of cardiovascular and coronary deaths has also been shown among depressed patients (166-168).

Alcohol use

The prevalence regarding alcohol use above safe limits is comparable to that in other Swedish primary care settings, where a study showed that half of the patients with harmful or hazardous alcohol use also had symptoms of depression and anxiety (169).

Discussion of the methods

Instruments used

The BDI is regarded as one of the best-validated instruments for screening for depression, but a BDI with a higher cut-off score (≥ 14) than used here is recently recommended by SBU (133). A higher cut-off score would have reduced the number of repeat visits here, but some patients with mild depression would have been missed.

The GS, including questions on changes in the use of alcohol and pills or intense working and sport activities, overlooked five cases of mild depression. Whether answers in these questions were associated with depression has not been analysed yet. Interestingly, some depressed men mentioned spontaneously that they found the GS questions concise and clear and 'nailed it' regarding their problem.

MADRS has been shown to have high inter-rater correlation properties in primary care also among multicultural patients, and is a reliable method (159).

The diagnostic process

According to the exclusion criteria of MDD, somatic disease as reason for depression must be ruled out. The researchers met the depressed patients twice before the diagnosis, and systematically used the DSM-IV criteria. In addition, somatic examinations were also performed by the physicians to find and treat possible somatic reasons for the patients' symptoms.

Risk of over-diagnosis?

Recently, a meta-analyses has reported on primary care physicians' accuracy in detecting depression using unassisted screening – 'gut-feeling' (156). They found that

the number of patients misidentified as depressed was higher than the missed cases, but they were good at ruling out depression.

It has been pointed out that there is risk of over-diagnosing when using DSM criteria since heavy dysfunction is not mandatory for the diagnosis of MDD (170). Also the book 'Pillret' reports on the history of how SSRI marketing in Sweden resulted in high prescription levels for depressed mood and anxiety (171).

Correct diagnosis is the first step to good treatment. The ideal diagnostic process follows a methodology named LEAD (Longitudinal, Experts, All Data Procedure), described in detail in the SBU report (133). The method involves having all data, sometimes also from close family members, medical records, diagnostic interviews and the questionnaires are all evaluated by experts in a team. Such methods can be used in primary care in severe cases, when psychiatric specialists are consulted as well.

Risk of under-diagnosis?

To confirm the diagnosis of MDD, the patient's symptoms must be evaluated against the diagnostic criteria in ICD-10 or DSM-IV. It is a problem for the physician to keep in mind the symptoms in MDD, while discussing the patient's other treatments, and the risk of missed diagnosis is highest when comorbid somatic diseases are present (172). The questionnaires about depressive symptoms are helpful as the depressive symptoms are systematically registered.

Here, the use of BDI seemed to facilitate discussion about the patients' mental feelings. Patients' depressed thoughts are made visible to the physicians and perhaps also to the patients in their answers. Discussing the answers also helped to keep the focus on mental problems, so often 'pushed aside' by other medical needs.

An investigation conducted by the National Board of Health and Welfare found that today in Sweden about one quarter of primary care physicians always or sometimes use a questionnaire when investigating depression, and MADRS or MADRS-S were the most commonly used questionnaires (133).

There might be a risk of missed diagnosis of depression among men since only a few of the men mentioned mental symptoms at least when visiting the drop-in clinic. Asking men about their social situation and stress proved to be important.

Here the GS did not improve the detection rate.

Strengths and limitations

The major strength of this project is the action research design including two female specialists in primary care who involved their patients in their own practices with a low dropout rate. It resulted in new insights into screening and detection of depression in primary care practice as well as long-term mortality from a gender perspective. Another strong point is that the physicians met the depressed patients at least twice before the diagnosis, and that they continued caring for them. Furthermore, valid and reliable tools to diagnose depression and to assess the severity of depression were used and the studies also included lifestyle factors and alcohol questions.

There are limitations such as reduced ability to generalise due to its single-site design, although the results should be possible to transfer to similar settings.

Moreover, somatic diseases were not systematically recorded and the rate of possible depression among those patients having BDI or GS ratings below cut-off values were not assessed, preventing a calculation of predictive values.

CLINICAL IMPLICATIONS

Patients who attend primary care physicians' drop-in clinic have varying problems, ranging from common colds to serious diseases and depression is as prevalent among them as among other patients.

For patients with comorbid diseases access to care with continuity is important, a drop-in clinic is only one form of access to the primary care physician.

A possible cue for depression was identified when a patient mentioned mental symptoms. In this situation the physician would recommend further examination and use diagnostic instruments for depression. Primary care physicians can combine this with a physical check-up of the initial problems.

Questions about family relations and other psychosocial stressors can be applied in almost all types of consultations, and can be used as an indicator of depression or as a rule-out question for depression, in men and women alike.

Answering the BDI or other validated questionnaires for depression might be a signal to the patient that the physician is ready to discuss mental problems. In addition, answering for example the BDI might arouse the patients' consciousness about their depressive thinking. Communication about depression between the patient and physician is thereby facilitated.

Examination of depressed patients regarding somatic health and care of somatic diseases according to best practice is very important as they might have a risk for preterm death.

Patients with e.g. diabetes and coronary heart disease comorbid with depression are high risk patients for preterm death and must be followed attentively.

CONCLUSIONS

The prevalence and severity of depression was comparable to that in other primary care settings. Depressed women had often mentioned mental symptoms. Questions about family and working situation, feelings of stress and feelings about one's physical health could be used as risk indicators for depression in clinical practice for both men and women. Moreover, the long-term follow-up results underline the importance of finding patients with depression and thoroughly examine them also regarding their somatic health.

FUTURE STUDIES

It would be valuable to study further gender issues in diagnostics and detection of depression in different settings using multiple-site research centres, and also to study how men and women recognise depressive symptoms, e.g. by a qualitative design. Performing long-term studies on intervention methods for depression in primary care would be valuable, e.g. regarding outcome, sick-leave and mortality and mortality cause, comparing them to a non-depressed group and to those with multiple health problems.

SAMMANFATTNING PÅ SVENSKA

SYFTEN

Avhandlingens syften var att undersöka förekomsten och svårighetsgraden av depression hos oselekterade patienter på en "drop-in" mottagning på en vårdcentral i centrala Stockholm samt att identifiera för depression typiska kliniska kännetecken, och att bedöma användbarheten av skattningsformulär. Dessutom undersöktes eventuella samband mellan depression, psykosociala stressfaktorer och livsstilsfaktorer i ett könsperspektiv och användbarheten av en ny skattningsskala för depression bland män. Slutligen undersöktes i en långtidsuppföljning dödstalen bland de deprimerade patienterna jämfört med patienterna utan depression och svenska befolkningen.

BAKGRUND

Primärvårdspatienter har ofta många olika, både akuta och kroniska åkommor och samtidig förekomst av depression kan vara svår att upptäcka vid ett besök. Depression medför lidande och funktionsnedsättning för den som drabbas och stora kostnader för samhället och det är därför viktigt att upptäcka och behandla depression.

Studier under 1990-talet hade visat att ungefär hälften av fallen med depression inte blev diagnostiserade vid ett givet tillfälle. Att förbättra upptäckten och diagnostiken av depression kändes särskilt angeläget under 1990-talet då de nya läkemedlen för behandling av depression, serotonin-återupptagshämmarna (SSRI), med färre biverkningar än tidigare läkemedel hade kommit ut på den svenska marknaden.

Depression är känd som dubbelt så vanlig hos kvinnor som hos män. Låg socioekonomisk status är en känd riskfaktor för depression liksom negativa livshändelser, dålig kroppslig hälsa, relations- och alkoholproblem samt migrationsstress, men om riskfaktorerna var likartade för män och kvinnor var okänt.

Självmord är vanligare bland män än bland kvinnor. Depression kan uttrycka sig på andra sätt hos män an hos kvinnor, vilket skulle kunna medföra att depression hos män lättare förbises av sjukvårdspersonalen. Förekomst av "manlig depression" hade diskuterats som en möjlig faktor, inkluderande attacker av ilska, irritabilitet, sänkt impulskontroll, överaktivitet inom arbete eller idrott eller bruk av alkohol i lugnande syfte. En särskild skala hade därför utvecklats för att hitta män med depression "Gotlandsskalan för skattning av manlig depressivitet" (GS) där även sådana frågor ingår. Denna hade dock inte testats i primärvården.

Studier hade också visat att patienter med hjärt-kärlsjukdom eller diabetes har högre dödlighet om de är deprimerade. Få långtidsstudier rapporterar om dödligheten bland deprimerade primärvårdspatienter.

Diagnostik av depression och mätning av svårighetsgraden

Diagnosen depression är i denna avhandling ställd enligt kriterierna i det psykiatriska diagnossystemet DSM-IV. Det centrala i kriteriet för depression (Major depression) är sänkt sinnesstämning och/eller oförmåga att känna glädje i kombination med minst fyra

andra symptom, till exempel initiativlöshet, sömnbesvär, koncentrationsstörning och mindervärdighetskänslor.

Depressionens svårighetsgrad klassificeras som mild, måttlig eller svår. Vid mild depression orkar personen genomföra sina vanliga aktiviteter och vid svår depression har personen svårt att genomföra även vardagliga göromål och plågas av skuldkänslor och självmordstankar. Montgomery-Åsberg Depression Rating Scale (MADRS) används i klinisk verksamhet och forskning för skattningen av svårighetsgraden i ett depressivt tillstånd.

PATIENTER OCH METODER

Screeningsmetod för depression

En "tvåstegsmetod" användes för att hitta patienter med depression. Det innebar att patienter först svarade på frågor om depressiva symptom i ett screeningformulär. I nästa steg intervjuades de med poäng över ett tröskelvärde med syfte att avgöra om kriterierna för depression är uppfyllda. Metoden användes på två sätt: 1. för att screena alla patienter i målgruppen utan selektion (opportunistisk screening) eller 2. screening riktat till de patienter som hade tecken eller symtom som kan förekomma vid depression (riktad screening).

Beck Depression Inventorium (BDI) (21 frågor, totalpoäng 0–63) har en hög känslighet vid screening av depression och innehåller frågor om depressiva symptom och tankemönster och användes för screening med tröskelvärdet BDI $\geq$ 10. Män screenades dessutom också med GS (13 frågor, totalpoäng 0–39) där tröskelvärdet $\geq$ 13 användes.

Övriga data

Ett frågeformulär med sociala bakgrundsdata (SC) användes, där även frågor om stressfaktorer samt alkoholförbrukning och rökvanor ingick.

Uppgifter om vilka symtom patienten angivit vid läkarbesöket erhölls från patientjournalen. De klassificerades som kroppsliga eller mentala.

I Studie IV hämtades data från Socialstyrelsens dödsorsaksregister, Folkbokföringsregistret, och Statistiska centralbyrån.

Målgrupp, procedur och diagnostik

Målgruppen var patienter i åldern 18–75 år som sökte på två läkares (specialister i allmänmedicin) "drop-in" mottagning på en vårdcentral i centrala Stockholm. Alla läkarna på vårdcentralen hade sin "drop-in" mottagning varje dag mellan 10.00 och 12.00, då patienterna kunde besöka sin husläkare utan föregående tidsbeställning. Rekryteringen av patienter till studien pågick mellan åren 1997 och 2001.

En sjuksköterska frågade patienter i väntrummet om deltagande i studien (opportunistisk screening) och de som accepterade besvarade i frågorna i BDI, SC och GS och återlämnade dessa till sjuksköterskan före läkarbesöket.

De dagar då sjuksköterskan inte var på mottagningen tillfrågade läkarna själva de patienter som vid besöket på den öppna mottagningen visade tecken på eller uppgav symtom som kunde tyda på depression att delta i studien (riktad screening). Dessa deltagare besvarade frågorna i BDI, SC och GS efter besöket och skickade sedan formulären till husläkaren.

Till diagnostisk intervju hos sin läkare enligt DSM-IV och MADRS kallades följande patienter: a) de med BDI ≥ 10, b) de med GS ≥ 13 samt c) de som angivit alkoholkonsumtion mätt i antal standardglas per vecka som kan innebära hälsorisk (män ≥ 15, kvinnor ≥ 10 standardglas). Vidare behandling och uppföljning planerades vid återbesöket.

Kvinnor och män med BDI < 10 klassificerades som kontroller samt de som vid intervjun befanns vara friska.

Studiepopulation i studierna I–IV

Deltagare var de kvinnor och män som screenades enligt ovan som hade lämnat in godkända frågeformulär. Deras medelålder var 45,3 år (95 % konfidensintervall 43,9–46,7).

Studie I: Totalt 135 kvinnor från den oselekterade screeningen som svarade i BDI och SC.

Studie II: Totalt 223 män, varav 190 från opportunistisk och 33 från riktad screening, som svarade i BDI, SC och GS.

Studie III och Studie IV: Totalt 404 patienter, 235 män och 169 kvinnor, från både opportunistisk och riktad screening som svarade i BDI och SC.

STATISTIK

Skillnader mellan grupper analyserades med Chi 2 eller Fisher's test. Logistisk regression användes för beräkning av riskkvoter (OR) för depression och för sammansatta riskfaktormodeller. Dödstal beräknades baserat på summan av observerat antal avlidna delat med varje individs risktid. Standardiserad dödlighet beräknades. Cox's regression användes för att beräkna den relativa risken att dö under observationstiden på 12 år vid förekomsten av de förklarande variablerna, och uttrycktes i hasardkvoter (HR).

RESULTAT

Studie I

Prevalensen av depression var 25 % bland de som initialt hade tackat ja till att delta i studien (n=43). Depressionen var mild i 43 % och måttlig i 53 %. Endast ett fall av svår depression identifierades. Ett kliniskt kännetecken var att flera deprimerade kvinnor än kontroller hade nämnt något psykiskt symtom vid det första besöket (69 % vs. 15 ; p<0,001). Vid det andra besöket identifierades även andra psykiska tillstånd, såsom krisreaktioner, och dessa kvinnor hade behov av och erbjöds hjälpinsatser.

Studie II

Totalt 40 deprimerade män identifierades. Prevalensen av depression i den opportunistiska screeningen var 11 % och 61 % i den riktade screeningen. Mer än hälften av depressionerna var milda, resten var måttliga. Endast en man hade svår depression. Inga ytterligare män med depression identifierades vid screeningen med GS. Nästan var sjätte screenad man (18 %) angav en alkoholkonsumtion på en nivå som kan innebära hälsorisker (≥ 15 standardglas per vecka), men andelen högkonsumenter var inte högre bland de deprimerade än bland kontrollerna.

Studie III

Riskfaktormodellerna innehöll samma riskfaktorer för depression hos män och kvinnor och var (i fallande ordning): missnöje med familjesituationen, upplevd hög stressnivå och upplevd dålig fysisk hälsa. Oddskvoterna (OR) varierade mellan 3,1 (95 % CI: 1,4–6,6) och 22,4 (95 % CI: 5, 8–86,8). Det negativa prediktiva värdet av modellen var 90,7 % för män och 76,5 % för kvinnor. Missnöje med arbetssituationen hade förhöjd OR hos båda könen, män OR 13,2 (95 % CI: 4,7–37,5) och kvinnor OR 32,5 (95 % CI: 4,1–254,7). Arbetslöshet och rökning var associerade med depression endast bland männen.

Studie IV

Flera av de deprimerade patienterna hade avlidit jämfört med de icke-deprimerade (11 % vs. 4 %) under observationstiden; sambandet var signifikant bara för männen (p=0,014). Dock hade de icke-deprimerade männen i vår studie en mycket låg dödlighet. De deprimerade patienternas standardiserade dödlighet skiljde sig inte signifikant från den svenska befolkningen. Den enda av de studerade variablerna som innebar signifikant förhöjd risk att avlida under observationstiden var att ha fått diagnosen depression, detta både som enskild faktor (HR 3,1 95 % CI 1,4–7,1) och i en sammansatt modell (HR 3,3; 95 % CI: 1,4–8,1). Onaturliga dödsorsaker, inberäknat självmord, oklar förgiftning och alkoholrelaterad leversjukdom förekom i ungefär en fjärdedel av alla dödsfall bland de deprimerade patienterna.

Tidigare ej publicerat material

Söksymptomen bland män i den opportunistiska screeningen granskades och grupperades på samma sätt som bland kvinnorna i Studie I. De deprimerade männen hade inte nämnt psykiska symptom oftare än de icke-deprimerade männen vid besöket. De deprimerade kvinnorna hade i signifikant högre grad nämnt något psykiskt symptom jämfört med deprimerade män (p=0,002).

SLUTSATSER

Eftersom studierna endast omfattar två läkares patienter är generaliserbarheten begränsad, men resultaten torde kunna överföras till liknande primärvårdspopulationer.

Var fjärde kvinna och var tionde man som sökte på den öppna mottagningen hade mild eller måttligt svår depression, med något enstaka undantag. Med GS identifierades inga ytterligare depressioner jämfört med screening med BDI. GS är dock det enda screeningsformuläret för depression som innehåller frågor om alkohol eller lugnande tabletter, en viktig fråga att ställa till patienter med depressiva symptom, oro och ångest.

Screening riktad till patienter som nämnde mentala symtom fungerade bättre än att screena alla patienter.

Tecken på depression hos kvinnor kunde identifieras i den kliniska bilden i att de oftare än icke-deprimerade hade nämnt psykiska symptom i den oselekterade screeningen; detta fann vi dock inte bland de deprimerade männen i motsvarande situation.

Tre frågor, som lätt kan ställas vid patientmöten, nämligen frågor om patientens familje- och arbetssituation, självupplevd hälsa och upplevd stress, tycks kunna användas som indikatorer för förekomst av depression både hos män och kvinnor och torde fungera bättre än en oselekterad screening. Om dessa riskfaktorer inte föreligger hos män är sannolikheten liten att de har depression.

Patienter med depression behöver följas upp noggrant avseende både kroppsliga sjukdomar och depression, eftersom de synes ha förhöjd risk att avlida.

Att be patienten besvara ett frågeformulär om depression kan fungera som en signal till patienten att läkaren är beredd att diskutera även sådana symtom och samtalet kring patientens svar kan underlätta kommunikationen och diagnostiken av depression. Detta är dock ett ämne för fortsatta studier.

ACKNOWLEDGEMENTS

I wish to express my deepest gratitude to everyone who has supported and helped me towards my doctoral thesis.

The Centre for Family Medicine CeFAM was the confident boat navigated by the professors with never-ending enthusiasm for research and with the skilled crew always ready to help me with any kind of problem. The courses in research methodology and statistics, and research meetings with deeply committed teachers and participants gave me an identity as a researcher to stand on.

Professor Emeritus Hans Åberg supported our study from the beginning, followed by Professors **Jan Sundquist** and **Lars Agréus** and today **Gunnar Nilsson.** They have all believed in the study and have shown great patience.

Associate Professor Anna-Karin Furhoff was my first supervisor and together with Professor **Anna Åberg-Wistedt** and my colleague **Estera Wernering** MD, we planned the studies and they are also co-authors of the first article.

Professor Emeritus Sven–Erik Johansson, co-supervisor, co-author and teacher in statistical epidemiology, gave me never-failing support with such speed in solving statistical problems that I forgot that it might be difficult. Without him I would have failed!

My main supervisor since 2008 has been **Associate Professor Monica Löfvander**. With never-failing energy and clarity she helped me to analyse data and to understand the contexts. Suddenly I was no longer lost in details; instead I could make research results comprehensible!

Lars G. Backlund, MD, PhD a reliable and perspicacious co-supervisor and co-author was always helpful with clever advice.

The major part of the time during these years I worked at the primary care centre. **All the colleagues and staff** have made essential contributions. Their efforts covered many areas, explaining to the patients why I was not there, taking good care of them and keeping a warm atmosphere. The sampling of participants for the study was made in cooperation with Estera Wernering, MD.

My husband, **Filipe de Sousa Soares**, has supported me, not only with practical things in daily life but also encouraging me to continue with our recreational activities and breaks in our country house together with our children **Sofia and Henrique** and their families.

My family in Portugal, **Luisa and Manuel de Sousa Soares** showed great generosity by inviting me to their peaceful house in Brejo where I worked with the thesis.

My close friends **Birgitta Danielsson** MD, PhD and **Margareta Granbom Holmquist**, MD have given me all the possible support that friends can give since our first term as medical students at Karolinska Institutet.

APPENDICES

Major depressive disorder diagnostic criteria DSM-IV

Major depressive disorder (MDD) is a mental diagnosis with defined symptoms in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). In MDD a combination of five mental symptoms have to be present most of the time for at least for two weeks.

Depressed mood and feelings of worthlessness and hopelessness or absence of feelings of gladness are mandatory, and a combination of at least four additional symptoms is required to fill the criteria of MDD. Some exclusion criteria also have to be evaluated.

List of symptoms in major depressive disorder
Mandatory symptoms: Depressed mood or loss of interest and pleasure
Together with at least four of the following seven symptoms:
Weight loss
Insomnia or hypersomnia
Psychomotor agitation or retardation
Fatigue or loss of energy
Feelings of worthlessness or inappropriate guilt
Diminished ability to think or concentrate or indecisiveness
Recurrent thought of death, recurrent suicidal ideation

Exclusion criteria are: 1. Criteria for mixed mania/depression are not fulfilled. 2. The symptoms result in suffering and decreased functions. 3. The symptoms are not a result of use of drugs, or medication, somatic illness or injury. 4. The symptoms are not better explained by grief.

Gotland Male Depression Scale (in this study)

Har Du eller andra hos Dig under den senaste månaden märkt någon av följande beteendeförändringar som varken Du eller andra riktigt känner igen?

1. *Minskad stresstolerans / mer än vanligt lättstressad.*

   ❑ Inte alls
   ❑ I viss mån
   ❑ Stämmer rätt väl
   ❑ Stämmer i hög grad

2. *Ökad aggressivitet, brusar lättare upp än vanligt, har "kort stubin".*

   ❑ Inte alls
   ❑ I viss mån
   ❑ Stämmer rätt väl
   ❑ Stämmer i hög grad

3. *Känsla av utbrändhet och tomhet.*

   ❑ Inte alls
   ❑ I viss mån
   ❑ Stämmer rätt väl
   ❑ Stämmer i hög grad

4. *Långvarig oförklarlig trötthet.*

   ❑ Inte alls
   ❑ I viss mån
   ❑ Stämmer rätt väl
   ❑ Stämmer i hög grad

5. *Att du är mer lättirriterad, rastlös, missnöjd.*

   ❑ Inte alls
   ❑ I viss mån
   ❑ Stämmer rätt väl
   ❑ Stämmer i hög grad

6. *Att det är svårt att fatta även enkla vardagsbeslut.*

   ❑ Inte alls
   ❑ I viss mån
   ❑ Stämmer rätt väl
   ❑ Stämmer i hög grad

7. *Sömnrubbningar som t.ex: svårt att somna, vaknar många gånger under natten, vaknar för tidigt, sover för lite eller för mycket.*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

8. *Oro / ängslan / obehagskänsla framförallt på morgonen.*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

9. *Att du använder alkohol eller tabletter i lugnande och avkopplande syfte.*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

10. *Överaktivitet eller avreagering med hjälp av hetsigt och rastlöst idrottande, jogging eller arbete, för mycket / för lite ätande.*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

11. *Att du har blivit förändrad på ett sätt som gör att varken Du eller andra känner igen Dig eller tycker att Du är omöjlig att ha att göra med.*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

12. *Har Du känt Dig eller verkat dyster, negativ eller hopplös till sinnes, "sett allt i svart"?*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

13. *Har du själv känt eller andra lagt märke till ökande tendenser till självömkan, klagande, "ynklighet"?*

- ❑ Inte alls
- ❑ I viss mån
- ❑ Stämmer rätt väl
- ❑ Stämmer i hög grad

14. *Finns i Din ursprungsfamilj anlag för missbruk av alkohol, tabletter eller droger?*

- ❑ Ja
- ❑ Nej

15. *Har det i din ursprungsfamilj förekommit anlag för nedstämdhet / depression eller självmordshandlingar?*

- ❑ Ja
- ❑ Nej

16. *Har det i din ursprungsfamilj förekommit anlag för risksökande beteende eller "spelmani"?*

- ❑ Ja
- ❑ Nej

REFERENCES

1. Alonso J, Angermeyer MC, Bernert S, Bruffaerts R, Brugha TS, Bryson H, et al. Disability and quality of life impact of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand Suppl. 2004(420):38–46.

2. Sobocki P, Lekander I, Borgstrom F, Strom O, Runeson B. The economic burden of depression in Sweden from 1997 to 2005. Eur Psychiatry. 2007 Apr;22(3):146–52.

3. Jansson SP, Andersson DK, Svardsudd K. Prevalence and incidence rate of diabetes mellitus in a Swedish community during 30 years of follow-up. Diabetologia. 2007 Apr;50(4):703–10.

4. Wittchen HU, Pittrow D. Prevalence, recognition and management of depression in primary care in Germany: the Depression 2000 study. Hum Psychopharmacol. 2002;17 Suppl 1:S1–11.

5. Berardi D, Leggieri G, Ceroni GB, Rucci P, Pezzoli A, Paltrinieri E, et al. Depression in primary care: a nationwide epidemiological survey. Fam Pract. 2002;19(4):397–400.

6. Vuorilehto M, Melartin T, Isometsa E. Depressive disorders in primary care: recurrent, chronic, and co-morbid. Psychol Med. 2005 May;35(5):673–82.

7. Callahan EJ, Bertakis KD, Azari R, Helms LJ, Robbins J, Miller J. Depression in primary care: patient factors that influence recognition. Fam Med. 1997;29(3):172–6.

8. Lepine JP, Gastpar M, Mendlewicz J, Tylee A. Depression in the community: the first pan-European study DEPRES (Depression Research in European Society). Int Clin Psychopharmacol. 1997;12(1):19–29.

9. Al-Windi A. Depression in general practice. Nord J Psychiatry. 2005;59(4):272–7.

10. Salokangas RK, Poutanen O, Stengard E. Screening for depression in primary care: development and validation of the Depression Scale, a screening instrument for depression. Acta Psychiatr Scand. 1995;92(1):10–6.

11. Whooley MA, Avins AL, Miranda J, Browner WS. Case-finding instruments for depression: two questions are as good as many. J Gen Intern Med. 1997 Jul;12(7):439–45.

12. Isacsson G, Bergman U. [Increased use of antidepressive agents: a correctly aimed development]. Läkartidningen. 1997;94(16):1484–6.

13. Rosholm JU, Gram LF, Isacsson G, Hallas J, Bergman U. Changes in the pattern of antidepressant use upon the introduction of the new antidepressants: a prescription database study. Eur J Clin Pharmacol. 1997;52(3):205–9.

14. Davidson JR, Meltzer-Brody SE. The underrecognition and undertreatment of depression: what is the breadth and depth of the problem? J Clin Psychiatry. 1999;60(Suppl 7):4–9; discussion 10–1.

15. Bertakis KD, Helms LJ, Callahan EJ, Azari R, Leigh P, Robbins JA. Patient gender differences in the diagnosis of depression in primary care. J Womens Health Gend Based Med. 2001 Sep;10(7):689–98.

16. Sjonell G. Relationship between use of increased primary health care service and other care in a Swedish urban area. III. Utilization of emergency house calls. Scand J Prim Health Care. 1984 Sep;2(3):133–9.

17. Sjonell G. Relationship between use of increased primary health care and other out-patient care in a Swedish urban area. I. Utilisation of public primary health care. Scand J Prim Health Care. 1984 Feb;2(1):33–9.

18. Socialdepartementet Lag 1993:588 om husläkare. Lag (1993:588 om husläkare) In: Socialdepartementet, editor. Stockholm 1993.

19. Scott AI, Freeman CP. Edinburgh primary care depression study: treatment outcome, patient satisfaction, and cost after 16 weeks. Bmj. 1992 Apr 4;304(6831):883–7.

20. WHO World Health Organisation. International statistical classification of diseases and related health problems: ICD-10. Geneva: World Health Organization; 2009.

21. Socialstyrelsen. Klassifikation av sjukdomar och hälsoproblem 1997. Primärvård. Stockholm: Socialstyrelsen; 1997.

22. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV. Quick reference to the diagnostic criteria from DSM-IV. Washington, D.C.: American Psychiatric Assoc.; 1994.

23. Feldman EL, Robbins A, Jaffe A. Selections from current literature: minor depression. Fam Pract. 1998;15(3):275–81.

24. Williams JW, Jr., Kerber CA, Mulrow CD, Medina A, Aguilar C. Depressive disorders in primary care: prevalence, functional disability, and identification. J Gen Intern Med. 1995;10(1):7–12.

25. Rapaport MH, Judd LL, Schettler PJ, Yonkers KA, Thase ME, Kupfer DJ, et al. A descriptive analysis of minor depression. Am J Psychiatry. 2002 Apr;159(4):637–43.

26. Alexanderson K, Norlund A. Swedish Council on Technology Assessment in Health Care (SBU). Chapter 1. Aim, background, key concepts, regulations, and current statistics. Scand J Public Health Suppl. 2004;63:12–30.

27. Socialstyrelsen. Utmattningssyndrom: stressrelaterad psykisk ohälsa. Stockholm: Socialstyrelsen; 2003.

28. Maslach C, Schaufeli WB, Leiter MP. Job burnout. Annu Rev Psychol. 2001;52:397–422.

29. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960 Feb;23:56–62.

30. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry. 1979;134:382–9.

31. Snaith RP, Harrop FM, Newby DA, Teale C. Grade scores of the Montgomery-Åsberg Depression and the Clinical Anxiety Scales. Br J Psychiatry. 1986 May;148:599–601.

32. Isacsson G. Suicide prevention – a medical breakthrough? Acta Psychiatr Scand. 2000;102(2):113–7.

33. Carlsten A, Waern M, Ekedahl A, Ranstam J. Antidepressant medication and suicide in Sweden. Pharmacoepidemiol Drug Saf. 2001 Oct–Nov;10(6):525–30.

34. Korkeila J, Salminen JK, Hiekkanen H, Salokangas RK. Use of antidepressants and suicide rate in Finland: an ecological study. J Clin Psychiatry. 2007 Apr;68(4):505–11.

35. Ankarberg PH. Antidepressant prescribing and suicide: antidepressants do not reduce suicide rates. Bmj. 2003 Aug 2;327(7409):288–9; author reply 9.

36. van Praag HM. Why has the antidepressant era not shown a significant drop in suicide rates? Crisis. 2002;23(2):77–82.

37. Rihmer Z, Rutz W, Pihlgren H. Depression and suicide on Gotland. An intensive study of all suicides before and after a depression-training programme for general practitioners. J Affect Disord. 1995;35(4):147–52.

38. Rihmer Z. Strategies of suicide prevention: focus on health care. J Affect Disord. 1996 Jul 8;39(2):83–91.

39. Vuorilehto MS, Melartin TK, Isometsä ET. Suicidal behaviour among primary-care patients with depressive disorders. Psychol Med. 2006 Feb;36(2):203–10.

40. Allgulander C. Suicide and mortality patterns in anxiety neurosis and depressive neurosis. Arch Gen Psychiatry. 1994 Sep;51(9):708–12.

41. Kessing LV. Severity of depressive episodes according to ICD-10: prediction of risk of relapse and suicide. Br J Psychiatry. 2004 Feb;184:153–6.

42. Andersen UA, Andersen M, Rosholm JU, Gram LF. Contacts to the health care system prior to suicide: a comprehensive analysis using registers for general and psychiatric hospital admissions, contacts to general practitioners and practising specialists and drug prescriptions. Acta Psychiatr Scand. 2000 Aug;102(2):126–34.

43. Stockholms Läns Landsting. Hälso- och sjukvårdsförvaltningen. Viss – medicinskt och administrativt stöd för primärvården [Internet] [uppdated March 2012]. Available from: http://www.viss.nu/.

44. Apoteket AB. Association of Swedish Pharmacies. Diagnos receptundersökningen: särtryck ur Svensk läkemedelsstatistik. Stockholm: Apoteket; 2000.

45. Socialstyrelsen.se. [Internet] Antidepressiva läkemedel vid psykisk ohälsa2006. Available from: http://www.socialstyrelsen.se.

46. Sartorius N, Ustun TB, Lecrubier Y, Wittchen HU. Depression comorbid with anxiety: results from the WHO study on psychological disorders in primary health care. Br J Psychiatry Suppl. 1996(30):38–43.

47. Klinkman MS. Competing demands in psychosocial care. A model for the identification and treatment of depressive disorders in primary care. Gen Hosp Psychiatry. 1997;19(2):98–111.

48. Salokangas RK, Poutanen O, Stengard E, Jahi R, Palo-oja T. Prevalence of depression among patients seen in community health centres and community mental health centres. Acta Psychiatr Scand. 1996 Jun;93(6):427–33.

49. Klinkman MS, Schwenk TL, Coyne JC. Depression in primary care – more like asthma than appendicitis: the Michigan Depression Project. Can J Psychiatry. 1997;42(9):966–73.

50. Thompson C, Ostler K, Peveler RC, Baker N, Kinmonth AL. Dimensional perspective on the recognition of depressive symptoms in primary care: The Hampshire Depression Project 3. Br J Psychiatry. 2001;179:317–23.

51. Kirmayer LJ, Robbins JM, Dworkind M, Yaffe MJ. Somatization and the recognition of depression and anxiety in primary care. Am J Psychiatry. 1993;150(5):734–41.

52. Rost K, Zhang M, Fortney J, Smith J, Coyne J, Smith GR, Jr. Persistently poor outcomes of undetected major depression in primary care. Gen Hosp Psychiatry. 1998 Jan;20(1):12–20.

53. Leon AC, Olfson M, Broadhead WE, Barrett JE, Blacklow RS, Keller MB, et al. Prevalence of mental disorders in primary care. Implications for screening. Arch Fam Med. 1995 Oct;4(10):857–61.

54. Maier W, Gansicke M, Gater R, Rezaki M, Tiemens B, Urzua RF. Gender differences in the prevalence of depression: a survey in primary care. J Affect Disord. 1999;53(3):241–52.

55. Ustun TB. Cross-national epidemiology of depression and gender. J Gend Specif Med. 2000 Mar–Apr;3(2):54–8.

56. Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. Br J Psychiatry. 2000 Dec;177:486–92.

57. Kuehner C. Gender differences in unipolar depression: an update of epidemiological findings and possible explanations. Acta Psychiatr Scand. 2003 Sep;108(3):163–74.

58. Roness A, Mykletun A, Dahl AA. Help-seeking behaviour in patients with anxiety disorder and depression. Acta Psychiatr Scand. 2005 Jan;111(1):51–8.

59. Spijker J, de Graaf R, Bijl RV, Beekman AT, Ormel J, Nolen WA. Duration of major depressive episodes in the general population: results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Br J Psychiatry. 2002 Sep;181:208–13.

60. van Weel-Baumgarten EM, Schers HJ, van den Bosch WJ, van den Hoogen HJ, Zitman FG. Long-term follow-up of depression among patients in the community and in family practice settings. A systematic review. J Fam Pract. 2000 Dec;49(12):1113–20.

61. Ustun TB. The global burden of mental disorders. Am J Public Health. 1999 Sep;89(9):1315–8.

62. Simon GE, VonKorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. N Engl J Med. 1999 Oct 28;341(18):1329–35.

63. Wittchen HU, Lieb R, Wunderlich U, Schuster P. Comorbidity in primary care: presentation and consequences. J Clin Psychiatry. 1999;60 Suppl 7:29–36; discussion 7–8.

64. Sobocki P, Ekman M, Agren H, Krakau I, Runeson B, Martensson B, et al. Health-related quality of life measured with EQ-5D in patients treated for depression in primary care. Value Health. 2007 Mar–Apr;10(2):153–60.

65. Karlsson H, Lehtinen V, Joukamaa M. Psychiatric morbidity among frequent attender patients in primary care. Gen Hosp Psychiatry. 1995;17(1):19–25.

66. Gill D, Dawes M, Sharpe M, Mayou R. GP frequent consulters: their prevalence, natural history, and contribution to rising workload. Br J Gen Pract. 1998 Dec;48(437):1856–7.

67. Gill D, Sharpe M. Frequent consulters in general practice: a systematic review of studies of prevalence, associations and outcome. J Psychosom Res. 1999 Aug;47(2):115–30.

68. Bergh H, Marklund B. Characteristics of frequent attenders in different age and sex groups in primary health care. Scand J Prim Health Care. 2003 Sep;21(3):171–7.

69. Ronalds C, Kapur N, Stone K, Webb S, Tomenson B, Creed F. Determinants of consultation rate in patients with anxiety and depressive disorders in primary care. Fam Pract. 2002;19(1):23–8.

70. Ormel J, Vonkorff M, Oldehinkel AJ, Simon G, Tiemens BG, Ustun TB. Onset of disability in depressed and non-depressed primary care patients. Psychol Med. 1999;29(4):847–53.

71. Isacson D, Bingefors K, von Knorring L. The impact of depression is unevenly distributed in the population. Eur Psychiatry. 2005 May;20(3):205–12.

72. Berndt ER, Koran LM, Finkelstein SN, Gelenberg AJ, Kornstein SG, Miller IM, et al. Lost human capital from early-onset chronic depression. Am J Psychiatry. 2000 Jun;157(6):940–7.

73. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care. 2001 Jun;24(6):1069–78.

74. Ferketich AK, Schwartzbaum JA, Frid DJ, Moeschberger ML. Depression as an antecedent to heart disease among women and men in the NHANES I study. National Health and Nutrition Examination Survey. Arch Intern Med. 2000 May 8;160(9):1261–8.

75. Swendsen JD, Merikangas KR, Canino GJ, Kessler RC, Rubio-Stipec M, Angst J. The comorbidity of alcoholism with anxiety and depressive disorders in four geographic communities. Compr Psychiatry. 1998 Jul–Aug;39(4):176–84.

76. Gilman SE, Abraham HD. A longitudinal study of the order of onset of alcohol dependence and major depression. Drug Alcohol Depend. 2001 Aug 1;63(3):277–86.

77. Wang J, Patten SB. Prospective study of frequent heavy alcohol use and the risk of major depression in the Canadian general population. Depress Anxiety. 2002;15(1):42–5.

78. Sher L. Alcohol consumption and suicide. QJM. 2006 Jan;99(1):57–61.

79. Allgulander C, Msghina M. [Benefits and risks of benzodiazepines. A current analysis of facts]. Läkartidningen. 2011 Oct 12–18;108(41):2025–9.

80. Ansseau M, Fischler B, Dierick M, Mignon A, Leyman S. Prevalence and impact of generalized anxiety disorder and major depression in primary care in Belgium and Luxemburg: the GADIS study. Eur Psychiatry. 2005 May;20(3):229–35.

81. Bovasso GB. Cannabis abuse as a risk factor for depressive symptoms. Am J Psychiatry. 2001 Dec;158(12):2033–7.

82. Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. Cannabis use and mental health in young people: cohort study. Bmj. 2002 Nov 23;325(7374):1195–8.

83. van Weel-Baumgarten E, van den Bosch W, van den Hoogen H, Zitman FG. Ten year follow-up of depression after diagnosis in general practice. Br J Gen Pract. 1998 Oct;48(435):1643–6.

84. Försäkringskassan. Sveriges officiella statistik 2005. [Internet] Available from: http://www.forsakringskassan.se.

85. Gottfries CG, Regland B, Zachrisson O, Walinder J. [Sick listing – "disaster" or incompetence in statistics and diagnostics?]. Läkartidningen. 2003 May 22;100(21):1912–4.

86. Perski A, Grossi G, Evengard B, Blomkvist V, Yilbar B, Orth-Gomer K. [Emotional exhaustion common among women in the public sector]. Läkartidningen. 2002 May 2;99(18):2047–52.

87. Paykel ES. Depression in women. Br J Psychiatry Suppl. 1991 May(10):22–9.

88. Brown GW, Moran PM. Single mothers, poverty and depression. Psychol Med. 1997 Jan;27(1):21–33.

89. Lorant V, Deliege D, Eaton W, Robert A, Philippot P, Ansseau M. Socioeconomic inequalities in depression: a meta-analysis. Am J Epidemiol. 2003 Jan 15;157(2):98–112.

90. Salokangas RK, Poutanen O. Risk factors for depression in primary care. Findings of the TADEP project. J Affect Disord. 1998;48(2–3):171–80.

91. Engström C, Thornlund AS, Johansson EL, Langstrom M, Chotai J, Adolfsson R, et al. Anticipation in unipolar affective disorder. J Affect Disord. 1995 Oct 9;35(1–2):31–40.

92. Johansson LM, Sundquist J, Johansson SE, Bergman B. Ethnicity, social factors, illness and suicide: a follow-up study of a random sample of the Swedish population. Acta Psychiatr Scand. 1997 Feb;95(2):125–31.

93. Westman J, Johansson LM, Sundquist K. Country of birth and hospital admission rates for mental disorders: a cohort study of 4.5 million men and women in Sweden. Eur Psychiatry. 2006 Jul;21(5):307–14.

94. Westman J, Sundquist J, Johansson LM, Johansson SE, Sundquist K. Country of birth and suicide: a follow-up study of a national cohort in Sweden. Arch Suicide Res. 2006;10(3):239–48.

95. Ronalds C, Creed F, Stone K, Webb S, Tomenson B. Outcome of anxiety and depressive disorders in primary care. Br J Psychiatry. 1997 Nov;171:427–33.

96. Nazroo JY, Edwards AC, Brown GW. Gender differences in the onset of depression following a shared life event: a study of couples. Psychol Med. 1997 Jan;27(1):9–19.

97. Mattisson C, Bogren M, Horstmann V, Tambs K, Munk-Jorgensen P, Nettelbladt P. Risk factors for depressive disorders in the Lundby cohort – a 50 year prospective clinical follow-up. J Affect Disord. 2009 Mar;113(3):203–15.

98. Roeloffs CA, Fink A, Unutzer J, Tang L, Wells KB. Problematic substance use, depressive symptoms, and gender in primary care. Psychiatr Serv. 2001 Sep;52(9):1251–3.

99. Bergman H, Kallmen H. [Swedish women have developed more risky and more harmful alcohol drinking habits. A survey of alcohol drinking changes among Swedes between 1997–2001]. Läkartidningen. 2003 Mar 20;100(12):1028–30, 33–5.

100. Moscicki EK. Epidemiology of suicide. Int Psychogeriatr. 1995 Summer;7(2):137–48.

101. Arsenault-Lapierre G, Kim C, Turecki G. Psychiatric diagnoses in 3275 suicides: a meta-analysis. BMC Psychiatry. 2004;4:37.

102. Rutz W. Improvement of care for people suffering from depression: the need for comprehensive education. Int Clin Psychopharmacol. 1999;14 Suppl 3:S27–33.

103. van Praag HM. Faulty cortisol/serotonin interplay. Psychopathological and biological characterisation of a new, hypothetical depression subtype (SeCA depression). Psychiatry Res. 1996 Dec 20;65(3):143–57.

104. Rihmer Z, Pestality P, Pihlgren H, Rutz W. 'Anxiety/aggression-driven depression' and 'male depressive syndrome': are they the same? Psychiatry Res. 1998;77(3):209–10.

105. Walinder J, Rutzt W. Male depression and suicide. Int Clin Psychopharmacol. 2001 Mar;16 Suppl 2:S21–4.

106. Rutz WR, Z. Daltag,A. Bech, P. Gotlandskalan til vurdering af depression hos mænd. Psychiatri Information. 1998(3).

107. Apoteksbolaget. Läkemedelsboken. 97/98. Stockholm: Apoteksbolaget; 1997.

108. Rost K, Smith R, Matthews DB, Guise B. The deliberate misdiagnosis of major depression in primary care. Arch Fam Med. 1994 Apr;3(4):333–7.

109. Spitzer RL, Williams JB, Kroenke K, Linzer M, deGruy FV, 3rd, Hahn SR, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. Jama. 1994;272(22):1749–56.

110. Coyne JC, Schwenk TL, Fechner-Bates S. Nondetection of depression by primary care physicians reconsidered. Gen Hosp Psychiatry. 1995 Jan;17(1):3–12.

111. Bodlund O. [Anxiety and depression as a hidden problem in primary health care. Only one case in four identified]. Läkartidningen. 1997;94(49):4612–4, 7–8.

112. Kessler D, Bennewith O, Lewis G, Sharp D. Detection of depression and anxiety in primary care: follow up study. Bmj. 2002 Nov 2;325(7371):1016–7.

113. Dowrick C, Buchan I. Twelve month outcome of depression in general practice: does detection or disclosure make a difference? Bmj. 1995;311(7015):1274–6.

114. Rost K, Humphrey J, Kelleher K. Physician management preferences and barriers to care for rural patients with depression. Arch Fam Med. 1994;3(5):409–14.

115. Nutting PA, Rost K, Smith J, Werner JJ, Elliot C. Competing demands from physical problems: effect on initiating and completing depression care over 6 months. Arch Fam Med. 2000;9(10):1059–64.

116. Hutton C, Gunn J. Do longer consultations improve the management of psychological problems in general practice? A systematic literature review. BMC health services research. 2007;7:71.

117. McDowell IN, C editor. Measuring Health. A Guide To Rating Scales and Questionnaires. Second Edition ed. New York: Oxford University Press; 1996.

118. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. J Psychosom Res. 2002;52(2):69–77.

119. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. Jama. 1999 Nov 10;282(18):1737–44.

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

121. Svanborg P, Åsberg M. A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS). J Affect Disord. 2001 May;64(2–3):203–16.

122. Cunningham JL, Wernroth L, von Knorring L, Berglund L, Ekselius L. Agreement between physicians' and patients' ratings on the Montgomery-Åsberg Depression Rating Scale. J Affect Disord. 2011 Dec;135(1–3):148–53.

123. Mulrow CD, Williams JW, Jr., Gerety MB, Ramirez G, Montiel OM, Kerber C. Case-finding instruments for depression in primary care settings. Ann Intern Med. 1995;122(12):913–21.

124. SBU. Swedish Council on Health Technology Assessment, editor. Diagnostik och uppföljning av förstämningssyndrom. En systematisk litteraturöversikt. Stockholm Statens beredning för medicinsk utvärdering 2012.

125. Arroll B, Goodyear-Smith F, Kerse N, Fishman T, Gunn J. Effect of the addition of a "help" question to two screening questions on specificity for diagnosis of depression in general practice: diagnostic validity study. Bmj. 2005 Oct 15;331(7521):884.

126. Williams JW, Jr., Mulrow CD, Kroenke K, Dhanda R, Badgett RG, Omori D, et al. Case-finding for depression in primary care: a randomized trial. Am J Med. 1999;106(1):36–43.

127. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961 Jun;4:561–71.

128. Beck AT, Beamesderfer A. Assessment of depression: the depression inventory. Mod Probl Pharmacopsychiatry. 1974;7(0):151–69.

129. Beck AT. Psychometric properties of the Beck Depression Inventory. Clinical Psychology Review. 1988;8:77–100.

130. Oliver JM, Simmons ME. Depression as measured by the DSM-III and the Beck Depression Inventory in an unselected adult population. J Consult Clin Psychol. 1984 Oct;52(5):892–8.

131. Zich JM, Attkisson CC, Greenfield TK. Screening for depression in primary care clinics: the CES-D and the BDI. Int J Psychiatry Med. 1990;20(3):259–77.

132. Lasa L, Ayuso-Mateos JL, Vazquez-Barquero JL, Diez-Manrique FJ, Dowrick CF. The use of the Beck Depression Inventory to screen for depression in the general population: a preliminary analysis. J Affect Disord. 2000 Jan–Mar;57(1–3):261–5.

133. SBU. Swedish Council on Health Technology Assessment Implementeringsstöd för psykiatrisk evidens i primärvården: en systematisk litteraturöversikt. Stockholm: Statens beredning för medicinsk utvärdering (SBU); 2012.

134. Zierau F, Bille A, Rutz W, Bech P. The Gotland Male Depression Scale: a validity study in patients with alcohol use disorder. Nord J Psychiatry. 2002;56(4):265–71.

135. World Health Organisation info package. Mastering depression in primary care. Report. Frederiksborg: WHO Regional Office for Europe Psychiatric Research Unit, Frederiksborg 1998.

136. Moller-Leimkuhler AM, Paulus, NC, Heller J. Male depression in a population sample of young males. Nervenartzt. 2007 Jun;78(6):641–2, 4–6, 8–50.

137. Gilbody S, House AO, Sheldon TA. Screening and case finding instruments for depression. Cochrane Database Syst Rev. 2005(4):CD002792.

138. Christensen KS, Sokolowski I, Olesen F. Case-finding and risk-group screening for depression in primary care. Scand J Prim Health Care. 2011 Jun;29(2):80–4.

139. Jackson JL, Houston JS, Hanling SR, Terhaar KA, Yun JS. Clinical predictors of mental disorders among medical outpatients. Arch Intern Med. 2001 Mar 26;161(6):875–9.

140. Baas KD, Wittkampf KA, van Weert HC, Lucassen P, Huyser J, van den Hoogen H, et al. Screening for depression in high-risk groups: prospective cohort study in general practice. Br J Psychiatry. 2009 May;194(5):399–403.

141. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption – II. Addiction. 1993 Jun;88(6):791–804.

142. Association AP. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: Washington, DC: American Psychiatric Association; 1994.

143. Skatteverket. The Swedish Tax Agency. Population Registration in Sweden. [www.skatteverket.se]: Swedish Tax Agency; 2011.

144. Statistiska Centralbyran Statistics Sweden. Livslängden i Sverige 2001–2010: livslängdstabeller för riket och länen = [Life expectancy in Sweden 2001–2010: life tables for the country and by county]. Stockholm: Statistiska centralbyrån; 2011.

145. StataCorp. Stata Statistical Software: Release 8.0. College Station, TX: Stata Corporation; 2003.

146. Statistics Sweden. Life expectancy in Sweden 2001–2010: life tables for the country and by county. Official Statistics of Sweden, Statistics Sweden 2011. Stockholm Statistics Sweden Statistiska centralbyran; 2011.

147. Fink P, Jensen J, Borgquist L, Brevik JI, Dalgard OS, Sandager I, et al. Psychiatric morbidity in primary public health care: a Nordic multicentre investigation. Part I: method and prevalence of psychiatric morbidity. Acta Psychiatr Scand. 1995;92(6):409–18.

148. Schulberg HC, Madonia MJ, Block MR, Coulehan JL, Scott CP, Rodriguez E, et al. Major depression in primary care practice: clinical characteristics and treatment implications. Psychosomatics. 1995;36(2):129–37.

149. Åsberg M, Nygren A, Leopardi R, Rylander G, Peterson U, Wilczek L, et al. Novel biochemical markers of psychosocial stress in women. PLoS One. 2009;4(1):e3590.

150. Malterud K. Action research – a strategy for evaluation of medical interventions. Fam Pract. 1995 Dec;12(4):476–81.

151. Johansson E. Beyond frustration: understanding women with undefined musculoskeletal pain who consult primary care. Umeå: Univ.; 1998.

152. Löfvander M. Illness, disease, sickness: clinical factors, concepts of pain and sick leave patterns among immigrants in primary health care: effects of different therapeutic approaches. Stockholm 1997.

153. Lindell O. On the rehabilitation of non-acute, non-specific spinal pain [Electronic resource]. Stockholm: Karolinska institutet; 2010.

154. Magnil M. Mild to moderate depression in the elderly in primary care: detection, patient centeredness and course [Electronic resource]. Göteborg: Department of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg; 2012.

155. Magnil M, Gunnarsson R, Björkelund C. Using patient-centred consultation when screening for depression in elderly patients: a comparative pilot study. Scand J Prim Health Care. 2011 Mar;29(1):51–6.

156. Mitchell AJ, Vaze A, Rao S. Clinical diagnosis of depression in primary care: a meta-analysis. Lancet. 2009 Aug 22;374(9690):609–19.

157. Lotfi L, Flyckt L, Krakau I, Martensson B, Nilsson GH. Undetected depression in primary healthcare: Occurrence, severity and co-morbidity in a two-stage procedure of opportunistic screening. Nord J Psychiatry. 2010 Dec;64(6):421–7.

158. Magnil M, Gunnarsson R, Björkstedt K, Björkelund C. Prevalence of depressive symptoms and associated factors in elderly primary care patients: a descriptive study. Prim Care Companion J Clin Psychiatry. 2008;10(6):462–8.

159. Löfvander MP, D. Cross-cultural psychiatric assessment of Greek and Swedish patients at a Swedish primary health centre. Nord J Psychiatry. 1993;47(3):179–83.

160. Hildebrandt MG, Stage KB, Kragh-Soerensen P. Gender and depression: a study of severity and symptomatology of depressive disorders (ICD-10) in general practice. Acta Psychiatr Scand. 2003 Mar;107(3):197–202.

161. Hickie I. Is depression overdiagnosed? No. Bmj. 2007 Aug 18;335(7615):329.

162. Perski A, Grossi G. [Treatment of patients on long-term sick leave because of stress-related problems. Results from an intervention study]. Läkartidningen. 2004 Apr 1;101(14):1295–8.

163. Nygren AL, Bernsprang B, Borg K. Rehabiliteringsrådets slutbetänkande: slutbetänkande. Stockholm: Fritzes; 2011.

164. Sundel KL, Stain-Mahngren R, Andersson A, Aberg-Wistedt A, Schenck-Gustafsson K. High frequency of anxiety and angina pectoris in depressed women with coronary heart disease. Gend Med. 2007 Jun;4(2):146–56.

165. Sundquist J, Li X, Johansson SE, Sundquist K. Depression as a predictor of hospitalization due to coronary heart disease. Am J Prev Med. 2005 Dec;29(5):428–33.

166. Aromaa A, Raitasalo R, Reunanen A, Impivaara O, Heliovaara M, Knekt P, et al. Depression and cardiovascular diseases. Acta Psychiatr Scand Suppl. 1994;377:77–82.

167. Barefoot JC, Helms MJ, Mark DB, Blumenthal JA, Califf RM, Haney TL, et al. Depression and long-term mortality risk in patients with coronary artery disease. Am J Cardiol. 1996 Sep 15;78(6):613–7.

168. Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. Psychosom Med. 2004 Nov–Dec;66(6):802–13.

169. Nordström A, Bodlund O. Every third patient in primary care suffers from depression, anxiety or alcohol problems. Nord J Psychiatry. 2008;62(3):250–5.

170. Parker G. Is depression overdiagnosed? Yes. Bmj. 2007 Aug 18;335(7615):328.

171. Carlberg I. Pillret: en berättelse om depressioner och doktorer, forskare och Freud, människor och marknader. Stockholm: Norstedt; 2008.

172. Keeley RD, Smith JL, Nutting PA, Miriam Dickinson L, Perry Dickinson W, Rost KM. Does a depression intervention result in improved outcomes for patients presenting with physical symptoms? J Gen Intern Med. 2004 Jun;19(6):615–23.