Aspects of management of depression in primary care

- use of a self-assessment instrument

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”To my beloved Åsa and my two children Love & Ingrid,
without you I am nothing”

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ABSTRACT

Aim: The general aim of this thesis was to evaluate effects of recurrent use of a self-assessment instrument in general practitioner (GP) consultations with the patient with depression in the primary care clinical context. Does the use of self-assessment instruments have an effect on depression course, as well as quality of life, well-being, anti-depressant medication use, sick leave, work ability, and health care use in a long-term perspective?

Introduction: Depression is a common mental disorder and leading cause of disability and is among the most common reasons for sick leave. Primary health care is the first line of care, and where 70% of all patients with depression are managed without referral to specialist psychiatry. As a tool to enhance accuracy and enable the GP to diagnose suspected depressions, there are recommendations to use some kind of structured interview. Self-assessment instruments such as MADRS-S (Montgomery Asberg Depression Rating Scale- Self rating) are well known in Swedish primary care, but not regularly used. MADRS-S includes nine items that the patient rates on a scale from 0 to 6: reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Higher scores indicate more severe depression and the maximum score is 54. MADRS-S is especially sensitive to change and is therefore suitable for measuring the effect of depression treatment. There are today no recommendations in guidelines to use MADRS-S or any other assessment tool on a regular basis; there are too few studies of good quality to provide enough evidence to defend its use. More studies are needed that evaluate structured use of such instruments and where outcomes are measured in long-term follow-up.

Methods: Paper I (n=258) was a randomized controlled study, evaluating the effects of recurrent use of MADRS-S in the depressed patient during regular GP consultations. Outcomes were measured by BDI-II, EQ-5D, GHQ-12, and medication use. Paper II used results from self-assessments from patients with

depression in 2 RCT studies (PRI-SMA and PRIM-NET), where the patients assessed their symptoms with both MADRS-S and BDI-II. The total scores were compared between MADRS-S and BDI-II. Paper III (n=9) invited patients with depression who had assessed their symptoms with MADRS-S to discuss their perceptions of such use in focus group discussions. The collected data were then analyzed with Malterud's systematic text condensation. Paper IV (n=183) evaluated the effects of recurrent use of MADRS-S in the depressed patient during regular GP consultations on work ability, job strain, sick leave, quality of life, and social support.

Results: Paper I showed no significant differences between the intervention and control group in depression severity reduction or remission rate, change in quality of life, psychological well-being, sedative prescriptions, or sick leave during the entire 12-month follow-up. However, significantly more patients in the intervention group continued anti-depressants until the 6 month follow-up (86/125 vs 78/133, $p < 0.05$). Paper II showed a good correlation between the two instruments (MADRS-S and BDI-II): 0.66 and 0.62. The reliability was also good for both MADRS-S (Cronbach α: 0.76 for both cohorts) and BDI-II items (Cronbach α: 0.88 and 0.85). Paper III showed that three categories emerged from the analysis: (i) confirmation; MADRS-S shows that I have depression and how serious it is, (ii) centeredness; the most important thing is for the GP to listen to and take me seriously and (iii) clarification; MADRS-S helps me understand why I need treatment for depression. Paper IV showed a significantly steeper increase of WAI at 3 months in the intervention group, although this levelled off at 6 and 12 months. In both groups approximately 20% showed decreased job strain with no significant difference between intervention and control groups. Sick leave did not show any significant difference. Social support was perceived as positive in a significantly higher frequency at 12 months in the intervention group compared to the control group ($p= 0.009$).

Conclusion: The studies in this thesis have expanded knowledge of use of self-assessment instruments in the management of depression in primary care with regard to a number of aspects. Using a self-assessment instrument in recurrent consultations can strengthen the patient's perceptions concerning confirmation, centeredness, and clarification. The use of a self-assessment instrument increases the adherence to anti-depressant medication, WAI, and the perception of positive social support. However, the use does not reinforce beneficial effects concerning depression course, quality of life, or sick-leave.

Implication: It is important for GPs and nurses in primary care to have knowledge of the possible effects of the use of a self-assessment instrument and to explore during contact with the individual with depression, whether the individual is positive to the use of a self-assessment instrument. Further, the MADRS-S instrument corresponds well to the BDI-II instrument in all domains and could be used as a reliable instrument to follow a person's course of depression with the

knowledge that it yields indications comparable to the BDI-II. The use of depression self-rating scales should perhaps not be mandatory in primary health care but rather left to the discretion of the GP and the patient.

Keywords: depression, primary care, self-assessment rating scale, patient reported outcome measures

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SAMMANFATTNING PÅ SVENSKA

Depression är en folksjukdom och bland de vanligaste orsakerna till sjukskrivning. Under sin livstid drabbas ungefär var fjärde man och cirka hälften av alla kvinnor av minst en period som kan klassas och diagnostiseras som depression. Svensk primärvård är första linjens vård och de allra flesta med besvär som kan vara depression söker sig i första hand till primärvården. Där tas cirka 70 % helt och hållet om hand utan att behöva remitteras till specialistpsykiatrin. Som ett hjälpmedel för att öka träffsäkerheten och möjliggöra att hitta fler individer med depression, rekommenderas läkaren använda sig av ett så kallat självskattningsinstrument. Det är ett papper innehållande ett batteri av frågor ämnade att låta patienten själv ta ställning till hur den skattar sig själv. Men, det finns inga rekommendationer att man ska använda dessa rutinmässigt, då det vetenskapliga underlaget hitintills inte visat att instrumenten gör att primärvården identifierar fler personer med depression, eller att kvalitén i vården ökar. Syftet med vårt forskningsprojekt har varit att undersöka om regelbundet användande av ett självskattningsinstrument som patientens eget instrument i mötet med läkaren på vårdcentralen positivt påverkar depressionsförlopp och andra faktorer som livskvalitet, sjukskrivning, antidepressiv medicinering och vårdkonsumtion i större utsträckning än vid enbart den sedvanliga behandling som vanligtvis genomförs i primärvården i Sverige idag.

Avhandlingen ” Aspects of management of depression in primary care – use of a self-assessment instrument” har genom 4 delarbeten beskrivit olika sidor av och vilka effekter ett strukturerat användande av självskattningsinstrument har för patienten med depression i den personcentrerade konsultationen i primärvården. Genom delarbetena beskrivs dels vilka utfallsmått som påverkas när skattningsskalan (MADRS-S) används, såsom depressionssymptom, livskvalitet, sjukskrivning, arbetsförmåga, upplevt socialt stöd och självskattad hälsa, dels har patienternas egna upplevelser fångats genom fokusgruppsdiskussioner. och dels har de vanligast förekommande skattningsinstrumenten (MADRS-S och BDI-II) jämförts för att se om deras resultat överensstämmer. Genom en stor randomiserad studie som genomfördes i Västra Götalandsregionen på 22 vårdcentraler, kunde studien tillsammans med 91 läkare rekrytera 258 patienter till studien (PRI-SMA). Hälften av patienterna fick sedvanlig behandling (kontrollgrupp), och den andra hälften erbjöds en intervention (interventionsgrupp). Interventionen bestod av 4 inplanerade besök där patienterna med depression i tillägg till den sedvanliga behandlingen fick skatta sina egna depressiva symptom med skattningsskalan MADRS-S. Alla patienter (både kontroll och intervention) fick träffa en forskningssköterska den dag de gick med i studien. Vid det besöket samlades demografiska data in och ett antal frågeformulär besvarades. Denna procedur

upprepades sedan vid 3, 6 och 12 månader (6 och 12 månader sköttes via brevutskick).

Resultat: Användande av MADRS-S vid upprepade besök i primärvården ger samma effekt som vid sedvanlig behandling gällande depressionsutfall. Inga skillnader kan ses mellan interventionsgruppen och kontrollgruppen. Däremot visar det sig att patienterna i interventionsgruppen är mer följsamma vad gäller anti-depressiv medicinering och fortsätter med sina förskrivna anti-depressiva mediciner enligt dagens rekommendationer. Detta är ett viktigt fynd. MADRS-S och BDI-II visade sig korrelera över hela depressionsspektret. Studien betyder att primärvården kan använda sig av MADRS-S (som är kortare, tar mindre tid och är gratis) och känna sig trygg i att utfallet blivit det samma om BDI-II hade används istället.

Patienterna upplever positiva sidor med användande av MADRS-S såsom att skalan hjälpte dem att få en bekräftelse på hur de mådde och vad det rörde sig om, de upplevde att det viktigaste var att läkaren visade att patienten togs på allvar och blev lyssnad till, samt att MADRS-S kunde göra det mer förståeligt varför viss behandling kunde vara fördelaktig. I gruppen av patienter som var i arbete (inte pensionärer, studenter och arbetssökande) utvärderades om återkommande skattningar med MADRS-S kunde påverka sjukskrivning, upplevd arbetsförmåga och upplevelse av socialt stöd på arbetsplatsen. Det visade sig att det sociala stödet upplevdes som större i interventionsgruppen och att den upplevda arbetsförmågan var större än hos kontrollgruppen.

Den kvalitativa studien visade tydligt att det finns positiva sidor med denna typ av självskattningsinstrument. Patienterna upplevde att genom att använda instrumentet så var det som att ”ta tempen” på depressionen. De fick ett kvitto, svart på vitt att det var en depression de hade, och den pedagogiska vinsten med att lära sig vilka delar som tillsammans bidrog till det depressiva tillståndet upplevdes som någonting positivt. När läkaren använde MADRS-S visade denne att patienten hade blivit lyssnad till och att man tagit patientens ord på allvar. Resultaten av de fyra delarbetena visar att primärvården inte behöver använda sig av skattningsskalor rutinmässigt, eftersom det inte påverkar själva depressionsförloppet, livskvalitén eller sjukskrivningslängd för patienten, men att patientfaktorer såsom följsamhet, upplevd arbetsförmåga och socialt stöd på arbetsplatsen i vissa fall positivt kan påverkas. Slutsatsen är att det är viktigt för primärvårdens personal att ha denna kunskap om självskattningsinstrumentens effekter och att det kan vara upp till varje läkare och patient att tillsammans själva avgöra om man vill använda dem eller ej.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Wikberg C, Westman J, Petersson E-L, Larsson MEH, Andre M, Eggertsen R, Thorn J, Ågren H, Björkelund C. Use of a self-rating scale to monitor depression severity in recurrent GP consultations in primary care – does it really make a difference? A randomized controlled study. BMC Family Practice. 2017, 18:6.

II. Wikberg C, Nejati S, Larsson MEH, Petersson EL, Westman J, Ariai N, Kivi M, Eriksson M, Eggertsen R, Hange D, Baigi A, Björkelund C. Comparison Between the Montgomery-Asberg Depression Rating Scale–Self and the Beck Depression Inventory II in Primary Care. Prim Care Companion CNS Disord. 2015; 17(3): 10.

III. Wikberg C, Pettersson A, Westman J, Björkelund C, Petersson EL. Patients' perspectives on the use of the Montgomery Asberg Depression Rating Scale self-assessment version in primary care. Scand J Prim Health Care. 2016; 34(4): 434-442.

IV. Petersson EL, Wikberg C, Westman J, Ariai N, Nejati S, Björkelund C. Effects on work ability, job strain and return to work of monitoring depression using a self-assessment instrument in recurrent person-centered GP consultations– a randomized controlled study. Submitted.

CONTENT

ABBREVIATIONS

BDI-II	Beck Depression Inventory second edition
CI	Confidence interval
CMD	Common Mental Disorders
CME	Continuing Medical Education
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders – fourth edition
EPR	Electronic Patient Record
EQ-5D	Euro Quality 5 Dimensions
ESEMED	European Study of the Epidemiology of Mental Disorders
GP	General Practitioner
ICBT	Internet Cognitive Behavior Therapy
MADRS-S	Montgomery Åsberg Depression Rating Scale – Self rating
OR	Odds ratio
PCC	Primary Care Centre
PRIM-NET	Primary Care Internet-Based Cognitive Behavioral Therapy Study
PRI-SMA	Primary Care Self-Assessment Montgomery-Åsberg Depression Rating Scale-Self Study
PROMs	Patient Reporter Outcome Measures
RR	Relative risk
SBU	Swedish Agency for Health Technology Assessment

STC	Systematic Text Condensation
TAU	Treatment as Usual
WAI	Work Ability Index
WHO	World Health Organization
WONCA	World Organization of National Colleges Academies Academic Associations of General Practitioners/Family Physicians

PREFACE

I had just finished my exam as district nurse, when Jeanette Westman (supervisor for the program) handed out a call for applicants. The job for which she was searching for applicants was as research assistant for a new project, a randomized trial in primary care. I immediately took the application, went home and wrote my CV, and sent the necessary papers to apply. A few weeks later, I had the job. I met Cecilia Björkelund, professor and project leader. She threw me right into the boiling pot from the beginning – applying to the board of ethics for approval to begin inclusion of patients, structuring protocols, logistics, and selling the study to primary care centers. Together with co-worker Eva-Lisa Petersen, we had a hectic start to this exciting project. Now almost seven years later, I can easily say it has been worthwhile.

The project had originated from a meeting that Cecilia had had about doing a study about the effects and usefulness of internet based treatment of depression. She had said, OK I can do a trial on that, but then I would like to do a trial that evaluates the effect of regular visits to the general practitioner and use of person-centered methodology together with self-assessment in patients with mild/moderate depression as well. Said and done, the two trials were on. As in many cases when regarding randomized trials, and as we learned along the road, it is one thing to have ideas and protocols on paper that describe how things are going to be done, and another thing how reality plays out.

Depression was a very new subject for me. I had some basic knowledge about it, and I came from Cardiology and Medicine at Sahlgrenska University hospital and had been doing percutaneous coronary interventions and treating ischemic heart failure patients for the last 7 years. The step towards becoming a district nurse was a part of leaving the hospital and raising the horizon towards public health. I was interested in how to prevent illness and diseases in populations, rather than treating and preventing death in the acute phase. During the course of becoming a district nurse, Jeanette opened my eyes to public health, and the many aspects that were connected with primary, secondary, and tertiary preventions.

First day at my new job, Cecilia handed me some literature that covered the current state of depression treatment in Sweden. I began my journey. Moreover, all the experiences, knowledge, and insightful moments I have collected during these years, I want to put to use for future improvements in the treatment of one of worst epidemics of our times, and to try help to "beat the blues".

Why this thesis? (Rationale)

Depression is common and mostly treated in primary care[1]**.** Depression guidelines recommend General Practitioners (GPs) to use some tool as an assistance when diagnosing a suspected depression, as the clinical consultation is not regarded as being sufficient, and GPs may miss diagnosing many depressions.

About 60 different types of instruments and scales assess a broad spectrum of common metal disorders (CMD). Most of them have been developed and evaluated in psychiatric care.

Since most people with CMD and especially depression and anxiety are treated in primary care, it is important to evaluate the effects of the very use of such instruments. Do they make a difference? How do the instruments affect depression outcomes, quality of life, sick leave and work ability? Should we use them, and if so, how are they best used, keeping both the patient and the GP perspective in mind?

In this thesis, I will describe the use and effects of the intervention consisting of regular, structured use of self-rating scales in the person-centered GP consultation in primary care. Do they affect important outcomes such as depression, medication use and adherence, quality of life, sick leave, work ability, job strain and positive social support? I will explore how patients with depression perceive the use of MADRS-S in primary care consultations with GPs. I will also examine care consumption and treatment as usual.

These aspects will be addressed with reference to the papers that have originated out of the PRI-SMA trial, which was an RCT study in Region Västra Götaland between 2010 - 2014.

1 INTRODUCTION

To set the stage for this thesis, some parts need to be assembled to form the framework. First I will provide an overview of depression and its prevalence in Swedish primary care, then I will describe other related concepts such as patient/person-centered care, work ability, adherence to medication, and last but not least, screening/diagnostic instruments and self-assessment.

1.1 Depression

Depression is a common mental disorder and leading cause of disability world-wide [2] and commonly associated with sick-leave and early retirement [3, 4]. WHO states that in 2020 depression will be the second leading cause of disability [2]. Depression causes a significant burden to society, economy, and to healthcare providers and policy makers [5]. Recently, national epidemiological surveys reported an increase of depressive symptoms in the younger portion of the Swedish population to levels equivalent to those of the elderly [6]. The lifetime depression risk for women is almost 45% and for men about 20% [7]. In Sweden, depression is now one of the leading causes of sick-leave [8]. The question has been raised as to whether depression is the ticking bomb of our generation [9]. The word depression comes from Latin depressionem (nominativ depressio) and deprimere, “To press down, depress” [10], and suggests that something is lower than it usually is. The fundamental and important difference between normal mood swings and being depressed is the quality of symptoms, as well as the time factor. Anyone can feel “down”, or not to up to one’s normal standards during a day or two, but the depressed person experiences a longer period (over two weeks) of the same perceived symptoms [11]. The symptoms when taken together form the depression. Depression is more than a sum score of its parts. It is a cluster of identified symptoms that form the depressive syndrome [12].

1.2 Epidemiology

Depression is a common disorder, which is closely entwined with low quality of life, work ability, function, pain, medical morbidity, and higher mortality [13-15]. The causes of depression are widespread, but are often a combination of factors: environmental, interpersonal, and social [16]. Prevalence of depression differs somewhat between countries, and although there is vast knowledge about prevalence, we do not have a total

global picture of depression due to the lack of prevalence studies from many countries. Lifetime prevalence in international studies differs between 1.5% in Taiwan to 19.0% in Beirut [17], and Kessler et al. reported 16.2% across cultures [18, 19], but in Sweden, a few studies have reported prevalence (diagnoses) from 2.4% [20] to 10-15% in the report from Swedish Agency for Health Technology Assessment (SBU) [21]. Månsson et al reported in a publication from 2011 that 9.3% of the diagnoses in patient encounters in primary care were mental and behavioral disorders, and Åsbring et al reported that 7% of primary care patients were diagnosed with common mental disorder (CMD) [22, 23].

The truth is probably that the prevalence of common mental health problems in primary care is somewhere around 10-15%. This corresponds to Ferarri et al's findings, that depression is a leading cause of disability and affects 10-15% of the populations in most countries [24]. We do have to bear in mind that many somatic concerns and chronic diseases increase the risk of mental health problems, and the comorbidity with depression is high [25]. In a large study among European countries (ESEMED), mood disorder was reported among 14% of the participants [26]. The prevalence of major depression is higher among patients with long-term medical illness (diabetes, coronary heart disease and stroke) [27-30]. Women are more often diagnosed with depression than men at about a ratio of 2:1 [31], but there are yet no established determinants to explain this [32]. A Swedish study showed prevalence among women attending primary care as high as 23 % [33], but this included sub-threshold depressions. Schuch et al [34] presents possible reasons for the skewed prevalence, with earlier onset of depression and higher comorbidity with agoraphobia and panic disorder, although many researchers still are uncertain about the reasons underlying the gender distribution [34].

It is difficult to measure prevalence because mental disorder is defined in several different ways. There is today no "gold standard" in Sweden that defines exactly how the diagnostic procedure should proceed. Procedures as various as waiting room screening with single questions where patients testify as to "feeling bad" to structured diagnostic interviews that take up to 60 minutes have been used as the basis for diagnostics in different studies.

Depression is associated with several risk factors, such as chronic medical illness, traumatic events, domestic abuse or violence, major life changes,

family history of major depression or substance abuse, stressful life events, and recent losses [7].

The course of depression differs from patient to patient. It is important to recognize this as a clinician when making decisions concerning treatment options [35]. Epidemiological studies show that people have recurrent (50% after one episode and 80% after two episodes) [11, 36] and chronic depressions, yet there is still uncertainty about the levels of disability associated with this risk [19, 37]. Untreated depression constitutes a huge risk, with suicide as the worst endpoint. Back in the 90s, Sweden had high suicide rates, but this has changed since the introduction of SSRI anti-depressant medication [38].

1.3 Primary care

In Sweden, as in many other countries, primary care is the base of the healthcare system. As a part of the healthcare system, primary care should according to the law [39] "respond to people's need for basic medical treatment, care, prevention and rehabilitation that do not require medical and technical resources offered by the hospitals or other instances". The development of the cornerstones of primary healthcare emphasizes universal access, dealing with the health of everyone in the community with a comprehensive response to people's expectations and needs, spanning the range from risks and illnesses to multi-morbidity [40]. Accessibility and continuity form the prerequisites for developing high quality of care, as well as access to high communication ability for the health care users and the community. The first international declaration that underlined the importance of primary health care was presented at the Alma-Ata conference 1978. "Health for all" was the slogan that came out of that conference, and it was proposed that work should be started towards health equality in all countries. The goals set forth by the WHO for primary care are better health services for all, and the elements to obtain this goal are described as: integrating health care everywhere, reducing social disparities, organizing health services according to people's needs and expectations, using collaborative models, and increasing participation from stakeholders [41].

1.3.1 Depression in primary care

There are many reasons for treating mental health problems in primary care. The WHO presents in a report seven reasons why: [42].

1. The burden of mental disorders.

In all societies common mental disorders are prevalent, and create a burden for individuals and their families. CMD produces significant economic and social drudgery that affects the society as a whole.

2. Mental and physical health problems are interlacing.

People often suffer from both mental and physical problems. Integrated care ensures a holistic treatment manner.

3. Treatment gap for mental disorders

There is in all countries a gap between the prevalence of mental disorders and the number of people needing and receiving treatment. Primary care can help decrease this gap.

4. Enhanced access

With integrated care, people can access mental health care closer to their homes. This enables maintenance of daily activities and keeping the family together. Primary care also facilitates long-term monitoring and management.

5. Promotes respect of human rights

When treating mental health disorders in primary care, stigma and discrimination are minimized, and human rights violations that may occur in in-patient psychiatric settings are avoided.

6. Affordable and cost effective

Primary care can provide less expensive treatment than psychiatric wards and hospitals. The treatment is cost effective, and if governments invest, additional cost-benefits may be achieved.

7. Generates good health outcomes

Most people treated in primary care have good outcomes, especially when connected to a secondary level service provided by the community.

Epidemiological studies show that primary care manages more than 70% of all patients with depression/anxiety [14, 43]. Moreover, about 75% of

prescribed anti-depressant medications are prescribed by general practitioners (GPs) [44]. In Sweden about 13% of the adult female population and about 7% of the adult male population use anti-depressant medications [45]. Many of the patients in primary care do not primarily seek medical attention because of depression, but rather for concurrent symptoms such as chest pain, stomach ache, or back problems [21]. In most cases, somatic disease must be excluded and eliminated, or simultaneously treated, before depression can safely be diagnosed. This is in contrast to when a patient attends psychiatric care where somatic causes of ill health are more or less already eliminated either by the referring doctor or by the patient her/himself, thus facilitating the diagnostic process [12].

Most patients can safely be treated within primary care and most cases will lead to remission [46]. Luppa et al highlighted the association between depression and high economic burden. [47].

1.3.2 Detection of depression in primary care

It has generally been claimed that GPs miss identifying about 50% of all patients with depression [48]. Since there are so many patients attending primary care, and the prevalence of depression symptoms is so high in patients who seek care for somatic reasons, it has been proposed that one way of increasing the detection and diagnostics of depression should be waiting room screening. Improvements in the detection and treatment of depression in primary health care have been investigated in several trials. However, detection of depression using approaches such as screening alone does not appear to produce any significant or lasting benefit [49]. Recently, a Cochrane systematic review was published of randomized controlled trials conducted in non-mental health settings that included case-finding or screening instruments for depression [50]. Use of screening or case-finding instruments was associated with a modest increase in the recognition of depression by clinicians (relative risk (RR) 1.27, 95% confidence interval (CI) 1.02 to 1.59), but when questionnaires were administered to all patients and results were given to clinicians irrespective of baseline score, the ability to recognize depression was not improved. The outcomes of depression did not improve, screening or case finding did not significantly increase the use of any intervention. The authors concluded that, if used alone, case-finding or screening questionnaires for depression appeared to have little or no impact on the

detection and management of depression by clinicians and that "recommendations to adopt screening strategies using standardized questionnaires without organizational enhancements should not be justified" [50].

The Nice guideline [51] suggests that two questions be asked when depression is suspected in a person who seeks care: "During the last month, have you often been bothered by feeling down, depressed or hopeless? During the last month, have you often been bothered by having little interest or pleasure in doing things?" If the person says yes to either of these questions, there should be no hesitation regarding referral to an appropriate professional. All persons working with people seeking care should be familiar with these questions. These questions have been validated for case finding [52, 53], and are diagnostically accurate [54].

1.3.3 Depression diagnostics in primary care

Depression can manifest itself in many ways, both mainly as somatic and mainly as mental symptoms, and it can therefore be difficult for the GP to make a proper diagnosis at the first visit. Depression can affect very many aspects of a person's life, leading to e.g. apathy, irritability, changes in eating and sleeping patterns, agitation, concentration difficulties, pain and much more. The clinical interview (consultation) is not enough for a diagnosis; the GP needs more tools to ensure a correct diagnosis. Today, there are some validated worldwide used systems upon which the GPs can base their diagnosis.

Symptoms are identified and classified in the Diagnostic and Statistical Manual of Mental Disorders (DSM) [11]. The DSM-system is used worldwide, and since 2013 the fifth version is in use. For a diagnosis of depression, the patients should have had symptoms that correspond to the duration criteria of at least two weeks. The DSM-IV is broadly used and at the time of the PRI-SMA study on which this thesis is based, DSM-IV was most adequate. The DSM-IV is also used in almost every study examined and reviewed by the NICE Guidelines for adult depression [51]. The DSM IV is based on four pillars.

- Depressed mood or a loss of interest or pleasure in daily activities for more than two weeks.

- Mood represents change from that person's baseline.
- Functions are impaired; social, occupational and educational.
- Five out of nine specific symptoms are present nearly every day.

The symptoms are as follows:

1. Depressed mood or irritable most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)

2. Decreased interest or pleasure in most activities, most of each day

3. Significant weight change (5%) or change in appetite

4. Change in sleep: Insomnia or hypersomnia

5. Change in activity: Psychomotor agitation or retardation

6. Fatigue or loss of energy

7. Guilt/worthlessness: Feelings of worthlessness or excessive or inappropriate guilt

8. Concentration: diminished ability to think or concentrate, or more indecisiveness

9. Suicidality: Thoughts of death or suicide, or has suicide plan.
Healthcare personnel report that it is sometimes very hard to tell if someone has a depression solely by appearance. In Sweden primary care physicians use ICD-10-SE, which is an international classification system for diseases. It is primarily used to group different types of diseases and causes of death to enable statistical compilations and analyses [55].

The ICD system was developed by WHO [56], where depression is defined as a combination of symptoms; a certain number of symptoms must be present and durable for the past two weeks. Core symptoms are low mood, low energy and low activity. In the ICD system, patients are classified according to the severity of the symptoms, and the classification

levels are mild, moderate, or severe. The ICD also takes function into consideration, which then provides the foundation for the choice of treatment and evaluation [7, 21]. The main difference between the ICD-system and DSM-IV is that the ICD was developed by a global health agency and the DSM was developed by a single national association. The ICD is multidisciplinary and multilingual versus the DSM which primarily was derived by US psychiatrists. The ICD system is of low cost, whereas the DSM generates a substantial part of the American Psychiatric Association's revenue [57].

With regard to case finding, several instruments have been developed for diagnostics of depression. The PRIME-MD [53], based on the DSM-III was developed especially for use in primary care and is a tool for identifying mental disorders in primary care practice and research. Mean time for the diagnostic process is estimated to be 8.4 minutes. Another structured diagnostic interview is the Mini International Neuropsychiatric Interview (M.I.N.I), which has been recommended by the SBU [12]. This is a diagnostic instrument, validated for psychiatric contexts, and is time-consuming. It takes about 30 minutes to complete [58] and therefore is less suitable for the short consultations that the GPs in Sweden often have (15-20 minutes per session). However, it is a good method to use as a differential diagnostic instrument to get an assessment when the course of the suspected depression is in any way deviant, in order to obtain a more complete picture.

1.3.4 Depression rating scales

Depression rating scales are instruments used to assess the patients' symptoms. Generally, there are two types of scales, those that the GP fills out, and scales that the patient him/herself fills out (self-assessment). There are in principle three types of scales, i.e. the VDS (verbal description scale) that has a set scale, the graphic rating scale (GRS) that has options along a fixed line, and the visual analogue scale (VAS) with a start and endpoint, such that the rater can choose anywhere between the two points.

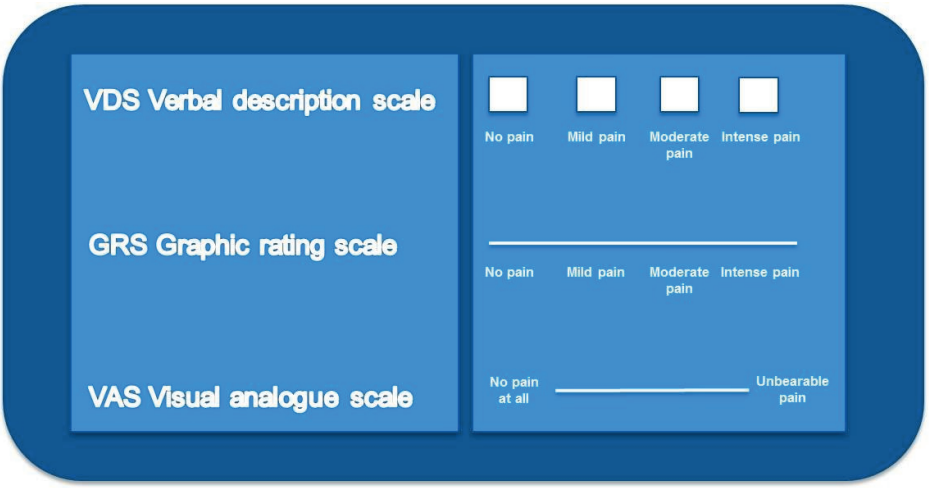


Figure 1. Three types of commonly used scales.[59]

The use of patient reported outcomes, such as self-assessment instruments, has been promoted in recent years, as they are assumed to get the patients more involved, activate participants, and make better decisions about treatment options together with their GP [60-62]. A correct diagnosis is crucial in order to decide which treatment is most suitable, and as objective methods such as blood-sample tests have yet to be developed [63], the clinical interview is a helpful tool.

For the evaluation of the level of depression, mild, moderate or severe, depression-rating scales have been developed. As concerning diagnostic instruments, there are rating scales developed for use in contexts as primary care. The rating scale most used in research is BDI-II, but the rating scales most used in clinical contexts are the Montgomery-Åsberg Depression Rating Scale- self (MADRS-S) [64] and the PHQ-9 [65]. In Sweden, every third GP in primary care says that she/he uses an instrument for target screening, and the most commonly used instrument is MADRS and MADRS-S [12]. Depression rating scales should not be used as diagnostic instruments, but are often used as screening instruments. They generally are sensitive with few false negatives but on the other hand often less specific (many false positives) [66]. By sensitivity we mean the attribute of a diagnostic method (percentage of sick patients that the method correctly identifies) [12] and by specificity we mean percentage of healthy patients that the method correctly identifies.

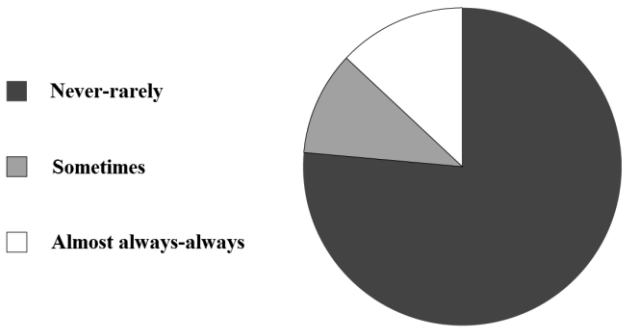


Figure 2. Description of common use of assessment scales in primary health care in Sweden

In primary care it is of course the GP and the nurse her/himself who are the important case finders, and here the ability/experience and communication technique used by the GP and the nurse play an important role in detecting and suspecting depression. Evidence suggests that a GP could exclude depression with great precision by the use of only two questions during the consultation [66]. The GP can in many cases rule out depression, but misses about 20% to up to (in some publications) 50% of patients with depression [48, 67, 68], and GPs are encouraged to re-assess patients whom they suspect have depression. Non-psychiatric GPs' accuracy of depression detection is low [69] and research indicates the need to develop standardized methods. Magnil suggests a person-centered approach with key questions, and Mitchell suggests reassessment. To achieve this there is a need of continuity of care.

Since most instruments used to measure different aspects of depression have originated from psychiatry, but most people seeking treatment for depression attend primary care as the first line of care, more studies evaluating the use of self-assessment instruments in primary care are warranted [12].

The use of self-assessment instruments as a tool to screen for depression is not the issue, according to Gilbody et al. [49], who conclude that without organizational collaborative structure, the use of assessment instruments to identify depression is of little value. There is still little information available as to whether using these instruments in primary care affect depression symptoms, recovery, rehabilitation, and treatment [70].

1.3.5 Screening

There is a distinct difference between screening and diagnostics. It is important to know the difference when talking about self-assessment instruments and depression in primary care. A screening instrument is a tool (often rapidly administered, and easy to use) developed to find candidates, i.e. possibly depressed patients, and a diagnostic instrument (often takes more time and requires some education to use) is used to ensure and categorize the diagnosis.

BDI-II is one of the instruments that showed evidence-based support with regard to reasonable sensitivity in the SBU evaluation in 2012 [12]. SBU concluded in their report that there are too few studies that have scrutinized the effects of using self-assessment scales to evaluate the lapse, cost, and depression outcomes in primary care [12]. There is a need to evaluate structured diagnostics as a part of a systematic trial, in order to measure the effect on recovery, patient/doctor relation, and costs [12].

Screening could be divided into two major groups, i.e. universal and case finding. Universal means that one screens all individuals in a category (for example all people above 18). Case finding means that one screens certain smaller groups of people based on, for example, the presence of risk factors. Every time one screens a population, one needs to be aware of the existence of false positive and false negative results, which means that one will most certainly get positive scores for people who are not depressed, as well as negative results for people who are depressed. These are ethical issues that require serious consideration [71].

In primary care, where the prevalence of depression is lower than e.g. the psychiatric ward, the positive predictive value (PPV) as well as the negative predictive value (NPV) are more important when describing the quality of an instrument [72]. To be useful in primary care with a modest prevalence of the affliction, an instrument must have high PPV. Usually instruments with high sensitivity have low PPV in low-prevalent populations. On the other hand, a high NPV can be useful for the GP/nurse to rule out depression [66].

1.3.6 Treatment of depression in primary care

The Swedish National Guidelines for Treatment of Depression and Anxiety syndromes were published in 2010 [73]. Recommendations for primary care management apply especially to the following:

- high accessibility - the primary health care system should conduct a first assessment with high accessibility
- high continuity of care
- collaborative care - according to the principles of tailor-made stepped care activities
- to not screen for depression and anxiety in samples of patients without known risk for psychiatric disease within primary care [73].

There is no "gold standard" as to what treatment as usual should be regarding depressed patients. It all depends on the severity of the depression, how the person with the diagnosis would like to be treated, and which regimens are available.

The stepped care approach to treating depression has gained more popularity since it is in alignment with most guidelines (high accessibility, effective and efficient services at a low cost). The stepped care model for first depression episode often looks something like this:

Step one: "Watchful waiting", as depression symptoms, especially sub-threshold and mild, can improve as a result of the patient having had a first, supporting care contact and having been acknowledged. A new visit in around a week's time is a confirmation and a start of a continuous and often therapeutic process in itself [73].

Step two: Guided self-help, sometimes through the internet, if the patient is positive to Internet Cognitive Behaviour Therapy (ICBT). This is both efficient and cost effective [73, 74].

Step two-three: Brief face-to-face psychotherapy [73].

Step four: Longer face-to-face psychotherapy and consideration of anti-depressant medication [73]. However, if the person previously has had a depression that was successfully treated with anti-depressant medications, the guidelines indicate prompt start of anti-depressant medication treatment again [73].

The idea behind stepped care is that both the person and the GP can evaluate the depression and find the right level of treatment for the ongoing depression, and if a milder regimen does not give results, they have the possibility to move up a step [75].

The Nice guidelines suggest almost the same:(Figure 3)

Focus of the intervention	Nature of the intervention
STEP 4: Severe and complex[a] depression; risk to life; severe self-neglect	Medication, high-intensity psychological interventions, electroconvulsive therapy, crisis service, combined treatments, multiprofessional and inpatient care
STEP 3: Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions; moderate and severe depression	Medication, high-intensity psychological interventions, combined treatments, collaborative care[b] and referral for further assessment and interventions
STEP 2: Persistent subthreshold depressive symptoms; mild to moderate depression	Low-intensity psychosocial interventions, psychological interventions, medication and referral for further assessment and interventions
STEP 1: All known and suspected presentations of depression	Assessment, support, psychoeducation, active monitoring and referral for further assessment and interventions

[a] Complex depression includes depression that shows an inadequate response to multiple treatments, is complicated by psychotic symptoms, and/or is associated with significant psychiatric comorbidity or psychosocial factors

[b] Only for depression where the person also has a chronic physical health problem and associated functional impairment (see 'Depression in adults with a chronic physical health problem: treatment and management' [NICE clinical guideline 91]).

Figure 3. The stepped care model from NICE guidelines. [51]

Therefore, GPs have a variety of tools they can use in the treatment of depression. We do know that psychological treatment is effective [76] and that antidepressant medications are an effective treatment [77].

Since the mid-90s, the foundation of Swedish primary care has been a patient/person-centered approach for patient-doctor communication, and this has been a part of the education for new physicians ever since, both in the academic undergraduate education and in the Continuing Medical Education (CME) [78, 79]. Most GPs in Region Västra Götaland have taken part in person-centered communication method education in the 90s and onwards as tutors in the undergraduate education at all PCCs and/or

as undergraduate students, and person-centered communication is continuously included in CME and the specialist education (ST) of general practice. This means (in most cases) that persons who receive treatment for depression in primary care in Sweden can be assured of a person-centered communication approach.

1.3.7 Evaluation of depression and MADRS-S in primary care

There is a substantial amount of literature covering depression, but less that covers treatment and use of MADRS-S in primary care. I will present some of the most relevant related to this thesis. Search results from PubMed is presented in Table 1.

Table 1. Search results from PubMed with search strings depression; primary care; MADRS-S

Search String	**Hits**
Depression	362785
Depression AND Primary Care	15807
Depression AND Primary Care AND MADRS-S	13

The thirteen hits on the string Depression AND Primary Care AND MADRS-S are presented below.

McIntyre 2006 [80] – A study that implied a reciprocal interaction between depressive symptoms and somatic symptoms, and suggested that GPs should track and target somatic symptoms of depressed patients.

Horn 2007 [81] – Investigated patient satisfaction after hospitalization in psychiatric institutions. This is not a study performed in primary care and therefore is not considered relevant.

Magnil 2008 [67] - Prevalence of depressive symptoms and associated factors in elderly (aged ≥60) primary care patients: a descriptive study. Showed a 15% prevalence in the depressive range, and sedatives were more common among these patients than non-depressed. Perceptions of

good health and leisure time activities were higher among non-depressed patients. The study also showed good prognosis for patients with ongoing treatment for depression in primary care.

Holländare 2010 [82] – Showed that MADRS-S can be transferred to online use. This also applied to the BDI-II. An online questionnaire opens possibilities for the clinician to save resources.

Magnil 2011 [66] – Concluded that the clinical consultation screening procedure might be as useful as the Prime-MD screening questionnaire, and that the GP can rule out depressive symptoms with high accuracy.

Magnil 2013 [35] – Described three course patterns for elderly depressed patients and called attention to risk factors that facilitate identification of patients at high risk of poor prognosis.

Flyckt 2014 [83] – Identified cues for recognizing people with undiscovered depression, and highlighted that a two-stage procedure with screening and a structured interview is recommended in patients with sleep disturbance and lowered function.

Hedman 2014 [84] – Showed that ICBT for depression is as effective as treatment delivered in routine psychiatric care when delivered in a controlled setting.

Kivi 2014 [74] – Showed that ICBT can successfully be delivered in primary care and is on a par with treatment as usual (TAU).

Wang 2015 [63] – Presented results indicating a biomarker that potentially could be related to depression.

Wikberg 2015 [85] – Concluded that MADRS-S and BDI-II have comparable results, thereby opening up for the possibility that clinicians may use the easily administrated and free instrument MADRS-S to follow the lapse of depression with the knowledge that the results would have been the same if the licensed and costly instrument BDI-II had been used.

Enander 2016 [86] – This was a study on CBT treatment on body dysmorphic disorder, and therefore not relevant for this thesis.

Wikberg 2016 [87] – This study used focus groups interviews to ask depressed patients about their perception using MADRS-S in the GP consultation in primary care.

This demonstrates the limited number of studies regarding MADRS-S in primary care, and in particular, the lack of studies evaluating the effects MADRS-S as a part of the primary care consultation.

1.3.8 Primary care context of the study

Primary care plays an important role in improving outcomes and plays an essential role in the prevention, treatment, and rehabilitation of common diseases [88]. In Sweden there are about 1200 PCCs, and in Region Västra Götaland there are about 200 PCCs. These are the first line of healthcare. Most PCCs have GPs, nurses, and psychologists. There are some additional personnel as well, such as counselors, administrators and assistant nurses, and sometimes occupational and physio-therapists. There are several ways for the individual to get help at a PCC; one is to go to a drop-in session, in order to see a GP or a nurse, and the other is to call/make internet contact for a booked appointment. Usually, at the drop-in for a GP visit at the PCC, only one problem can be managed at each appointment, due to the lack of time and few available bookable appointments. For a longer consultation time of around 20 minutes, there is usually around a week's waiting time.

At the time when we began the PRI-SMA RCT in 2010, a large reorganization took place in the primary care organization called Vårdvalet, roughly translated as "The choice of care". The implication of Vårdvalet was that patients should be able to choose freely which PCC they wanted to attend with their problems. Vårdvalet also meant a deregulation of the public health services, meaning that private actors could compete on equal terms. This reformation was a part of LOV 2008:962 [89] (The law of system of free choice). Patients were now able to switch PCC if they liked, were not happy with their treatment, or for any other reason. This forced the PCCs to change to a more person-centered orientation. The PCCs were to see the patients more as individuals than patients. Enrolling patients became important due to remuneration. PCCs were allotted payment from the region depending on several factors. One factor was the number of patients listed. Other factors were quality indicators such as results of blood pressure treatment,

asthma, diabetes, and other measures to name a few. The national guidelines for depression called for high accessibility with regard to offering an assessment, continuity throughout the chain of care, a collaborative stepped care that is tailor-made for the individual [73]. However, in contrast to high accessibility, continuity of care was not included in the quality indicators by the region.

1.4 Adherence to medication

One aspect and one of the usual regimens for treating depression includes the use of antidepressants. National guidelines for depression state that antidepressant medication has a good effect on symptoms and ability to function regarding moderate depression, but often a very small effect when regarding the first episode of a mild depression [73]. Yet antidepressants are one of the most commonly used strategies by GPs when treating a depressed patient. About 75% of all antidepressants are prescribed in primary care [7]. Counted in terms of DDD (Defined daily dose) and based on statistics from the Board of Social Welfare 2009, antidepressants are on the list of the most used drugs in Sweden [90]. A recent meta-analysis [91] showed that SSRI and TCA antidepressants have a solid evidence base compared to other drugs regarding effectiveness in primary care, although the effects are small compared to placebo. It is easy to prescribe an SSRI, but studies show that it is harder to maintain adherence [92, 93]. Depressed patients have a three times greater risk of noncompliance to medication than non-depressed patients [93]. Geddes et al showed that if patients do use the antidepressants for the time called for in the guidelines, the risk of relapse is reduced [94].

The relationship between the GP and the patient plays a vital role in the results and outcome regarding adherence. Collaboration between the treatment giver and the receiver is essential to gain satisfaction, improve outcomes and reduce non-adherence [95]. The term adherence or compliance is used to describe to which degree the patient follows advice or in the case with antidepressants, follows the prescription and treatment.

Adherence to medication plays an important role in depression treatment [96]. Adherence to prescriptions plays a vital part in the remission rate for patients with depression [97]. Poor adherence is associated with higher risks of relapse [98]. Thus, if primary care could enhance adherence, perhaps better outcomes could be attained in reducing depressive symptoms.

1.5 Sick leave, work ability and function

Most people who attend primary care are of working age, and a majority of them are employed. Depression and work ability are closely entwined meaning that depression affects work ability to a large extent and on several dimensions [99-101]. In Sweden today there are increasing numbers of people who are on sick leave due to depression and other mental health disorders, such as stress reactions, anxiety, and burnout syndrome [8]. After the seventh day of sick leave, the patients need a certificate that is written and approved by a physician

In Sweden physicians need to address the patients work ability in three stages to write recommendation certificate for sick leave to the Swedish Social Insurance Agency: i) diagnose; what kind of illness does the patient have ii) disability; describe what functions that are disabled due to the diagnosis and iii) limits of activity; to what extent the diagnose and disability have consequences for the job [102].

When a person is on sick leave the employer pays a reduced salary the first 14 days, and thereafter the Swedish social insurance agency pays sick leave salary. This system sometimes makes it hard to get a truthful picture of how long a patient has been on sick leave from registers, because all data is not reported to the Swedish Social Insurance Agency.

Common mental disorders (CMD) account for a large proportion of sick leave days in many industrial countries [103], and the work capacity is substantially reduced among people with depression [99, 100, 104, 105]. Depression and back disorders are the diagnoses that represent the major part of decreased work ability among employees [106]. This is not so apparent on the individual level, but since the diagnoses are so prevalent, there is a large effect in larger populations. About 50% of people with depression or anxiety reported their work ability to be good [107] , and when patients recover from depression, their work ability does not recover at the same pace as the depression does [108, 109].

The ability to work, i.e. work ability, is a multidimensional concept that is not easy to define. Illmarinen defines work ability as “the balance between human resources and the demands of work”[110]. Tengland has a more divided perspective regarding the term work ability [111]. He describes work ability as a concept in need of two definitions, one for jobs that require specific education and one for jobs that most people can manage.

Work ability is the employees' ability to complete the tasks required for the job that they were hired to do, and if they become ill/disabled or in any way become unable to complete the tasks that they were hired for, the second definition comes in use, i.e. the ability to complete a task that lies within most people's range to complete.

Illmarinen describes work ability using the following "house" metaphor: In this house there are four stories – the ground floor contains health and functional capacities, the second floor is competence, the third floor contains values, attitudes and motivation, and finally, the fourth floor accommodates work, work community and leadership. Above these floors you reach the roof, which is protecting the stories below. All four floors together embodies the concept work ability. There is also a line separating the third floor where the external operational environment comes into play. Outside the work ability house you will find the family and the immediate social environment, as factors that affect the outcome [112, 113].

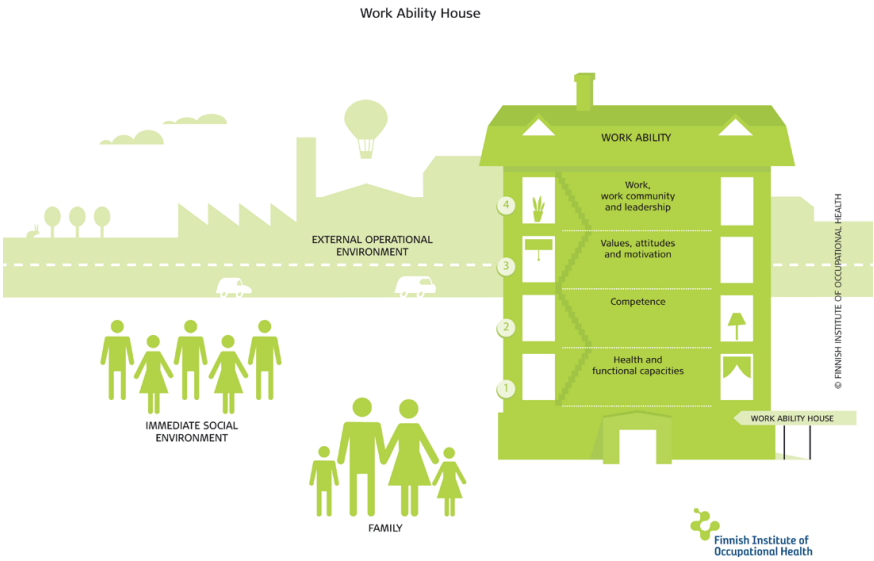


Figure 4. Work ability house

Internationally and in Sweden the International Classification of Function (ICF) is used to categorize function and disabilities [114].

There are numerous factors that need to be accounted for, but non-medical staff can hinder or promote return to work (RTW). There is a need to assess work ability early during a person's sick leave to improve outcome [115]. Many employees and managers call for better links to enhance collaborations and work performance [116]. Decreased work ability is also associated with loss of productivity [117, 118] and patients with depression account for a large portion of health care consumption, costs for both the individual patient as well as for society due to reduced work ability and delayed ability to return to work [119]. The largest economic detriment associated with depression seems to be the loss of productivity occurring after the individuals have returned to work, which stands for a substantial cost for society [108, 120]. It is also important to include functional impairments as an outcome when studying depression, because the two are highly coexisting [121].

Function comes from Latin *Functio* and means a performance, execution. Depression is associated with occupational impairments [108, 109]. The following is an example: a person is working as secretary; one function is to write, using her/his hand. If she/he damages the hand and will not be able to use the hand properly, then that function is considered diminished. There is an increasing body of evidence pointing towards the importance of including these factors when developing new interventions or programs in order to enhance treatment of CMD in primary care. Kamenov et al in their large review have called for more studies that evaluate the comprehensive tools, provisions of detailed information and functional areas [122], and a recent Cochrane review found that including a work-directed intervention would reduce number of sick days compared to just a clinical intervention [123]. We cannot exclude the workplace, work ability, and function if we want to achieve successful interventions in the future.

1.6 Person/Patient-Centered care

In Sweden GPs have been trained (in medical school and tutoring programs) in the use of patient/person-centered consultation methods since 1993, and since then it has been evolving and become a natural part of the medical school education. The term person-centered care is a well-known concept, which should and could be applied in all disciplines that concern people's health and care [124]. Person-centered care is a central component for sustainable high quality in healthcare [125]. The relation between the patient and the GP/nurse/care personnel is central in the

primary care context. The understanding of the patient's "agenda" is one of the prerequisites for building a good patient/GP-alliance [126, 127]. GPs and other personnel in contact with patients in primary care should have a person-centered orientation, taking the patients' needs and preferences into account [51, 78, 128]. This requires a good patient/practitioner communication and is an essential part of the consultation. All communication needs to be supported by evidence-based information tailored to the patients' needs. [51]. A person-centered approach is important to lower patients' anxiety and improve satisfaction at work, and over the last decades there has been a substantial amount of research evidence supporting this [129]. The supposition has to be that each individual has his or her own way of handling, experiencing, and coping with health-related problems within their life world [88].

Person-centered care and patient-centered care are commonly used concepts within research and even though they often are used synonymously, there are differences [129, 130]. When "person" is used, this often refers to a holistic standpoint, and the equal value of every individual [131]. It is hypothesized that the use of "patient" tends to be a stigmatizing term that is more reductionist and differentiates between persons, hence the reduction of humanity [132]. In general practice, person- centered consultation methods have been used and taught since the 1980s in the UK, and are now widely spread and used in the medical curriculum in Sweden and other Nordic countries [79, 133, 134]. The cornerstones of the person-centered consultation methodology are to elicit the patient's main problems and the patient's perceptions of these, and to elicit the physical, emotional and social impact of the patient's problems on the patient and family [78]. This in turn gives the possibility to tailor the information to what the patient wants to know, and to engage the patient in the decision-making. We used the person-centered approach in our RCT, due to the patient's own involvement. The patients graded their own perception of symptoms, with the help from the instruments. Then they discussed their answers together with the GP. The GPs in our RCT had all undergone brief education/instructions on how to use the instruments in the consultations. Most GPs earlier in their career had had consultation training regarding the person-centered approach. Therefore, this methodology was not something new to the participating GP's.

In summary, it should be emphasized that a person with any sickness or disorders, risk of illness or disabilities should not be judged/be seen primarily by her/his sickness or disability. Person-centeredness is to a greater degree a focus on the resources. One approach can be to use the

word “person” instead of “patient”, in that some advocates of person-centeredness think that the word “patient” is more focused on the illness and the connection to the healthcare system, rather than on the person with her/his unique experiences and needs [135]. There are tools available to assess a more person-centered approach in primary care, and they deserve a more generous use [136]. A person-centered approach is regarded as effective for patients with depression, mild to moderate, and even severe depression [137].

1.7 Etichal issues

The Regional Ethical Review Board in Gothenburg, Sweden approved this study PRI-SMA (Dnr 746-09; T612-10). The trial was registered at ClinicalTrials.gov [138]. All studies have considered the Helsinki declaration. All patients received written and oral information on the study procedures and aims. All patients were informed that they at any time during the study were free to withdraw without any reason and without any consequences concerning future care. All collected data from the study were filed in a computer, the data were coded, and the key to the file was solely available to the study personnel. All patients were informed that the information they provided on the various forms would be handled confidentially.

2 AIM

2.1 General aims

The general aim of this thesis was to evaluate the effects of regular use of a self-assessment instrument in GP consultations with the depressed patient in primary care. Does the use of self-assessment instruments have an effect on depression course, as well as quality of life, well-being, anti-depressant medication use, sick leave, work ability, and health care use in a long-term perspective?

2.2 Specific aims

1. To evaluate in a randomized controlled trial whether using a depression rating scale (MADRS-S) in recurrent person-centered GP consultations affected depression severity, quality of life, overall psychological well-being, antidepressant and sedative use, sick leave, and healthcare use in a long-term perspective.

2. To assess the comparability of the BDI-II and MADRS-S self-assessment instruments in primary care to evaluate differences between the instruments in the self-assessment of depressed patients in primary care.

3. To understand how patients with depression perceive the use of MADRS-S in primary care consultations with GPs.

4. To investigate whether the continuous monitoring of the depression symptoms by a self-assessment instrument in recurrent person-centered GP consultations has any long-term effect on work ability, job strain, and social support for the patient with depression in primary care.

3 PATIENTS AND METHODS

This thesis consists of four studies, three quantitative and one qualitative. Overviews of these studies are shown in Table 2.

Table 2. Overview, design, study groups, data collection methods and data analysis of papers I-IV.

Paper	**I**	**II**	**III**	**IV**
Study Design	RCT Longitudinal cohort study	Retrospective cohort study	Qualitative	RCT Longitudinal cohort study
Study groups	258 PCC patients aged ≥18 diagnosed with mild/moderate depression.	146 PCC patients from PRI-SMA and PRIM-NET study	9 PCC patients who have undergone the PRI-SMA intervention	183 PCC patients from PRIS-SMA who worked or were on sick leave
Data collection method	Questionnaires, EPR	MADRS-S and BDI-II	Focus Group Discussion	Questionnaires, EPR
Data analysis	Descriptive, comparative	Descriptive, comparative	STC	Descriptive, comparative

3.1 Patients

All patients were recruited from primary care context at PCC in the Region Västra Götaland. The majority of the patients were recruited in the PRI-SMA study, which is described in paper I, except for 72 patients in paper II, who also were recruited from the PRIM-NET study. All patients were recruited when they had attended the primary care centers, and were thus "real" primary care patients. The recruitment period in the PRI-SMA study was between 2-4 weeks at each PCC, enabling a consecutive procedure. Patients in PRIM-Net study were recruited between 2010-2013. Figure 4 describes the number of participants in each study originated from the PRI-SMA cohort. The additional patients from the PRIM-NET study is also shown (Figure 4).

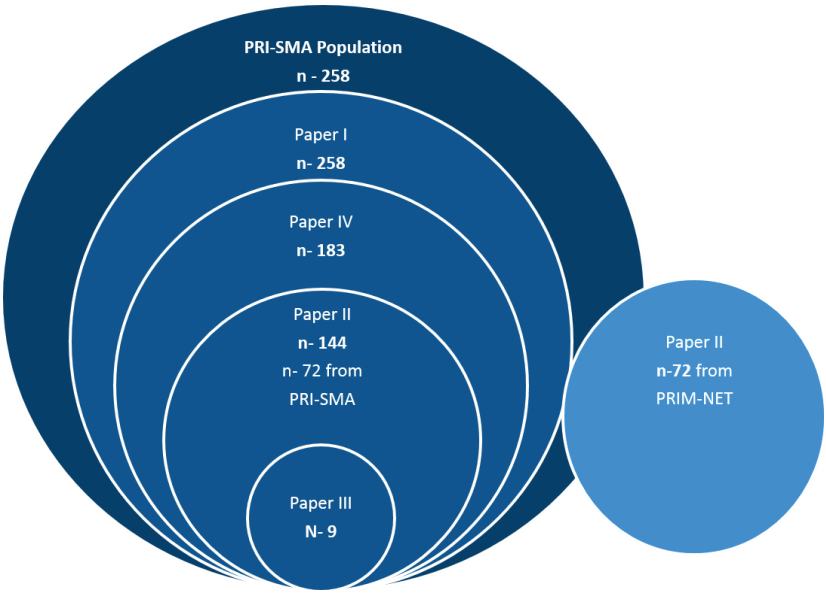


Figure 4. Distribution of PRI-SMA patients presented in circle diagram. PRI-SMA population enrolled 258 patients, and from that study, this thesis presents four papers.

Flowchart of the PRI-SMA study describes, randomization, intervention and control methods, and follow up and outcomes in the four papers is presented in figure 5.

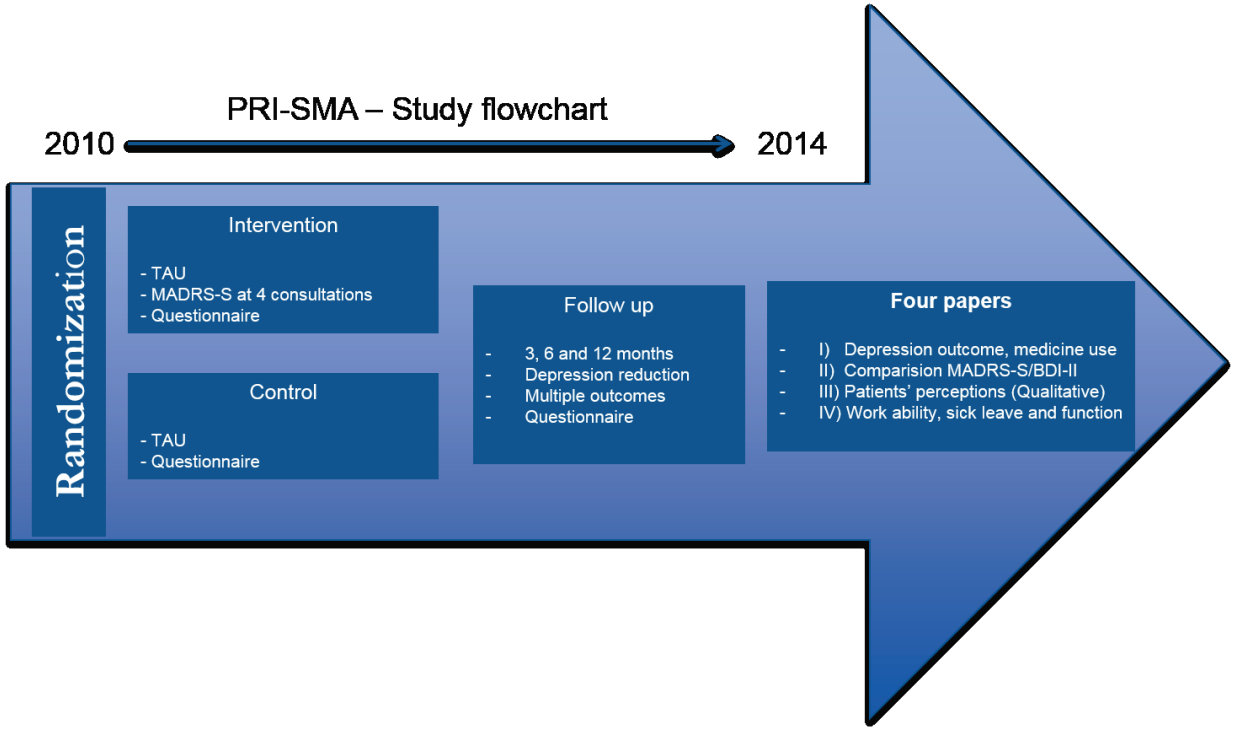


Figure 5. Flowchart of the PRI-SMA study.

Carl Wikberg

3.2 Methods

3.2.1 Instruments

PRIME-MD

Prime MD is a diagnostic instrument developed for primary care, based on the DSM-IV criteria [139]. Prime MD consists of a self-administered part where the patient completes a 26-item questionnaire and a second part for diagnostic purposes that should be used by the physician, psychologist, or trained nurse. The questionnaire screens for common disorders in primary care such as depression disorder, anxiety syndromes, eating disorder, alcohol disorder and somatoform disorder [53]. In the PRI-SMA study, solely the diagnostic part of the PRIME-MD was used (depression module) by the GPs to confirm the depression diagnosis. The Prime MD is evaluated and validated in primary care [53, 139, 140].

MADRS-S

The original MADRS (Montgomery Åsberg Depression Rating Scale) instrument was developed in the late 70s by Marie Åsberg and Stuart Montgomery [141] as an instrument sensitive to changes in depression symptoms and well suited to follow treatment and course of depression. MADRS-S is suitable when regularly following symptoms over time [142]. The instrument measures how the patients have felt during the last three days. The instrument has nine items where each item may be scored between 0 and 6 and has a maximum score of 54.

MADRS-S differs from the original MADRS instrument in two major ways. Firstly, the original instrument is administered by the interviewer and contains 10 items. In MADRS-S, the item concerning depressive thoughts content (item nine) is removed. Further, the main difference between the two instruments is that MADRS-S is the patient's own instrument, where the patients themselves score their symptoms. The two instruments have been validated and cross-validated in several studies [143, 144]. The nine items that the patients are requested to score are sadness, inner tension, reduced/changed sleep, reduced/changed appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. The cut-off levels are 0-12 indicating no (or minimal) depression, 13-19 mild depression, 20-34 moderate, and 35 and above indicating severe depression. The MADRS-S is a free to use instrument, is validated in several languages and it is the most commonly used instrument for self-assessment regarding depression in Swedish primary care [12].

BDI-II

Dr. Aaron Beck developed the BECK Depression Inventory instrument back in the 60s [145], and later on in 1996 [146], the BDI-II. The instrument lets the patient rate her/his own symptoms and has 21 items; for each of the items the patient assigns a score ranging between 0-3. The patient is instructed to take the last two weeks into consideration when scoring the items. Cut-off levels for BDI-II are reported to be 0-13 indicating no (or minimal) depression, 14-19 mild depression, 20-28 moderate depression, and 29 and above indicating severe depression [147, 148]. Maximum score is 63 The BDI-II is validated in several studies [149-153], and is one of the instruments that the SBU recognized as reliable enough to be used during the diagnostic process of depression [12]. However, comparison between cut-off levels for MADRS-S and BDI-II in primary care patients shows that the cut-off level for severe depression is set too low for the BDI-II (Study II). The cut-off score level should be increased from 29 to around 36 to match the MADRS-S cut-off level for severe depression.

GHQ-12

The General Health Questionnaire-12 is a twelve item self-assessed instrument developed from the GHQ [154]. It was developed as a screening instrument for the primary care setting, to identify psychological distress [155]. GHQ-12 measures self-assessed general psychological health in populations and was developed to identify "case" rather than the opposite "non-case". It is more of a specific instrument than a general. The GHQ-12 has been extensively used in a number of countries and languages. It takes about 2 minutes to complete and there are four possible response options on each of the twelve items (Likert score 0, 1, 2, 3) with a maximum score of 36 [154, 156]. The GHQ is a well-known validated instrument [157].

EQ-5D

EQ-5D is an instrument used to measure health outcome [158]. The EQ-5D consists of two parts: one part is a descriptive system with 5 dimensions, where the respondent ticks the box that is most accurate for each part. The second part is an analogue VAS scale where the respondent indicates "how good or bad your own health is today, in your opinion". The EQ-5D is a well-known and validated instrument for quality of life and useful in health economic calculations [157, 159].

WAI

Work ability index (WAI) is an instrument used to assess work ability during health examinations and work place surveys [113]. Through a self-assessment questionnaire, WAI measures the individuals work ability. It is a summary measure of seven items (score range 7-49). WAI has been translated into more than 24 languages and is validated in several studies [160-162]. It measures the demands of work, the worker's health status, and resources. Eight subscales are included in the index: 1) estimation of current work ability compared with life-time best (0-10 points), 2) work ability in relation to physical demands of the work (1-5 points), 3) work ability in relation to mental demands of the work (1-5 points), 4) number of diagnosed diseases (1-7 points), 5) estimation of work impairment due to diseases (1-6 points), 6) sickness absence during the past year (1-5

points), 7) own prognosis of work ability 2 years from now (1, 4, or 7 points), and 8) mental resources (1-4 points). All 8 subscale scores are summed up to a total score (range 7-49). WAI score between 7-27 points indicates poor work ability, 28-36 points moderate work ability, 37-43 points adequate work ability, and 44-49 points excellent work ability [163].

KARASEK-demand-control

This model describes what affects the perceived stress and describes the outer demands in relation to the control one has over a situation and the support one can obtain. [164]. With regard to demands at work, Karasek means aspects such as demands regarding productivity and demands to achieve deadlines. Mental workload is the amount of mental energy needed to complete a task.

Control is the factor that involves the competence one has at work and the ability to make own decisions. Together this contributes to the control over the situation and the demands set. Support is the third factor; employees who perceive a functioning social support from fellow coworkers or their boss develop fewer stress symptoms. In paper IV, the Demand–Control–Support questionnaire contained 17 items: 5 for demands, 6 for control, and 6 for support. The response alternatives for demands and control were: “yes often”, “yes rather often”, “no, seldom” and “no”. Each answer alternative was given a value, and summary scores were calculated for each index and dichotomized using the median score as a cut-off point. The demand subscale ranged from 5-20 and was dichotomized into low demand (5-13 score) and high demand (14-20 score). The control subscale ranged from 6-24 and was dichotomized into low control (6-18 score) and high control (19-24 score). The support subscale regarding support intensity was based on the following response alternatives: “agree, totally,” “agree, rather well,” “do not agree particularly well,” and “do not agree at all”. The support subscale ranged from 6-24 and was dichotomized into low support (6-19 score) and high support (20-24 score).

Job strain

The job strain model was used to analyze the combination of demand and control [165]. Using median values, each index was dichotomized into high and low control and high and low demand, respectively. The dichotomized variables were combined into the job strain index as follows: low-strain jobs (low demand, high control), high-strain jobs (high demand, low control), passive jobs (low demand, low control), and active jobs (high demands, high control).

Additional demographic data was collected by the use of a questionnaire distributed at the time of study inclusion.

3.2.2 Focus group discussion

A focus group discussion is a session led by a group leader. Usually between 4-6 informants are participants, but there is no absolute number of participants that needs to be achieved [166]. The group leader uses an interview guide or questions with the purpose to discuss a specific topic. A focus group discussion is suitable for sensitive topics and can provide aggregate information from multiple participants [167]. For analysis we chose to use Malterud's systematic text condensation as inspired by Giorgi describes the standards for qualitative research in her article in a profound way [168, 169]. The conclusion is that qualitative research helps to prevent methodological separatism. With qualitative research, we can expand our views of clinical realities. We need to remind ourselves that no research method will ever be able to completely describe how people think or feel in their minds. Scientific knowledge is not always the most important information when dealing with persons. We could have used other qualitative methods, for example, Grounded Theory [170, 171] but due to the experience with qualitative methodology by the PhD student and the experience with STC by the supervisor we were satisfied with our choice of method.

STUDY I

This RCT aimed to evaluate whether using a depression rating scale (MADRS-S) in recurrent person-centered GP consultations affected depression severity, quality of life, overall psychological well-being, antidepressant and sedative use, sick leave, and healthcare use in a long-term perspective.

Setting and subjects

We invited all primary care centers (PCC) in Gothenburg and South Bohuslän, and twenty-two PCCs agreed to participate. We randomized on the GP level to avoid that the same GP would deliver both the intervention and the control treatment. Ninety-one GPs were randomized to either intervention or treatment as usual (TAU) in this two-armed RCT. All participating and randomized GPs received a brief education about how the MADRS-S was supposed to be used during the consultation. All GPs (both intervention and control) were given a refreshment education about the person-centered consultation approach. All patients who were diagnosed by the general practitioners as having a new episode of mild/moderate depression were invited to participate in the RCT.

Inclusion criteria were: age ≥18 years, diagnosed with mild/ moderate depression, and a written consent of participation.

Exclusion criteria were severe depressive disorder (BDI-II >36), diagnosed with severe mental disorder (i.e., bipolar disorder, antisocial personality disorder, psychosis, substance use disorder, or other serious mental disorder), suicidal ideation or earlier suicide attempts, prescribed anti-depressant medication with changes in dose during the preceding 2 months, drug addictions, not fully under-standing written Swedish, and cognitive impairments that hindered participants to fill out questionnaires.

Intervention

The intervention consisted of a consultation including re-assessment with MADRS-S as the patient's own instrument, once every month for 3 months (4 appointments in total). In addition to usual treatment, patients received monitoring and evaluation of depression severity and change in person-centered consultations by using the self-assessment instrument MADRS-S [141], at baseline, 4, 8 and 12 weeks follow-up.

Treatment as usual

Patients in the control arm received treatment as usual (TAU). Recommended treatment from national guidelines includes cognitive behavioral treatment (or other psychological treatment), and/or anti-depressant medication, and/or re-assessment (watchful waiting). It is important to describe treatment as usual (as done in introduction) since we are using it as control condition in this study. It is known that putting patients on waiting list could worsen the conditions and could be a nocebo condition, and the use of placebo is not ethical [172-174].

Study procedure

During regular medical consultations, the GPs screened for depression based on the methodology using Malterud's key questions [175]. For patients who were suspected as having mild/moderate depression, they made the Prime-MD diagnostic test. If positive and no documented dysthymia was recorded, patients were asked if they would like to participate in the trial. They were then directed to the onsite study nurse who gave further information. If the patient could not stay and meet the study nurse, an appointment was set up within the nearest days. The patients were given oral and written information, and signed a written consent to participate. Patients were then enrolled in study. All study data was collected on site, where a study nurse was placed at the PCC and included eligible patients continuously. The study nurse handed out questionnaires, including the BDI-II, GHQ-12, EQ-5D, WAI, Demand-Control and demographic data questionnaires. The participants filled out the documents in about 20-30 minutes, and were informed about long-term follow-up procedures.

STUDY II

This paper assessed the comparability of the BDI-II and MADRS-S self-assessment instruments to evaluate differences between the instruments in the self-assessment of depressed patients in primary care.

Before we started the study, a statistician performed a power calculation to give us the number of inputs needed to present trustworthy data. Nineteen cases with assessment were needed on each instrument, i.e. the

MADRS-S and BDI-II. We collected the data from two RCT studies, the PRI-SMA study[138] and the PRIM-NET study [74].

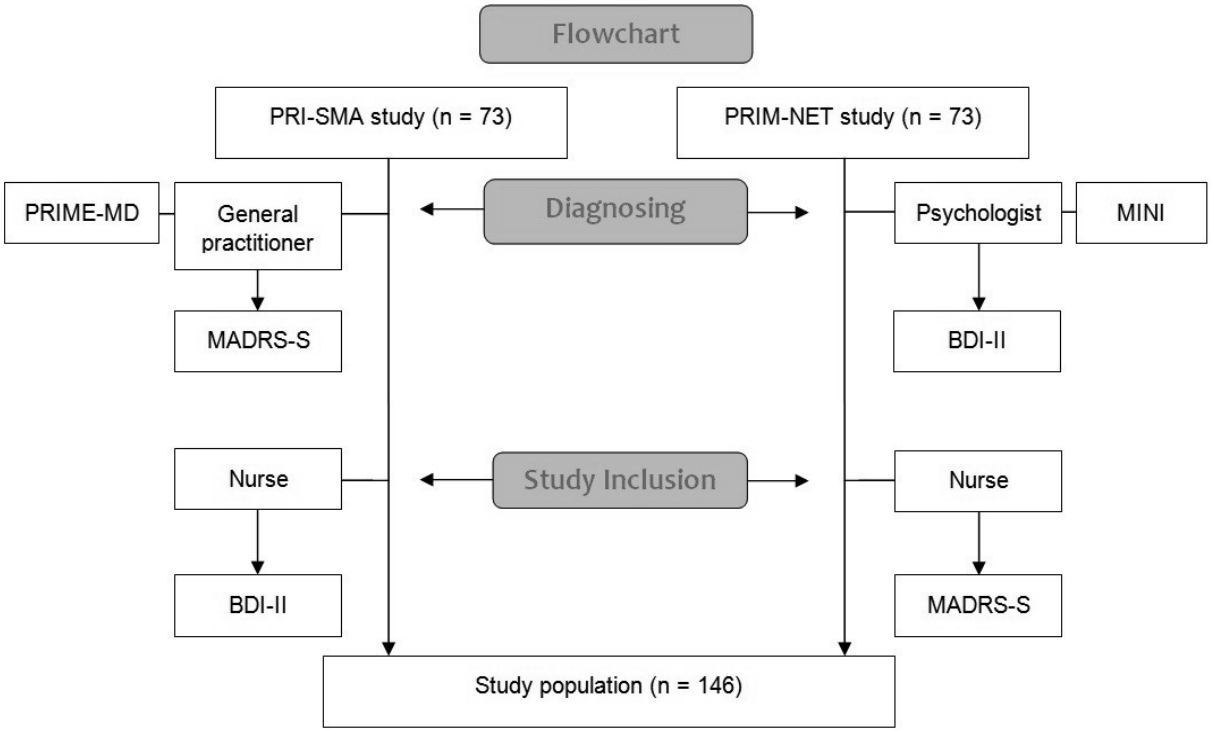


Figure 6. Order of assessment in separate RCTs explained

Inclusion criteria were similar in the PRI-SMA and the PRIM-NET study (similar to the inclusion criteria described for Paper I), and both were conducted in PCCs in Region Västra Götaland, also, exclusion criteria were the same. In paper II 146 patients were included, 73 from each RCT. We used all available data for this paper to increase power. The n=146 was a result of how many available full scores we had from the PRIM-NET study. A total of 73 patients had completed both MADRS-S and BDI-II at the same inclusion occasion in PRIM-NET, and consequently we included the same number of patients from the PRI-SMA study. All patients assessed their depression symptoms with both MADRS-S and BDI-II, but the order in which the patients assessed their own symptoms differed in the two RCTs, as shown in the flowchart (Figure 6).

Data analysis

The data was analyzed with SPSS statistics for Windows [176]. The association between the items from the two instruments was evaluated with intra-class correlation and Cronbach's alpha [177]. Cronbach's alpha was used to test the reliability of the BDI-II and MADRS-S items. Pearson product moment correlation was used to test the associations between BDI-II and MADRS-S total scores. Descriptive statistics were reported as number (%) and were compared with Pearson X^2 test. The level of significance was set at $p<0.05$.

STUDY III

This qualitative study recruited patients from PRI-SMA paper (I). Patients from the intervention arm, who had finished their intervention and where the time that had elapsed was no longer than 3 months, were invited to participate in a focus group discussion. The three-month restriction was intended to reduce memory bias.

We invited all possible patients by letter, and called them by phone after a few days to ask about participation (see paper III study flowchart). Patients who agreed to participate then received another letter with directions to the Research and Development Center in Gothenburg, where the focus group discussions were held. All participants were offered compensation and a snack (2 movie tickets, value approximately 20 Euros). A total of nine patients completed the three focus group discussions. All data were analyzed with Malterud's systematic text condensation [178], which is a method that is inspired by Giorgio [168]. It contains 4 stages, described below.

In the first step of systematic text condensation, the analyzers (one PhD student and the other co-authors) read the material to become familiar with it and to form an overall impression of the content. In the second step, they separately re-read the transcriptions in a more organized way. During this re-reading, they identified meaning units – those quotations that were relevant to the research question – and labelled them with a code. Then they organized the coded meaning units into a matrix that showed the relationship between the units, and they noted the row and page number from which each unit (quotation) came. The supervisor followed and validated this entire process. In a third step, the meaning units were sorted under sub-codes (overarching codes). To be more specific, each quotation was listed under the appropriate sub-code. Next, the meaning units were condensed, or in other words, simplifying the quotations by taking away unnecessary words, creating "artificial quotations." As necessary, multiple sub-codes were also collapsed into fewer sub-codes. These few codes then became the final categories that constituted the main results of the study. The supervisor followed and validated this process as well, and all authors participated in the creation and wording of the final categories. In a fourth step, the artificial quotations were used to create a description of what the patients said about each of the final categories during the focus group interviews. Quotations from the original transcriptions were used to illustrate these descriptions. All authors checked the quotations against the matrix to validate the findings.

STUDY IV

In this study, data from the PRI-SMA study was analyzed. The study sample was selected from the PRI-SMA population. We included patients who worked, who were on sick-leave or who in any other way were employed. The population in the analysis did not contain any PRI-SMA patients who were retired or students.

For this study, we used the same inclusion criteria as in paper I.

After exclusion of the above-mentioned groups, 183 patients were eligible for the analysis. The same exclusion criteria were used as described in above Study I. Data was collected the same way as in paper I. In paper IV all participants received the intervention described in paper I. Outcome measures for this paper was work ability, measured with WAI, and social support and job strain measured with the Swedish Demand-Control-Support Questionnaire. Quality of life measured using EuroQol-5D

(British tariff). Depression outcomes were measured with the BDI-II self-assessment instrument. Additional information concerning sick leave and medication use was collected through EPRs and from patients' questionnaires. All outcomes were measured at baseline, 3, 6 and 12 months.

Standard methods were used for descriptive statistics. Frequencies were compared by using Chi-square, means by the Mann Whitney U-test, all two-sided tests. Statistical significance was set at $p<0.05$. In order to compare change from baseline to 3, 6 and 12 months follow-up concerning age and gender, logistic regression analysis was used. Subgroup analysis concerning sick leave and number of work days was performed in the group of patients 18-65 years, taking age into consideration.

4 RESULTS

Paper I

In the PRI-SMA trial, 258 patients were enrolled to either the intervention or control group. Descriptive data is shown in Table 3.

Table 3. Baseline characteristics of participants in the PRI-SMA trial.

Characteristics	Total n (%)	Intervention n (%)	TAU¤ n (%)	p
Participants	258	125	133	
Age (years, mean)	43.48	44.84	42.19	0.2
men	76 (29.5)	31 (24.8)	45 (33.8)	
women	182 (70.5)	94 (75.2)	88 (66.2)	0.1
Marital status				
single	118 (45.7)	61 (48.8)	57 (42.9)	
married/cohabiting	140 (54.3)	64 (51.2)	76 (57.1)	
children <18 years at home	82 (43.2)	36 (40.4)	46 (45.5)	0.5
Lower educational level	71 (27.6)	32 (25.8)	39 (29.3)	0.5
Employment				
working/studying	181 (80.8)	90 (81.1)	91 (80.5)	
unemployed/retired	43 (19.2)	21 (18.9)	22 (19.5)	0.9
Born outside the Nordic countries	41 (16)	19 (15.3)	22 (16.7)	0.8
Smoking (yes or sometimes)	75 (29.4)	36 (29.3)	39 (29.5)	0.9
Leisure-time physical activity				
never	109 (42.4)	57 (46)	52 (39.1)	
at least 4 hrs/week	124 (48.2)	55 (44.4)	69 (51.9)	0.5
intensive	24 (9.3)	12 (9.7)	12 (9,0)	
Depression				
mild (BDI-II 12-19)	32 (13)	16 (13.6)	16 (12.4)	0.9
moderate (BDI-II 20-28)	82 (33.2)	39 (33.1)	43 (33.3)	
high moderate (BDI-II 29-36)	68 (27.5)	35 (29.7)	33 (25.6)	

¤TAU, treatment as usual

There were significantly more women than men enrolled. There were no statistically significant differences between the intervention and control groups at base-line (Table 3). Concerning dropouts (Figure 7) there was a statistically significant difference between participants and drop-outs during the study for age (mean age of drop-outs 37.3 years and 44.3 in participants), gender (male 14/62, 22.6%, female 16/166, 9.6%, p=0.034), and ethnicity (born in Sweden 21/194, 10.8%, and born outside Sweden 9/32, 28.1%, p=0.035).

STUDY FLOWCHART

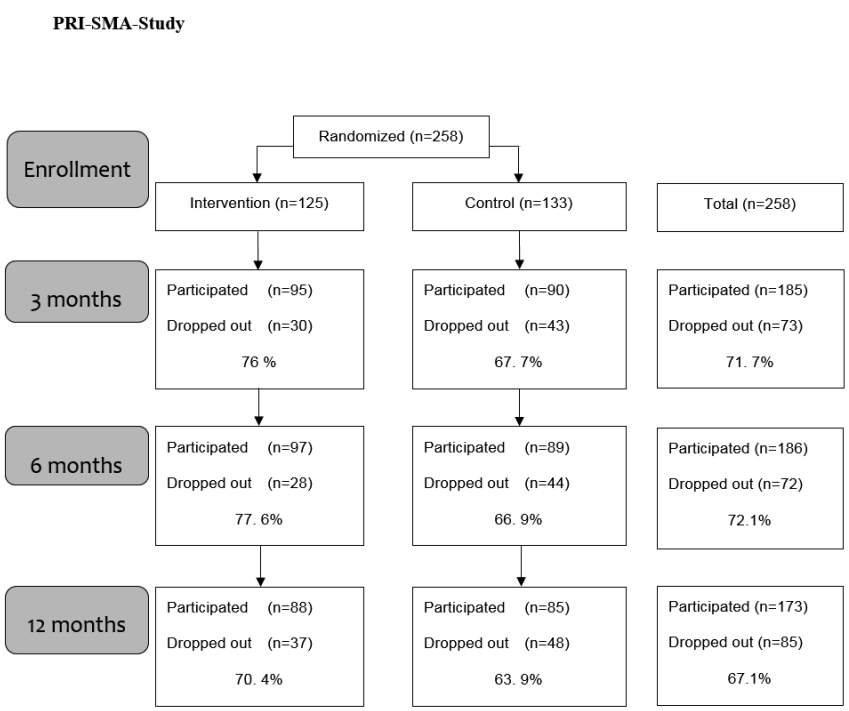


Figure 7. Flowchart and dropout rate for study I

The use of self-rating scales in recurrent primary care GP consultation showed no statistically significant differences between the intervention group and control group regarding depression outcomes over three, six and twelve-months follow up (Figure 8).

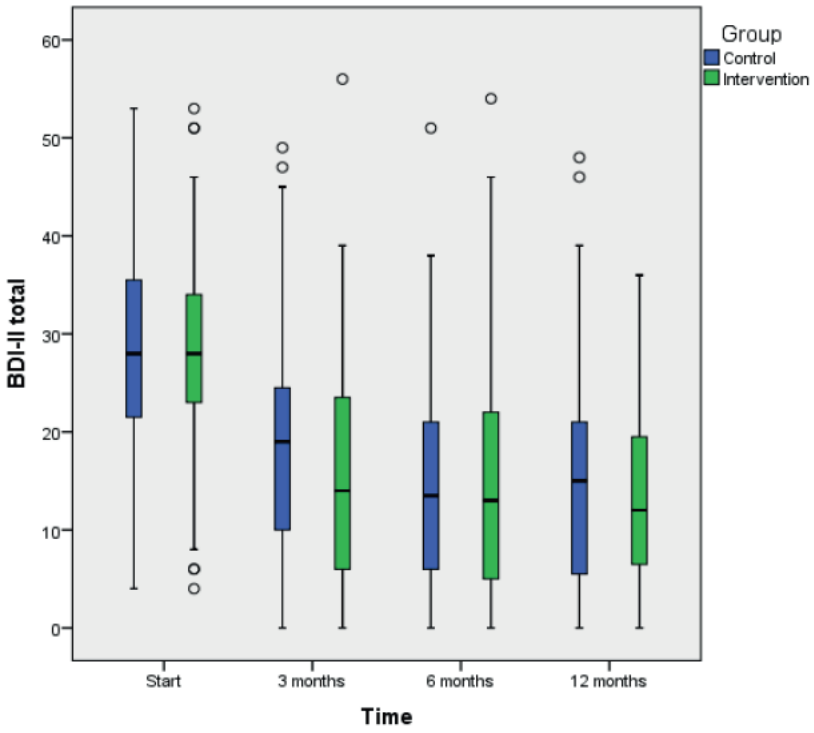


Figure 8. Depression severity (BDI-II values) in the intervention and TAU groups. Boxplots for baseline, 3 months follow-up, 6 months follow-up, and 12 months follow-up. The outcome variable is presented as box plot with medians, minimum and maximum values, and lower and upper quartiles. Y-axis: BDI-II, X-axis: time 0, 3, 6, 12 months. Outliers (circle) are cases with values between 1.5 and 3 times the interquartile range (5 cases with BDI-II >50 in patients with difficulties in Swedish language, where complementary diagnostic procedure by the GP yielded a diagnosis of moderate depressive disorder).

Patients participating in the study, both in the intervention and control groups, improved their depression outcome. Nearly half of the patients no longer had depression (BDI-II <13) at the 3 month follow-up (49% in the intervention group and 47.3% in the TAU group). There was a rapid decrease in total score on BDI-II from baseline to 3 months, and slightly less improvement from 3 to 6 months, and then almost no further improvement from 6 to 12 months, both in the intervention and control groups.

Figure 8 and 9 show results concerning quality of life (EQ-5D) and psychological well-being (GHQ-12).

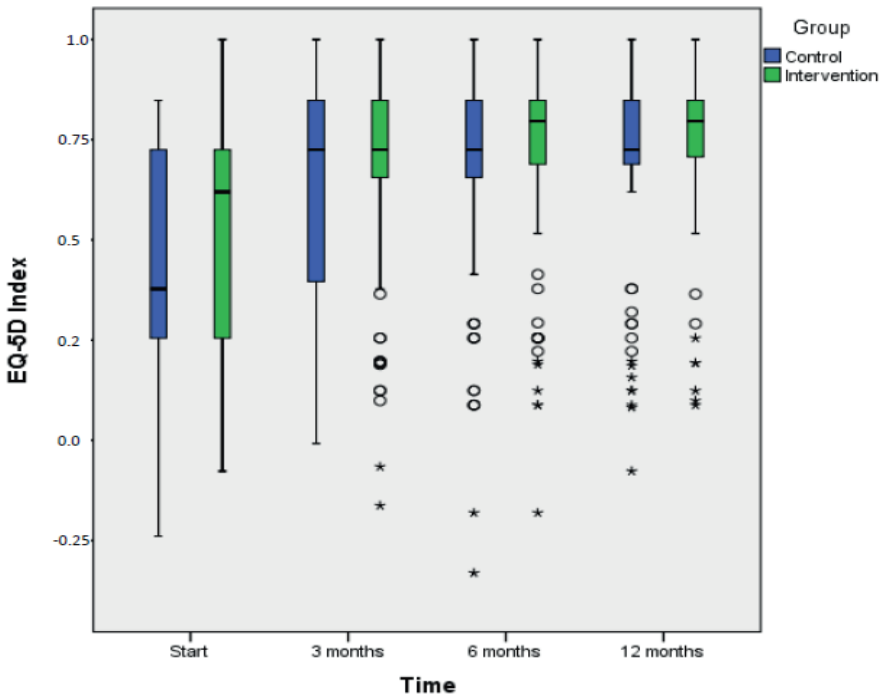


Figure 9. Quality of life (EQ-5D values) in the intervention and TAU groups. Boxplots for baseline, 3 months follow-up, 6 months follow-up, and 12 months follow-up. The outcome variable is presented as box plot with medians, minimum and maximum values, and lower and upper quartiles. Y-axis: EQ-5D, X-axis: time 0, 3, 6, 12 months. Outliers (circle) are cases with values between 1.5 and 3 times the interquartile range; extremes (x) are cases with values more than 3 times the inter-quartile range.

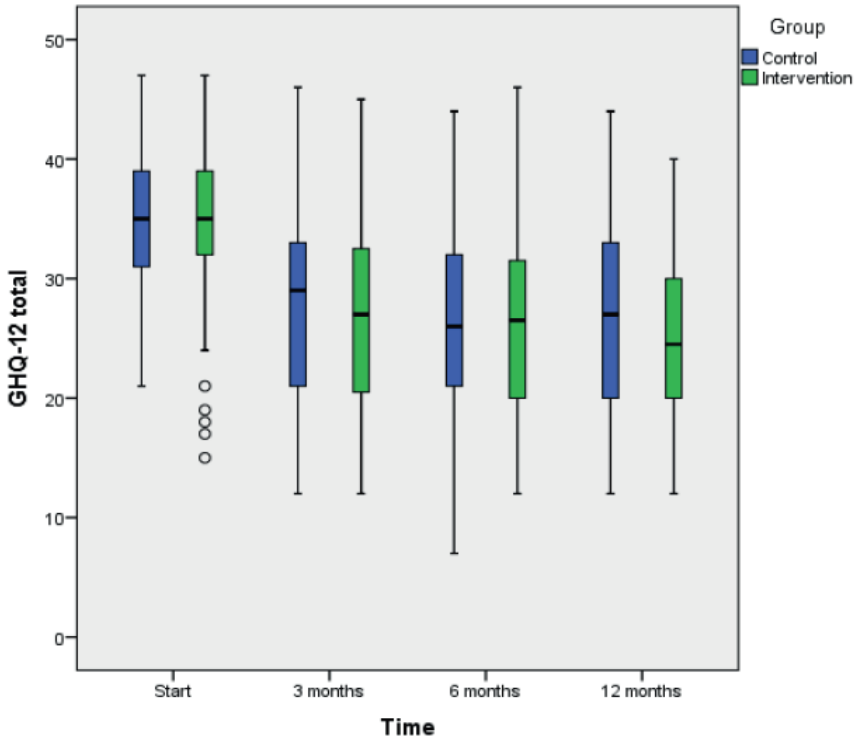


Figure 10. Overall psychological well-being (GHQ-12 values) in the intervention and TAU groups. Boxplots for baseline, 3 months follow-up, 6 months follow-up, and 12 months follow-up. The outcome variable is presented as box plot with medians, minimum and maximum values, and lower and upper quartiles. Y-axis: GHQ-12, X-axis: time 0, 3, 6, 12 months. Outliers (circle) are cases with values between 1.5 and 3 times the interquartile range.

There were no significant differences between intervention and control groups concerning increase of EQ-5D and no significant differences between intervention and control groups concerning reduction of GHQ-12 index.

Results concerning antidepressant and sedative prescriptions followed the similar patterns: from baseline to 3 months there is an increase, and thereafter a leveling off. As for the whole PRI-SMA cohort we found a significant difference between intervention and TAU concerning level of antidepressants at 6 months (Table 4).

Table 4. Number and percent of patients who had prescriptions for anti-depressant medications and sedatives and stated medication at baseline and 3, 6, and 12 months follow-up, respectively, in the intervention and TAU groups antidepressant medications after 6 months, p= 0.007

	Baseline		3 months follow-up		6 months follow-up		12 months follow-up	
	n	(%)	n	(%)	n	(%)	n	(%)
Antidepressants								
Intervention (n=125)	27	(22)	90	(72)	86	(69)**	74	(59)
TAU¤ (n=133)	43	(32)	96	(72)	78	(59)	77	(58)
Sedatives								
Intervention	26	(21)	64	(51)	53	(42)	52	(42)
TAU¤	32	(24)	73	(55)	56	(42)	51	(38)

¤TAU, treatment as usual.

**Significantly higher proportion of patients in intervention group still on antidepressants.

There were significantly more visits to psychologists in the control group, but significantly more visits to GPs in the intervention group during the first 3 months, but not thereafter, and when comparing over the total 12 months, no significant differences concerning visits could be seen between intervention and control group (Table 5).

Table 5. Number of patients' contacts with GPs, nurses, and psychologists between baseline to 3 months, and 4 to 12 months for intervention and TAU groups, based on information obtained from electronic patient records.

Profession	Type of contact	Intervention 0-3 months m (SD)	TAU 0-3months m (SD)	p
GP	visit	3.44 (1.214)	2.59 (1.354)	0.066
Nurse	visit	0.32 (0.829)	0.32 (0.875)	0.878
Psychologist/Therapist	visit	0.40 (1.320)	0.89 (1.776)	**0.0001**
Total visits to PHCC	visit	4.16 (2.398)	3.81 (2.692)	**0.006**
		Intervention 4-12 months m (SD)	TAU 4-12 months m (SD	p
GP	visit	2.54 (2.337)	2.38 (2.595)	0.301
Nurse	visit	0.68 (1.484)	0.62 (1.551)	0.581
Psychologist/Therapist	visit	0.90 (2.504)	0.83 (1.908)	0.401
Total visits to PHCC	visit	4.11 (4.586)	3.83 (4.403)	0.619
		Intervention total 0-12 months m (SD)	TAU total 0-12 months m (SD)	p
GP	visit	8.26 (5.842)	7.64 (5.976)	0.304
Nurse	visit	0.99 (1.978)	0.94 (2.088)	0.967
Psychologist/Therapist	visit	1.30 (3.129)	1.73 (3.222)	0.167
Total visits to PHCC	visit	8.26 (5.842)	7.64 (5.976)	0.812

Carl Wikberg

There were no significant differences in the percentage of patients on sick leave in the intervention and TAU groups between baseline and 3 months, or 4 -12 months, or during the entire study period (Table 6). The mean total duration of sick leave (days) was not significantly different between the intervention and TAU groups.

Table 6. Number and percent of individuals on sick leave, mean days of sick leave, and p-values for difference in mean days of sick leave between participants in intervention and TAU groups, based on information obtained from electronic patient records.

	Intervention			TAU			
	n (%)	mean days of sick leave	SD	n (%)	mean days of sick leave	SD	P for difference mean days
0-3 months	31(25)	63.1	29.8	48 (36)	55.8	27.7	0.221
4-12 months	35(28)	100.8	87.3	47(35)	102.7	85	0.922
Total 0-12 months	49(39)	124.8	102.5	64 (48)	123.3	85.0	0.942

Paper II

The results were based on the data from two combined RCT cohorts: the PRIM-NET study and the PRI-SMA study [74, 138]. The total number of participants were n=73 in each cohort, yielding a total of n=146 participants in this study.

There were significant differences in age and education levels between the cohorts that might be explained by the inclusion criteria in the PRIM-NET study that also required being positive to internet-based CBT (ICBT) (Table 7). The participants in the PRIM-NET study had to have a computer at home and be willing to receive treatment through the ICBT program. The age differences could be explained by the fact that more younger participants had computers and were more keen to obtain and try treatment that way. The population in the PRIM-NET cohort had lower

educational levels probably due to their age (younger participants would have lower educational levels) (Table 7).

Table 7 shows descriptive data

Table 7. Descriptive characteristics of patients in the study comparing BDI-II and MADRS-S results.

Characteristic	**Total**	**PRIM-NET Study**	**PRI-SMA Study**	***P*** ≤ †
No. of patients	146	73	73	
Sex				NS[a]
Male	39 (27)	21 (29)	18 (25)	
Female	107 (73)	52 (71)	55 (75)	
Age (y)				.005
< 40	83 (57)	50 (69)	33 (45)	
≥ 40	63 (43)	23 (31)	40 (55)	
Educational level				.02
Grade school (9 y)	13(9)	3 (4)	10 (14)	
High school	82 (57)	49 (67)	33 (46)	
University	50 (34)	21 (29)	29 (40)	

Data reported as number (%)

†Pearson chi-square test.

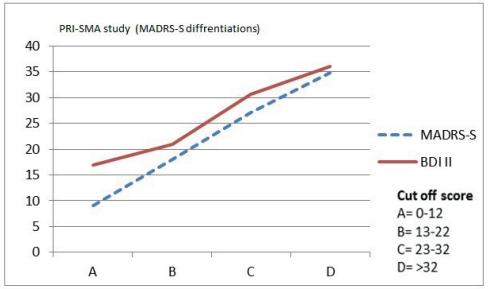
NS = not significant

[a] (P ≥ 0.05).

All patients assessed their depression symptoms with both MADRS-S and BDI-II according to the flowchart (Study flowchart)

MADRS-S and BDI-II had good comparability, among mild/moderate depressed patients in primary care. See Figure 10

I



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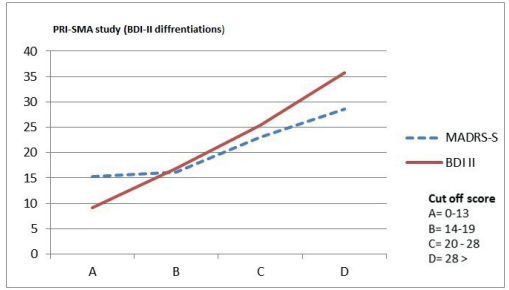
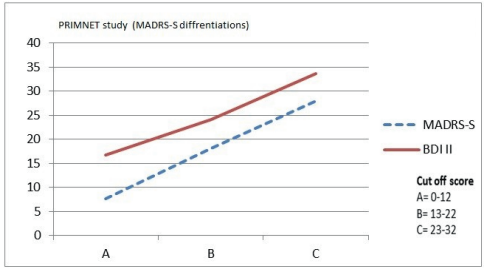


III



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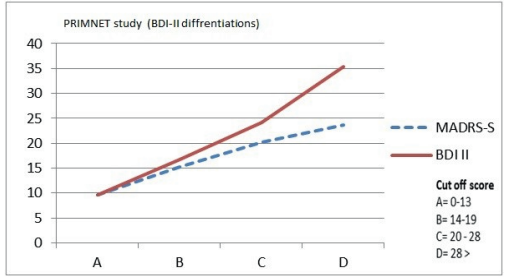

I	PRI-SMA (MADRS-S differentiations)				II	PRI-SMA (BDI-II differentiations)			
MADRS-S	9	18.05	27.17	34.78	MADRS-S	15.29	16.1	23.09	28.58
BDI-II	17	20.95	30.72	36.11	BDI-II	9.14	16.9	25.3	35.73
	A	B	C	D		A	B	C	D
III	PRIM-NET (MADRS-S differentiations)				IV	PRIM-NET (BDI-II differentiations)			
MADRS-S	7.57	18.13	27.95		MADRS-S	9.6	15.21	20.19	23.57
BDI-II	16.71	24.15	33.65		BDI-II	9.6	16.71	24.19	35.36
	A	B	C			A	B	C	D

Figure 10. Correlation between MADRS-S and BDI-II. Mean scores within each classification. MADRS-S and BDI-II scores were compared with MADRS-S (I,III) and BDI-II(II,IV)cut off scores as reference for the 73 participants in the PRI-SMA study and the 73 participants from the PRIM-NET study; the table below the graphs shows mean scores within each classification (MADRS-S and BDI-II)

Correlation statistics showed 0.66 and 0.62 in the two cohorts, and the reliability within the two study cohorts was good for both MADRS-S (Cronbach's alpha 0.76 both cohorts) and BDI-II items (Cronbach's alpha 0.88 and 0.85).

The study showed differences between male and female depressed patients regarding total score on BDI-II where female patients scored significantly higher than the males (Table 8).

Table 8. Scores for two depression instruments with patients from two study samples.

Patient Characteristics	**Total**	**PRIM-NET Study**	**PRI-SMA Study**
No. of patients	146	73	73
MADRS-S total score			
All patients	22 ± 7	20 ± 7	24 ± 8
Male	21 ± 8	18 ± 7	24 ± 8
Female	22 ± 7	21 ± 6	24 ± 8
Age < 40 y	23 ± 8	20 ± 7	27 ± 7
Age ≥ 40 y	21 ± 6	20 ± 5	21 ± 7
Grade school (9 y)	22 ± 8	24 ± 7	22 ± 8
High school	21 ± 7	20 ± 7	23 ± 8
University	23 ± 7	19 ± 6	27 ± 6
BDI-II total score			
All patients	27 ± 10	26 ± 9	27 ± 10
Male	**23 ± 8**[b]	**22 ± 7**[b]	25 ± 9
Female	**28 ± 10**[b]	**28 ± 9**[b]	28 ± 10
Age < 40 y	28 ± 10	26 ± 9	31 ± 10
Age ≥ 40 y	25 ± 9	27 ± 10	24 ± 9
Grade school (9 y)	**21 ± 11**[c]	26 ± 11	**20 ± 11**[c]
High school	27 ± 9	27 ± 9	27 ± 9
University	29 ± 10	25 ± 10	31 ± 9

[a] Data is reported as mean +- SD

[b] Sex, t-test: P ≤0.02 in total sample; P ≤0.02 in PRIM-NET sample.

[c] Education, partial correlation: P ≤0.02 in total sample; P ≤.001 in PRI-SMA sample.

Paper III

The results from this paper were derived from three focus group discussions conducted between 2012-2013. The sample included n=45 participants who had completed the intervention from paper I. The sample was purposive, and the aim was to study patients who regularly completed the self-assessment scale MADRS-S together with the GP consultation. The analysis was based on the systematic text condensation according to Malterud. Figure 11 presents the results from the invitations, letters and phone calls. A total of 9 patients completed the discussions. Preliminary reading of the transcript from focus group I showed that despite a somewhat low number of participants, the data were adequate and detailed. The same outcome emerged from focus group discussions II and III.The three focus group discussions were the foundation for the analysis.

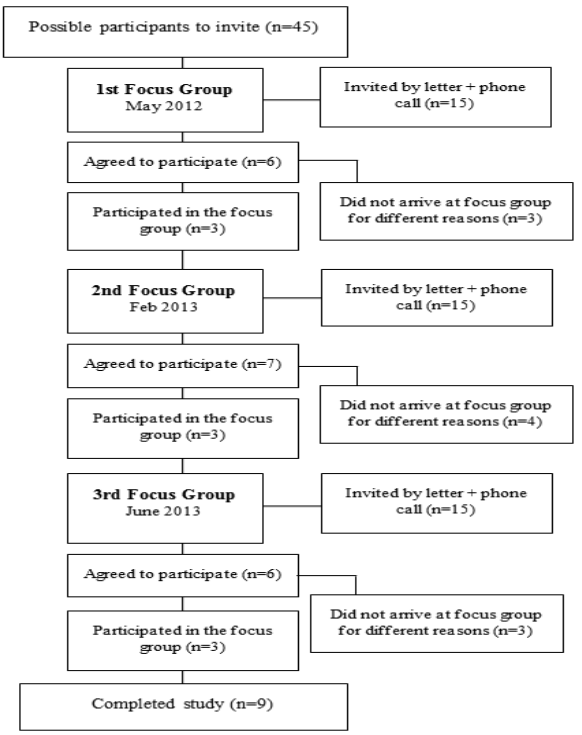

Figure 11. Timeline and number of patients invited, number of patients who accepted participation, and number of patients who finally took part in the focus groups.

Descriptive data of the participants in the focus groups is shown in Table 9

Table 9. Sample distribution in the PRI-SMA patient focus group study.

Category	Variables	n
Gender	Female	8
	Male	1
Age	18 – 45	5
	>45	4
Married/cohabitant		9
Educational level	Lower (primary, vocational or high-school)	4
	Higher (college or university)	5
Children at home	Yes	4
	No	5
Occupation	Working	5
	Studying	2
	Unemployed/sick-leave	2

The three following categories emerged during the process of the analysis:

***Confirmation* – MADRS-S shows that I have depression and how serious it is.**

The participants described that they perceived the use of MADRS-S as something that confirmed the depression, something to lay their hands on. The participants said that it was almost like taking your temperature, when you have a fever. The MADRS-S score was something black on white that acknowledged how they were feeling. The participants expressed the notion that the self-assessment was unique and subjective regarding their situation. Completing the MADRS-S gave them a clearer picture of the symptoms and how these symptoms fit together. Some participants stated that completing the MADRS-S gave the GP an opportunity to step them through the symptoms. The MADRS-S gave the participants something black on white: a receipt of the depression. The participants expressed the importance of being honest and truthful when filling out the assessment, so that the results could be useful in the treatment. One participant expressed how the MADRS-S organized the depressed condition, that the patient could go from point to point, rethink every part, and re-consider. The self-assessment was perceived as a good

basis for discussion. Also, it opened their eyes to the fact that depression is not static, it is changing over time, and symptoms change as well. *"I think it was pretty good, actually, to divide it up, because it organizes how you really feel. You had to go forward from point to point. How is it with that part, that part, that part, because it could be different for each. It was a good base, actually."* When filling out the instrument, participants emphasized the importance of having enough time. Some questions demanded more consideration than others. This category was represented in all of the focus group discussions. It seemed as if MADRS-S was perceived as something that confirmed the depression, a tool that helped both the patient and the GP to put a finger on what was causing the problems. The use of MADRS-S helped to confirm the condition that the participants in some cases had felt before seeking care. It was experienced as a relief for the patients to discover what was going on.

***Centeredness* – The most important thing is for the GP to listen and to take me seriously.**

In this category, the participants emphasized the importance of being listened to by the GP. Participants perceived that the GP acknowledged their condition, when the GP used the MADRS-S. The participants perceived that the instrument facilitated the communication between the patient and the GP. If the patients thinks the GP takes her/him seriously, this could enhance the consultation. When the GP handed out the MADRS-S, the participants expressed that it felt like the GP wanted to know more about what they had talked about, and how the patient would rate and describe her/his depression. It seemed to matter whether the GP was paying attention and listened to the patients, as some described how some GPs turned away from them and stared into the computer monitor, and then just looked at the scores when finished. Some liked that the GP turned away, it made them feel more at ease, but no one appreciated if the GP just collected the scores without any discussion. The participants described during the discussions how GPs who had an understanding attitude and really talked about the depression was seen as persons who took the patient serious. The very use of an instrument confirmed that the GP had listened and was interested in knowing more about the patient.

***Clarification* – MADRS-S helps me understand why I need treatment for depression.**
The self-assessment instrument should be used as a help for the GP to explain and motivate the suggested treatments. MADRS-S helped the participants understand the necessity for the use of, for example, antidepressants. The instruments should be used as a help for the GP to explain treatment options and why certain treatments are recommended. The participants felt that the GP with the help of the patients' assessment could provide a more accurate treatment. During the group discussion the participants talked about how the GP reviewed the results from the instruments and how they compared the results from previous assessments. By using the MADRS-S, the GP gained a rapid access to the patient's condition. Some of the participants perceived that there was a lack of information as to how and why to fill out the instrument, and they felt that if receiving more information and if the GP taught them more about depression with MADRS-S as a pedagogic tool, the suggested treatment would make more sense.

Taken together, the three categories illustrated the participants' perceptions of using MADRS-S during the GP consultation in primary care.

Paper IV

The aim of this paper was to investigate whether the continuous monitoring of depression symptoms by a self-assessment instrument in recurrent person-centered GP consultations had any long-term effect on work ability, job strain, social support and return to work for the patient with major depression in primary care.

In the main PRI-SMA study 258 patients were enrolled, but in this study solely the 183 patients who stated in the patient questionnaires that they were working were included. The participation rates are shown in Figure 12.

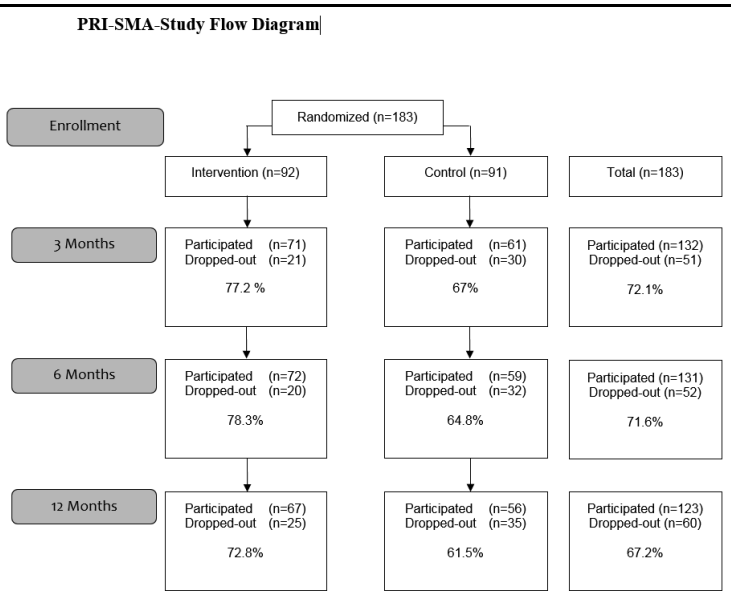

Figure 12. Participation flowchart for PRI-SMA study of n=183 working patients.

The patients' characteristics at baseline are described in Table 10. There were no significant differences between the intervention and control group in this cohort of working patients at baseline.

Table 10. Demographic characteristics of the intervention and TAU groups in the PRI-SMA trial for the group of participants who stated they worked: age, gender, social and lifestyle variables, and job strain. P-values indicate test of difference between intervention and control group. Missing values not included.

Characteristics	**Total** n= 183 (%)	**Intervention** n= 92(%)	**Control** n=91= (%)	P-value
Age (years, mean SD)	40.5	42	39	0.2
Men	51 (28)	22 (24)	29 (32)	0.11
Women	132 (72)	70 (76)	62 (68)	0.34
Marital status (n=183)				
Single	76 (41.5)	44 (47.8)	32 (35.2)	0.08
Children at home <18 (n=183)	65 (35.5)	29 (42.6)	36 (48.6)	0.47
Alcohol (n=183)				
2 - 4 times/week	32 (17.5)	17 (18.7)	15 (17)	0.78
Smoking (n=183)				
Yes+ sometimes	48 (26.2)	25 (27.5)	23 (25.3)	0.74
Educational level (n=183)				
Up to primary education	10 (5.5)	5 (5.5)	5 (5.5)	
Secondary education	82 (44.8)	47 (51.6)	35 (38.5)	
University or college	90 (49.2)	39 (42.9)	51 (56.0)	0.19
Occupational class (n=183)				
High white collar	60 (32.8)	29 (39.2)	31 (39.2)	
Middle/low white collar	51 (27.9)	29 (35.4)	22 (27.8)	
Blue collar/students	47(25.7)	21 (26.6)	26 (32.9)	0.46
Employment (n=183)				
Employment	150 (82)	72 (80.0)	78 (85.7)	
Working	31 (17.1)	18 (20.0)	13 (24.3)	
Studying	75 (29.3)	33 (26. 8)	42 (31.6)	0. 31
Country of birth (n=182)	182	91	91	
Nordic country	156 (85.7)	78 (85.7)	78	
Europe	8 (4.4)	5 (5.5)	(85.7)	
Outside the Nordic countries	18 (9.9)	10 (11.0)	3 (3.3)	0.70
Job strain (n=164)			8 (8.8)	
Active jobs	41 (25.0)	22 (27.0)		
	40 (24.0)	22 (26.0)	19 (24.0)	
Low-strain	44 (27.0)	23 (28.0)	18 (22.0)	
Passive jobs	39 (24.0)	16 (19.0)	21 (26.0)	0.58
High-strain			23 (28.0)	

There were no significant differences concerning age, gender, lifestyle variables, job strain, depression symptoms, or quality of life between the intervention group and control group at baseline. Table 11 presents change of job strain perception 0-12 months. There were no significant differences regarding job strain. Table 12 presents the patients' perception on how long time it would take to get back to work.

The results concerning depression symptoms, work ability, quality of life, and the perceived social support at 3, 6, and 12 months are presented in figures 13-16. Depression symptoms were reduced in both groups over time, and work ability and quality of life increased in both groups.

Table 11. Perceived intra-individual change regarding job strain during 0-3, 0-6, 0-12 months. Odds ratio (OR) and 95% confidence interval for difference between intervention and TAU group.

Job strain	Intervention better vs no change/worse n (%) / n (%)	Control better vs no change/worse n (%) / n (%)	OR (CI)
0-3 months [1]	10 (18) / 44 (82)	8 (15) / 44 (85)	1.48 (0.46-4.79)
0-6 months [2]	9 (18) / 42 (82)	10 (21) / 37 (79)	0.92 (0.30-2.80)
0-12 months [3]	12 (26) / 34 (74)	9 (21) / 35 (79)	1.26 (0.39-4.11)

[1]n=106, [2]n=98, [3]n=90

Table 12. Response at baseline to question "When will you be back at work" in individuals on sick leave (n=101). Number and percentage in intervention and control group, respectively. No significant difference between the intervention group and control group.

	Intervention n (%)	Control n (%)
Within 1-4 weeks	13 (34.2)	22 (51.2)
Within 1-6 months	16 (42.1)	13 (30.2)
Never	0 (0)	1 (2.3)
Don`t know	9 (23.7)	7 (16.3)

Work ability at 3 months follow up was statistically significantly different difference between intervention and control group (intervention 35.2, SD 1.07; control 32.0, SD 1.02, p=0.031).

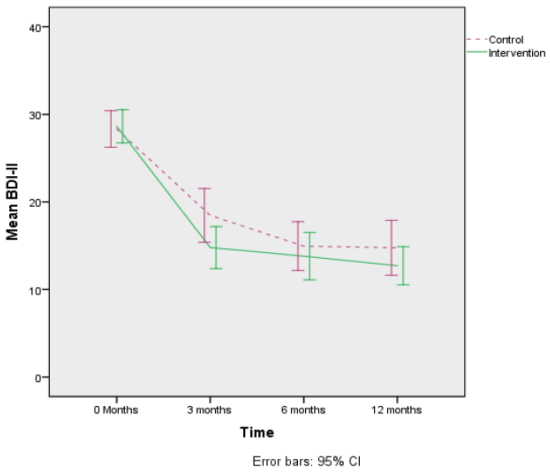

Figure 13. BDI-II mean values in intervention and control group at baseline, 3, 6 and 12 months. No statistically significant differences between the intervention and control group.

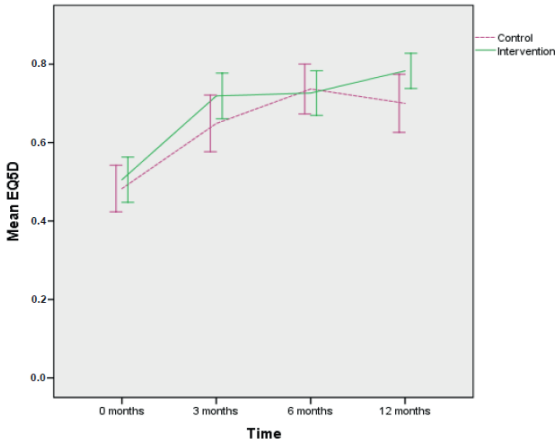

Figure 14. EQ-5D mean values in intervention and control groups at baseline, 3, 6, and 12 months. No statistically significant differences between the intervention and control group.

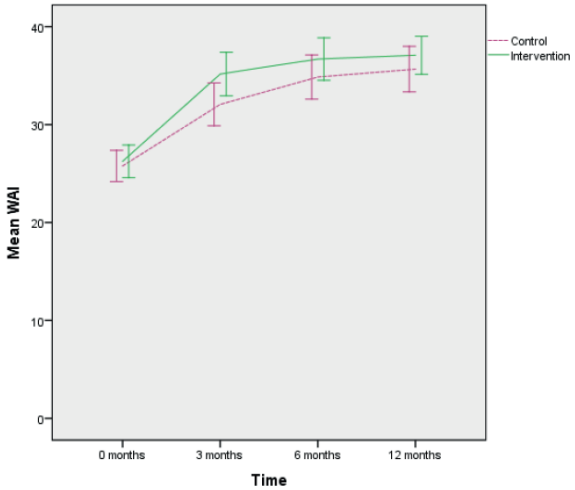

Figure 15. WAI mean values in intervention and control groups at baseline, 3, 6 and 12 months. Statistically significant difference at 3 months between the intervention and control group.

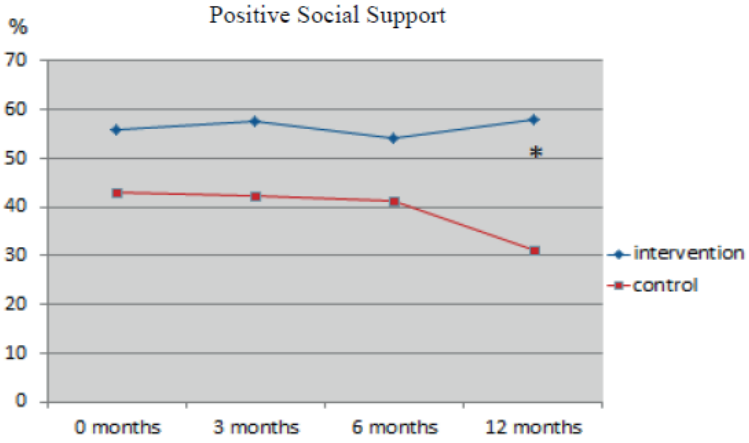

Figure 16. Perceived positive social support showed statistically significant differences between the intervention group and control group at 12 months follow-up, p=0.009.

There were no statistically significant differences regarding sick leave (percent-age on sick leave and sick leave days) for patients on sick leave between the intervention and control group.

The frequency of patients on anti-depressant medication was 72% in both groups (intervention and TAU) at 3 months. The medication continued longer in the intervention group at 6 months follow-up with 69% compared to 59% (p=0.01), leveling off to 59% and 58%, respectively, at 12 months follow-up.

There were no significant differences concerning referrals to psychotherapeutic treatment or visits to GP or nurses between the groups 0-12 months. Further, sick leave (frequency and days) showed no statistically significant differences over the 12 months observation period between the two groups (39% total frequency in intervention group vs. 48% in control group; mean 125 days vs. 123 days on sick leave at any time during the 12 month period that was observed). Further, the patient's own assessment of the probable duration of ongoing sick leave at the time of their inclusion did not differ between intervention and control groups.

We saw no significant differences concerning change in WAI, EQ5D, or social support for those without sick leave during the 12 month period.

5 DISCUSSION

5.1 General findings

The results in this thesis are based on the results from the PRI-SMA trial, which aimed to evaluate the effects of regular use of a self-assessment instrument in GP consultations with the depressed patient in primary care. Did the use of self-assessment instruments have an effect on depression course and also on quality of life, well-being, antidepressant use, sick leave, work ability, and health care use in a long-term perspective?

We found that regular use of a self-assessment instrument (MADRS-S) during the recurrent person-centered consultation affected adherence to anti-depressant medication and improved work ability to some extent. Social support was in a significantly higher frequency perceived positive after twelve months in the intervention arm. However, the very use of self-assessment instruments as a part of the consultation and the significantly higher frequency of SSRI adherence during 6 months did not affect essential depression outcomes compared to usual care (TAU).

Although the course of depression did not significantly change with regular use of a self-assessment instrument in a person-centered consultation intervention, the patients' perceptions of positive enhancements should not go unrecognized. The MADRS-S instrument is a fast, cost-free, and easily administered tool for the GP to use with the individual who is positive towards use of a self-assessment instrument in the consultation. Further, the GP can be assured she/he will get comparable results concerning reliability of depression level with and in alignment with the more extensive BDI-II instrument.

Papers I and IV showed similar results regarding the depression outcomes, but found significant results in adherence to antidepressants (I), and WAI and positive social support (IV), respectively. The comparison study of MADRS-S and BDI-II (II) gave new insights that clearly show the usefulness of MADRS-S during depression treatment in primary care. The study also found an interesting secondary finding in the significant effect regarding gender on total scores in BDI-II. Women's mean score was 28 versus men's 23, with a $p \leq 0.02$.

In the focus group discussions (III), patients shared their perceptions about MADRS-S during depression treatment. In the categories that

emerged from the analysis, we found that in contrast to our hypothesis the patients found positive aspects concerning the use of the instrument. MADRS-S added something to the consultation, something that GPs had not reported in a previous study [179].

These findings suggest that there are some valuable effects with the use of self-assessment instruments in primary care, provided it is used as the patients' instrument, but there is still a need for more studies that test and evaluate interventions and methodology regarding care in mild/moderate depressed patients. There is seldom one clear answer to a question, and the results of this thesis illustrate the importance of mixed methodology when doing research in a "reality context" environment. These findings are in alignment with a recent Cochrane review [180] that concluded that more and better research is needed, especially in primary care settings where most of the common mental health disorders are treated. Zhu et al compared the placebo and waiting list conditions in clinical trials and concluded that when evaluating effects of interventions, researchers have to consider the "no treatment" or psychological placebo's influence on the results [172], which can be one explanation for the small effect of the PRI-SMA intervention, where care as usual constitutes control.

Better adherence to anti-depressant medications at 6 months

In study I the results were very similar between the intervention group and the control group. Both groups showed the same reduction of depressive symptoms and enhanced quality of life and psychological well-being.

When we started this study (PRI-SMA), there was a lack of primary care RCTs that evaluated the long-term effects of self-assessment instruments in depressed patients [7]. The evidential base upon which clinical practice rested was limited. Our results describe reality from the actual perspective of the multi-facetted primary care environment. The pragmatic approach gives a more truthful answer to the research question [181].

Adherence is a major problem not only in Sweden but also globally. Health care professionals play a large role in adherence improvements, and as such, they need to identify barriers that exist on a person-centered level [182]. Depression guidelines do suggest use of anti-depressant medications as a part of treatment [51, 73] but the effects of medical treatment compared to placebo are still under debate [183].

Managing depression in primary care is not just about medication. There is a symbiotic relationship; management of depression improves the management of other diseases and vice versa [184]. Prior to this thesis, we knew that most antidepressant medication is prescribed in primary care [7]. Our findings show that a substantial part (over 50%) of study participants reported use of anti-depressant medications twelve months after baseline. Yet recent studies show that in this population (mild/moderate-depressed), there is no concern about over prescription [185]. Guidelines recommend anti-depressant medication treatment in depressed patients as a first choice if the patient is in recidivism and a potential treatment if psychotherapy or watchful waiting does not give effect in newly diagnosed first-episode patients.

Our findings show that when MADRS-S is used in the recurrent person-centered consultation, patients in primary care seem to continue to be more adherent in their anti-depressant medication usage. This is positive, since the MADRS-S was developed to be sensitive to change [141]. To use a self-assessment instrument could be a way to keep things simple, i.e. a pedagogic tool that the patient uses together with the GP to gain more knowledge about the depression itself and the progression of the treatment, and as a way to achieve clarification, centeredness, and confirmation. The MADRS-S is a tool that gives the patients a quick answer to the question of how the treatment is going. The idea of keeping things simple with the objective of increasing adherence is supported by Atreja [186] who introduced the following framework to increase adherence: i) simplifying the regime, ii) imparting knowledge, iii) modifying health beliefs, iv) patient communication, v) leaving bias and vi) evaluation [186]. All these parts in the framework that are worth taking into consideration are attainable with the recurrent use of MADRS-S in the consultation.

Treatment guidelines recommend use of antidepressants in recurrent depression [7]. Our findings support the use of MADRS-S to maintain adherence to pharmacological treatment. There is a need for more studies in primary care, although there has been a demand for this for a long time now [187]. Grenard et al. concludes that depression itself has an association with poor adherence, and that the focus must be on the depression in studies to improve this outcome [92].

We hypothesized that those patients who used MADRS-S as a part of the per-son-centered consultation would have a more rapid recovery from depression, shorter sick-leave, higher quality of life, and better adherence

to medication than patients receiving TAU. Our results showed almost no significant differences between intervention and TAU, but still gave a positive outcome for the population as a whole. For persons who seek treatment for depression or who are diagnosed with mild/moderate depression in primary care, the outcome is most likely to be positive, already after three months. As it is important that GPs treat the entire patient and take comorbidity into consideration to ensure best outcomes [1], it seems that "usual" depression care in primary care already reaches a satisfactorily high quality, and that use of a self-assessment instrument only can improve quality of care under special circumstances. One way to improve outcomes could be to implement quality improvement programs as suggested by Dietrich etal [189].

We found significantly higher adherence to antidepressants after 6 months in the intervention group, which is opposite to what DiMatteo found in a large review. In this review, the use of self-report and physical tests showed negative results concerning medication adherence [189]. There is also an ongoing debate on the pros and cons regarding anti-depressant medication for mild/moderately depressed patients [190]. Sometimes the best thing a GP can do for her/his patient is to carefully listen to their story and empower them to overcome the obstacles of every-day life problems [191]. There are several studies that have shown that use of a self-assessment instrument to communicate severity with the patient rarely modifies the treatment [192], findings that are notable. One can debate whether antidepressants have little or no clinical effects on the mildly/moderately depressed patient [193, 194], but there is still a scarcity of studies designed to evaluate interventions to improve adherence in depressed patients [195]. A large review from the Mayo clinic regarding medication adherence concluded that increased adherence could have a greater effect on health than improvements in specific medical therapy [196]. In paper I, we found improved adherence in antidepressants after 6 months, but no additional effects on depression reduction compared to TAU. Further, the review from Mayo clinic highlighted some interesting findings. Around 50% of all patients do not take their prescribed medications. Adherence is, however, not solely the patients' responsibility. The identification of non-adherence is a challenge and requires special consultation techniques. The behavior that controls medication-taking is complex, and both patient and GP need to be involved in the process [196].

Comparable results with MADRS-S and BDI-II in all domains

Comparison between different instruments regarding depression has been done before [197] and also between the BDI-II and MADRS-S [198]. Our results do not only show good comparability between the instruments, they also shed light upon the debate regarding cut-off points [199, 200]. The gender differences concerning scoring of the BDI-II instrument call for attention. As concluded by Salle et al in their work with high school students, there were significant differences in how girls versus boys rated their symptoms in several different instruments (BDI, CES-D, CRS and SRQ) [200]. Other studies have also acknowledged this finding, and addressed the future importance of further studying gender differences in rating depression symptoms [201]. While this issue was recognized as early as in 1975 by Monica Blumenthal [202], not much has been done yet to adjust the cut-off points. The idea for the current study emerged when meeting patients during inclusion in the PRI-SMA trial. There were patients who scored high on the BDI-II and yet the GPs had considered them to be in the mild/moderate spectrum. The patients from the intervention group had scored their symptoms during the GP consultation (with MADRS-S) and had been diagnosed and fulfilled the criteria for inclusion. The difference in levels reported in some cases led to a discussion about the eligibility criteria for inclusion, but for most of these patients the inclusion remained, as the conclusion was that the patients were moderately depressed and would not have been referred to psychiatry. This once again highlights the importance of repeated measurements, and to view every patient as a unique individual. In a context where so many different instruments have been and are in use, the results from paper II are comforting. Now GPs can use the MADRS-S during the entire course of treatment.

Patients' perceptions of MADRS-S worth taking under consideration

The perceptions of the MADRS-S instrument by primary care patients with depression are very much similar to the findings from Wen & Tucker [203], who concluded in their cross-sectional descriptive population study, that people want a doctor who listens to them, who cares and who is compassionate, and they also want a doctor who can explain well. In addition, the authors suggested that interventions should aim to strengthen the doctor-patient relationship. The PRI-SMA study did not have the doctor-patient relationship as an outcome, but paper III raises ideas and necessary reflections concerning the core values of primary care. The interaction between the patients and the doctors/nurses/other personnel

are at the heart of primary health care. The key to opening the door to the depressed patient seemed to be the ability to take the patient seriously and to listen. Savard [204] concluded that if GPs improved their communication, they would enhance their relationship with the patient and thereby improve patient symptoms and quality of life, an idea which is supported by our findings. On the other hand, Cheraghi-Sohi et al. found that patients placed technical quality of care and continuity higher than patient-centered care [205], meaning that patients' priorities in primary care should not go unrecognized. Again, this shows that it is important to pay careful attention to every patient's own expectations and needs. In today's primary care, continuity is difficult to achieve without a collaborative care organization where doctor-nurse cooperation can increase accessibility and continuity for the patient [206].

Sample size is often something discussed in qualitative research, and there is a need for more empirical research on the subject [207]. New approaches suggest that we shift the focus from concentrating on sample size to looking at the contribution of the analysis to new knowledge [208]. The more information there is in the sample that is relevant for the topic, the fewer participants are needed [209]. The researchers may have an a priori notion about the number of participants they require, but this is something that needs to be reconsidered during the process [209]. Our focus group study highlighted the importance of being taken seriously, and that the GP really listened to what the patients had to say. Gask reported that patients sensed that they were wasting their GP's time and that in a way it was impossible for the GPs to listen to them and understand how they felt [210], which is also in the line with our findings.

GPs take a risk when not applying fundamental person-centered principles in the consultation. It is known that not getting enough information, not being seen, listened to and acknowledged as a person with your unique needs and concerns leads to uncertainty in the interaction with the caretaker and to dissatisfaction with healthcare [211, 212] If used correctly, the self-assessment instrument could tick off all these boxes. During the entire RCT and the focus group discussions, my own experience was that many patients long for someone who can listen to them and take their words seriously. Although many patients do not initially seek treatment for being depressed, there is still an underlying need for human contact and for someone who is willing to take the time to be there and to really hear the patient out.

WAI and positive social support

Use of MADRS-S resulted in significantly better perceived social support for the intervention group compared to the treatment as usual group. This was a positive finding. Grav showed that there was an association between perception of social support and depression in the general population and called for attention to this in the continuing care of depressed patients, especially in the elderly population [213]. This speaks in favor of the use of the instrument, according to our findings. Previous studies have confirmed that reduced capacity to work is not always visible and easy to understand, and that the rehabilitation process benefits from deeper knowledge of the individual [214].

This seems to be in accordance with our findings, to the extent that the WAI was better in the intervention group at 3 months, and the probable cause was the recurrent use of MADRS-S, which allowed the GPs to gain access to the patient's own assessment of symptoms. This may have led to deeper knowledge of the patient, due to the methodology.

The number of total sick-leave days are increasing in Sweden, especially among younger women [215], and it seems clear that something needs to be done. The close relationship between the ability to work and CMD is well known, and therefore it would be reasonable to start intervening with collaborative methods that involve the employee and employers together with some involvement from the health care system (Care manager, Rehabilitation coordinator). Similar results were shown in a recent study from Canada, which concluded that the GP plays a significant role in the long-term prevention of work-related disability. Furthermore, the study concluded that there is need for more workplace involvement and the availability of a dedicated mental health nurse [216]. Our study shows the important aspect of soft values. Patients own experiences and assessments are valuable assets that need to be re-evaluated. Many patients with depression stay at work, some fulltime and some part-time, and this is a factor that many times is overlooked. Previous studies have shown significant losses of productivity when employees are working while being depressed [117, 118].

5.2 General considerations

Most of the results in this thesis are based on the data from the PRI-SMA trial. The participation rate in this trial was fairly high, with 76% after 3 months in the intervention group and 67.7% in the control group, with an overall 71.1% for the total study population. The participation rate after 12 months was 70.4% in the intervention group and 63.9% in the control group, with an overall 67.1% in the total study population. The participation rate differed some between 3 and 6 months in the intervention group, with more participants in the 6 months follow-up. The explanation for this is that we did not exclude patients who did not fulfill the 3-month appointment. We chose to follow all included participants from baseline, at 6 and 12 months, regardless of whether they had completed the 3 and 6 months follow-up.

The participation rate is an issue that needs to be taken seriously even if the rates are generally declining [217]. The population consisting of mild/moderately depressed patients in primary care is not a homogeneous group. Depression is prevalent at all socio-economic levels, but low socio-economic status is associated with higher prevalence of depression and this show that depression has a major impact on quality of life and that it is unevenly distributed in the population [218, 219]. In PRI-SMA we saw a major improvement in quality of life (EQ-5D) and depression outcomes (BDI-II) already after 3 months, both in the intervention group and TAU group, which is an indication that in Sweden, primary care is effectively treating depression for most patients attending primary care. Historically, it has been difficult to show large effects of interventions in pragmatic primary care studies due to optimal TAU [220]. However, the promoted collaborative care models seem to break this pattern and show large effects compared to usual care [221].

5.3 Methodological discussion

All papers originated from the same RCT study PRI-SMA. One of the papers (II) used additional data from the PRIM-NET study to add power to the results. Paper III used a qualitative approach (focus group discussions and STC) to add to the thesis the important aspect of the patient's perception.

Randomization

Randomization on a patient level would not have been possible, because in that case, the same GP would have delivered both the intervention and the control treatments. We did not randomize on the PCC level because we wanted to avoid bias in terms of large differences in socio-economic preconditions between PCCs.

The choice of method is crucial for the research. The method, whether quantitative or qualitative, cross-sectional or longitudinal, or survey or randomized con-trolled trials, has to be suitable to answer the research questions. Åsberg [222] argues that there is a need to free ourselves from the boundaries of labelling the research, because there are few studies that are purely the one or the other. To carry out clinical research in the "real world" in primary care, it is necessary to have research personnel placed at the site, with knowledge of both research methods and primary care clinical activity to accomplish adherence to the study protocol, but without having too much influence on the particular PCC's clinical "real world" activity [223, 224].

It is also important to note that there are persons behind the scores obtained on assessment instruments. When working with self-assessment instruments, it might be easy to rely solely on the scores. If a patient reaches a certain cut-off point, it is easy to put the numbers into the EPR. But the scores are only one piece of the puzzle. A patient who scores high on an instrument could very well have full function and be able to work, and the same might be true of the opposite. Thus, even patients with low scores may have productivity loss at work [118]. This is due to the "SELF" part in self-assessment. Every patient knows her/his perceptions best. Some patients will attain a low score even if they are obviously depressed, due to fact that this is just the way they rate their own symptoms. Other patients attain high scores, even if they do not have a depression. The clinical "fingerspitzgefühl" or one's own intuitive feeling is an attribute every GP and other PCC personnel should be sensitive to

and aware of. It is important to look at the entire picture. There are many aspects to consider and many times several consultations can help, which means that the continuity of care is equally important. In the studies in this thesis, different aspects of depression treatment in primary care are presented, and there are surely many more aspects that may be examined in the future. Nevertheless, it is of great importance not to forget the person in today's primary care.

5.3.1 Outcome measures

EQ-5D

The EQ-5D instrument have been successfully used as a tool to describe health and is usable in cost-utility analysis [225]. As with many instruments, it is crucial that the measurements are repeated over time, and that the health care system does not "sound the trumpet" after one deviant score. Nevertheless, it provides an important outcome measure for cost-effectiveness/health economic calculations and it is a good help for gaining a greater understanding of depression treatment and compliance [226].There is some critique to the use of EQ-5D regarding that it was developed from reviews and expert judgement rather than from what matters to patients [227]. These are aspects worth considering.

BDI-II

During the study inclusion, some high scores of BDI-II occurred, and when they did, the study personnel had a discussion with the GP about the patient. The discussion was mainly about the diagnosis "moderate" or "severe" depression, and if the GP assured that the patient had a moderate depression and did not need to be referred to psychiatry, the patient could remain included. These anomalies provided the impetus for the comparative study between MADRS-S and BDI-II. In addition, since there is an inpatient comparative study [199] that requested an outpatient equivalent, it seemed natural to compare our collected data from the PRI-SMA study [85].

MADRS-S

We chose to use the MADRS-S self-assessment instrument in our intervention. We knew it was easily administered, short, cost-free, sensitive to change, and suitable for use in clinical trials [64, 143]. It is and was an instrument well known to Swedish GPs [12]. The items that the patients have to consider and to respond to concerning how they feel are easy to understand and manageable for most patients. I never experienced or heard complaints from the patients whom I met during inclusion and follow-up. This seems consistent with previous research [82, 142]. With the knowledge gained from Pettersson's work and paper III [87, 179], we saw that there was diversity between the GPs' and the patients' perceptions. This suggests that there are beneficial uses of MADRS-S in primary care, but perhaps it is not primarily the GP who should be using it. There is ongoing research in Region Västra Götaland that is implementing a collaborative care model with a care manager who uses MADRS-S as a tool in the recurrent contacts with the depressed patient via tele-phone. The use of MADRS-S via telephone is a valid method and should not be underestimated [84].

In this study, we recruited patients at PCCs in Region Västra Götaland. It was a challenging task to get PCCs to participate in the RCT, although personnel are often positive to partake in studies and there is a need to involve all parts already in the design stage of an RCT [223]. We learned a great deal during this RCT and many of our working methods were in alignment with Hange's findings [223]. We continuously had communication with the involved PCCs, and during the inclusion periods the study personnel interacted with the entire PCC to inform about the ongoing study, to generate enthusiasm and to get the entire staff to feel included and a part of the study.

To be successful in a RCT one needs careful planning and monitoring during the entire process, which is in alignment with the conclusions of other studies [228]. The use of an RCT to evaluate the use of a self-assessment instrument in the primary care population with mild/moderate worked well. However, we need to be aware of the many obstacles to overcome to make a study successful [224, 229]. Hange et al used focus groups to collect data among primary care GPs and nurses, in order to explore how staff members experience participation in clinical trials. The results showed mostly positive experiences, but also some difficulties, such as difficulties in remembering the study purpose or uncertainty about study procedures [223]. In our RCT (PRI-SMA) we had a study nurse on

site during the inclusion period, and we experienced that this helped considerably. Once we had enlisted a PCC to our study, we could begin patient recruitment. All patients who visited the PCC booked visits or attended the drop- in reception, and those who received the diagnosis "mild/moderate" depression by their GP were asked to participate in the trial. The participants knew that they were part of an RCT and in which group they belonged. There was a blinding procedure for the researchers, who did not know which patient group that was the intervention or control group until after the inclusion and the 3 months follow-up were finished.

It is possible that the control GPs delivered exceptionally good treatment according to guidelines, due to their knowledge that that they were being compared to the intervention group. However, since we were interested in what effect the use of MADRS-S had on our chosen outcomes, it would be less important if the TAU component in the control and intervention groups was equally good.

Papers I and IV are closely related in their methodology with the exception of the excluded participants in paper IV, i.e. individuals who did not work, or were retired or students.

Focus group interviews

We knew beforehand that the focus group method would enhance the communicative interaction between the participants [166], and that focus groups are suitable to obtain new data about fields that are less researched. The logistics around the focus groups worked well, looking at how the research group split tasks between the focus groups. The researcher was a focus group leader at one session, a passive observer at another and a non-participant at a third. We were careful to describe our preconceptions in paper III, and the triangulation throughout the analysis gave us confidence that we were on the right track. We were fortunate to have an experienced researcher that had used the methodology several times before, which helped ensure consistency in data collection between the sessions. The use of focus group interviews was stimulating. It became a talkative, familiar atmosphere during the three sessions, which contributed to the rich material that we later transcribed verbatim and analyzed. There is good literature to support and guide young researchers to avoid bias, and I feel that we were aware of the possible pitfalls and traps that may occur [230, 231]. It is the responsibility of the group leader of a focus group discussion to put his/her preconceptions aside and let the participants be the ones who speak and interact. It is the perceptions of the

participants that the researcher should be interested in, and not the confirmation of own thoughts and beliefs.

Strengths and limitations

Generally we regard our studies to be solid and well conducted. We have used a pragmatic approach, meaning that we wanted to see the effects of our intervention as it would have been used in daily practice, rather than under optimal circumstances [232, 233]. This is both an advantage and a risk. When positive results are attained, we can be almost sure the intervention will work under normal conditions, but negative results on the other hand will leave unanswered the question as to whether the intervention would have worked under optimal conditions [234]. All studies have been approved by the regional ethical board. In paper I, we conducted an intervention aimed to reduce symptoms more rapidly, to facilitate a more rapid return to work, and to lower the number of sick leave days in primary care to patients with mild/moderate depression in the primary care context where most patients with these diagnoses are treated. Therefore, we can be confident that our results mirror the reality.

We chose to exclude patients who did not speak or understand Swedish, and this made our sample somewhat skewed according to the general Swedish population. This is one of the weaknesses of RCT studies and decreases the generalizability of the study. We could not include patients who did not understand, speak or read Swedish, as it is a large challenge to overcome such language barriers in order to include a more representative sample of the population. We know that exclusion of the non-native speaking population is a problem [235]. Perhaps future technical innovations could overcome this barrier.

The question about the role of self-assessment instruments used on regular basis in primary care is still not fully answered. Some knowledge gaps need to be filled. One can argue that GPs would be more prone to diagnose depression if they could manage and treat it, since it has been shown that diagnosis of depression follows treatment decisions [236]. In several studies evaluating treatment of patients with depression in primary care, the effect size is small compared to TAU [220, 237], which is interesting. Is treatment good enough as it is, or are we focusing on the wrong outcomes? We need more pragmatic large RCT studies in primary care evaluating long-term outcomes and interventions to be able to answer that question [91, 238, 239].

When the PRI-SMA trial started, there were, to our knowledge, no other studies that had evaluated the effects of recurrent use of self-assessment instruments in depression treatment in primary care. The SBU had called for studies like the one we conducted [12]. We accomplished the RCT in primary care, where most people with depression are treated, and where the real world conditions were available. The intervention and control group were very alike, and we found no statistically significant differences at baseline that potentially could affect the results. Our greatest weakness in the overall PRI-SMA study probably is the exclusion of patients who were not able to speak/understand Swedish. This situation is commonly occurring in research and it is something to discuss prior to designing new studies. We most certainly missed potential participants in our RCT due to this. Taking the "justice" principle of ethics in consideration [240], the researchers should not exclude persons who do not speak the language most commonly used in that country, just because it makes the research inclusion inconvenient.

One major strength of this study is that it is conducted within primary care, with real primary care patients, i.e. patients who seek their initial treatment in the first line of health care that society can offer. Study personnel were stationed at each site during inclusion and follow-ups. This enabled the possibility to keep enthusiasm up among PCC personnel. There are several advantages to having study personnel stationed on site, i.e. being able to monitor the course of the inclusion and to give the GPs and others insightful advice and input regarding the way to deal with situations that occur. The research group perceived that many PCCs were positive to having a study person on site, and that the study nurse's presence did not affect the way they worked to a large extent. The research personnel collected all EPR data.

The RCT we conducted was a pragmatic study. Schwartz and Lellouch introduced the concept of explanatory and pragmatic trials in 1967 [233]. Our trial is in alignment with the description of a pragmatic trial conducted in real life settings. The intervention is brought to the full range of the population that would be affected. Pragmatic trials are increasing, and in primary care this approach is very suitable, considering the broad range of persons attending its multifaceted environment [241].

A strength of pragmatic studies is the internal validity granted by their methods. Every step of the study is described and accounted for in the quantitative studies in a detailed study protocol. Our research group continuously held meetings during the entire RCT where we discussed the

progress of the study. This was a good way to keep everyone informed and to be able to prevent adverse events. These regular meetings were very constructive. We could report the number of included patients, difficulties, and positive experiences, etc. These meetings strengthened the internal validity, and give external reviewers good insight as to how the study was conducted. The inclusion and exclusion criteria also strengthen the validity. The blinding of the outcomes of the intervention and control arms enhances the credibility of the results. The RCT method is suitable when looking for the establishment of causation. The intervention given in study I and IV was possible to verify with EPR when collecting data for long term follow-ups. In retrospective, it would have been difficult to obtain the answers that were achieved by the RCT with other approaches. Perhaps in the future, large data registries could give us more, but until that becomes a reality, the RCT is the "gold standard" and is ranked as the highest level of evidence-based medicine [242]. Every step of the analysis is described, and we have followed the aims pre-registered for the study. All papers have followed consolidated standards for reporting quantitative trials and qualitative research [243-245]. In the qualitative study III, the inter-reliability is based upon the preconceptions described by the analyzers.

In the qualitative study (Paper III), we are aware of the small sample (n=9), and the possibility of non-representative participants for the research question makes the results less generalizable. On the other hand, sometimes it is important to look beside this, to look at the study as a whole, i.e. what was the design, the procedures, and the analytic strategies. We did not claim the results to be generalizable [166], but they do shed light upon an important aspect of treatment, i.e. the patient's own perceptions. We could have added some single interviews with patients, who had been part of the PRI-SMA study to obtain a higher "n", but we feel content about the choices we made during the collection of data, and we feel confident that they reach the research standards of today [207]. Our aim in paper III was to understand how patients perceive the use of MADRS-S in the primary care consultation with GPs. For that purpose we chose a qualitative method, and used focus group discussions. This we thought appropriate and would broaden the perspective with regard to the overall aim of the thesis [246]. We realized that if we were to access the whole picture of the use of self-assessment, we had to ask the patients who had used them in the clinical context. Only by asking them "How did you perceive that the GP asked you to complete the form?" and many other questions we could get closer to the core of the assessment. Since the process from start to a finished paper is time consuming, we had to be

aware that patients' understanding of context and situations could change with time. We chose to invite patients no less than 6 months after they had finished their intervention to minimize change in perceptions. To be trustworthy in our method we have to consider the credibility, dependability, confirmability and transferability.

Credibility: We believe that by using focus group discussions we gained access to different views and experiences that could lead to further discussions about the topic, how, why etc [247]. We have already discussed the sample size but nevertheless it is an important factor to discuss. Perhaps our results would have been different if our focus groups had been larger.

Dependability is the factor that refers to the stability of the findings. We completed the three focus groups at the same location in a non-medical environment, which we think grants stability. Outer circumstances were the same for all patients.

Confirmability: This factor describes to what degree we as researches may have influenced the findings. We were a district nurse, a GP, an Health assessment manager and an occupational therapist that conducted the study. All except the GP were involved in completing the focus group discussions. Everyone switched turns and were discussion leader, and passive listener at one session each. All researchers took part of the analysis. The preconceptions and understanding of the field differed between the researchers. All had experience from primary care, and theoretical knowledge about the field that was explored. Since all researchers were active throughout the process and we used triangulation to discuss findings and ensure we were on the same track, we feel we have dealt with most biases that could occur.

Transferability, i.e. how the results can be transferred to other settings and groups, is up to the reader to judge and decide upon. To help the reader we have tried to be as transparent as possible in describing the methodology, how patients were recruited, how we analyzed the data and how the group discussions played out [248].

Interpretations of results

I

When GPs used a depression self-rating scale in recurrent consultations, patients with mild/moderate depression more often continued antidepressant medication according to guidelines, compared to TAU patients. However, reduction of depressive symptoms, remission rate, quality of life, psychological well-being, sedative use, sick leave, and health care use 4-12 months were not significantly different from the TAU group. These findings suggest that frequent use of depression rating scales in person-centered primary care consultations has no further additional effect on patients' depression course or well-being, sick leave, or health care use compared to treatment-as-usual.

II

The two BDI-II and MADRS-S instruments showed good comparability and reliability for low, middle, and high total depression scores. The MADRS-S may be used as a rapid, easily administered, and inexpensive tool in primary care and has results comparable to BDI-II in all domains.

III

Use of MADRS-S was perceived as a confirmation for the patients that they had depression and how serious it was. MADRS-S showed the patients something "black and white" that described and confirmed the diagnosis. The informants emphasized the importance of person-centeredness, i.e. of being listened to and being taken seriously during the consultation.

IV

Recurrent consultations with the GP and self-assessment with feedback to the patient lead to some extent to improved work ability but not to significantly decreased experience of job strain among individuals with depression in comparison to treatment as usual. Rehabilitative efforts that seek to influence both work ability as well as return to work for depressed patients should probably include workplace engagement.

Taken together, the studies provide gained knowledge of importance for depression treatment in primary care. There is a desire among patients to be seen, recognized, and to be taken seriously. Previous studies indicating that GPs miss about up to 50% of all patients attending PCC with a possible diagnosis of mild/moderate depression have prompted efforts to improve detection. The use of waiting-room screening without

organizational backup has long since been regarded as insufficient, and it seems that we are more and more dependent upon the patients themselves and the ability of GPs to improve their consultation skills. It is futile to expect that every GP could exclude every possible disease when having a short consultation with the patient. There is always a possibility to re-assess the patient for a second appointment, hence the importance of continuity of care. A GP who is familiar with her/his patient has the advantage of knowing when the unusual occurs in the consultation. By using the person-centered consultation methods, the detection of depression can be around 80% [66]. The use of self-assessment instruments has also been driven in part by the unspoken demands from actors such as the social insurance system and even within the own organization. As a GP, one must support the provision of a sick-leave certificate, and one way to do that is to use a quantitative measurement of the depression with the help of a depression scale. However, a depression diagnosis cannot be based alone on a depression scale.

Lately, the rise of the use of self-assessment instruments has been an effect of the increased need for patients to partake in the decisions regarding treatment. The expert on how one actually feels must be the person himself/herself. There-fore, in that respect, the use of self-assessment scales are justified. One argument against using the scale as an argument for the provision of sick leave is that a patient who really wants to be given sick leave could score higher to get what he or she wants. The GPs have a great responsibility not to act solely on just the scores from these instruments but to use them, when the patient is positive to its use, as one communication aid, together with the consultation, and previous knowledge of the patient's wellbeing, EPR, and reassessments. There is a body of evidence suggesting that collaborative care models are the effective way of managing depression in primary care [249]. If incorporated, measurement-based stepped care and treatment can improve patients' health and function substantially and reduce costs at the same time [250]. A metaphor for being depressed has been formulated as being out in deep water and suddenly forgetting how to swim. Everything around one's self becomes very unimportant. To get out of this, one not only needs to get up to the surface to breathe air, but one will also have to relearn swimming. Antidepressants are often the help that is needed to get up to the surface to breathe again. However, unfortunately, statistics indicate that there is a strong likelihood of sinking again, if one does not learn how to swim again. Anti-depressant prescriptions with poor adherence are like a badly inflated life ring. It will work for a while, but eventually one will get into deep water again. Recurrent visits to the GP

with a self-assessment instrument as an integrated part of the consultation did not affect the depression outcomes compared to TAU, but antidepressant adherence improved and the patients perceived positive aspects that are worth taking notice of. Primary care should stand for accessibility and continuity, and in Sweden we do have good accessibility but we need to improve continuity. The quality of care will improve if continuity is improved [251]). The recurrent use of an assessment instrument could be one way to enhance continuity of care.

Unanswered questions

There are probably many aspects from the patients' view that we have not covered. We have concluded from our findings that workplace engagement from primary health care probably could have influence on sick leave and return to work, but this remains to be further explored. We still do not know why there is a difference between men and woman concerning self-assessment scores. Are there research models that allow control arms with no treatment at all? Is it unethical and dangerous to include in a study patients who are unaware of their participation, since the worst outcome in untreated depression is death?

6 CONCLUSION

The studies in this thesis have expanded our knowledge of use of self-assessment instruments in the management of depression in primary care concerning a number of aspects:

Using a self-assessment instrument in recurrent consultations can strengthen the patient's perceptions concerning confirmation, centeredness, and clarification. The use of a self-assessment instrument increases the adherence to antidepressant medication, WAI, and the perception of positive social support. However, the use does not reinforce beneficial effects concerning depression course, quality of life, or sick-leave. It is important for GPs and nurses in primary care to have knowledge of the possible effects of use of a self-assessment instrument and to explore during contact with the individual with depression, whether the individual is positive to the use of a self-assessment instrument. Further, the MADRS-S instrument corresponds well to the BDI-II instrument in all domains and could be used as a reliable instrument to follow a person's course of depression with the knowledge that it yields indications comparable to the BDI-II. The use of depression self-rating scales should perhaps not be mandatory in primary health care but rather left to the discretion of the GP and the patient.

7 FUTURE PERSPECTIVES

Could self-assessment instruments used to follow the lapse/course of depression find their place in clinical practice and reduce depression symptoms and enhance quality of life if used as an integrated part of a collaborative care model by a care manager nurse? The results from these studies further emphasize the importance of more longitudinal studies with long-term follow-ups, and this is valid not only in the depression field but in the entire primary care context.

In the light of this thesis and the current state of mental health in Sweden and globally, there is an urgent need for studies of several organizational factors of importance for the management of depression in primary care. Firstly, an important factor is continuity of care. In Sweden today, primary care has undergone an organizational change since 2009 that has steered towards a more consumer-oriented health care. Accessibility is often especially valued, but not continuity, which means that consultations get shorter when many patients are squeezed in before lunch or the end of the day. There is a risk that the nurse and GP only focus on the symptoms that the patient presents, and not the underlying cause.

Secondly, collaborative care interventions are needed to meet the challenge of common mental disorders. Many hopeful strategies have been developed and need to be evaluated in large studies, RCTs, and registry-based studies.

A care manager who together with the GP follows the patient through the course of depression is a method that has been shown to have significant effects on patient outcome in the US and Great Britain [252]. A care manager strengthens the primary care organization concerning accessibility and continuity and gives support and continuous contact with depression patients. Here, the self-assessment instrument could be a way to provide person-centered support. Increased prevention activities, on health care, community, and public health levels are important. I personally think we also need to focus on prevention not only on primary care level but also on the public health level and via early education among schoolchildren to raise awareness concerning mental health, detection, and treatment to avoid medicalization of entire generations to come.

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APPENDIX

MADRS-S
(självskattningsskala)

Namn	Datum

Genom att besvara följande nio frågor kan du och din läkare få en detaljerad bild av hur du mår och om du har symtom, som är typiska för depression. Genom att lägga ihop den "poäng" du får på frågorna får du och din läkare en bild av graden av depression. Sätt en ring runt siffran som du tycker bäst stämmer med hur du mått de senaste tre dagarna. Använd gärna mellanliggande alternativ. Tänk inte alltför länge, utan försök arbeta snabbt.

1. Sinnestämning
Här ber vi dig beskriva din sinnesstämning, om du känner dig ledsen, tungsint eller dyster till mods. Tänk efter hur du har känt dig de senaste tre dagarna, om du har skiftat i humöret eller om det varit i stort sett detsamma hela tiden, och försök särskilt komma ihåg om du har känt dig lättare till sinnes om det har hänt något positivt.

0 Jag kan känna mig glad eller ledsen, alltefter omständigheterna.
1
2 Jag känner mig nedstämd för det mesta, men ibland kan det kännas lättare.
3
4 Jag känner mig genomgående nedstämd och dyster. Jag kan inte glädja mig åt sådant som vanligen skulle göra mig glad.
5
6 Jag är så totalt nedstämd och olycklig att jag inte kan tänka mig värre.

2. Oroskänslor
Här ber vi dig markera i vilken utsträckning du haft känslor av inre spänning, olust och ångest eller odefinierad rädsla under de senaste tre dagarna. Tänk särskilt på hur intensiva känslorna varit, och om de kommit och gått eller funnits nästan hela tiden.

0 Jag känner mig mestadels lugn.
1
2 Ibland har jag obehagliga känslor av inre oro.
3
4 Jag har ofta en känsla av inre oro som ibland kan bli mycket stark, och som jag måste anstränga mig för att bemästra.
5
6 Jag har fruktansvärda, långvariga eller outhärdliga ångestkänslor.

3. Sömn
Här ber vi dig beskriva hur bra du sover. Tänk efter hur länge du sovit och hur god sömnen varit under de senaste tre nätterna. Bedömningen skall avse hur du faktiskt sovit, oavsett om du tagit sömnmedel eller ej. Om du sover mer än vanligt, sätt din markering vid 0.

0 Jag sover lugnt och bra och tillräckligt länge för mina behov. Jag har inga särskilda svårigheter att somna.
1
2 Jag har vissa sömnsvårigheter. Ibland har jag svårt att somna eller sover ytligare eller oroligare än vanligt.
3
4 Jag sover minst två timmar mindre per natt än normalt. Jag vaknar ofta under natten, även om jag inte blir störd.
5
6 Jag sover mycket dåligt, inte mer än 2-3 timmar per natt.

4. Matlust
Här ber vi dig ta ställning till hur din aptit är, och tänka efter om den på något sätt skiljt sig från vad som är normalt för dig. Om du skulle ha bättre aptit än normalt, sätt din markering vid 0.

0 Min aptit är som den brukar vara.
1
2 Min aptit är sämre än vanligt.
3
4 Min aptit har nästan helt försvunnit. Maten smakar inte och jag måste tvinga mig att äta.
5
6 Jag vill inte ha någon mat. Om jag skulle få någonting i mig, måste jag övertalas att äta.

5. Koncentrationsförmåga

Här ber vi dig ta ställning till din förmåga att hålla tankarna samlade och koncentrera dig på olika aktiviteter. Tänk igenom hur du fungerar vid olika sysslor som kräver olika grad av koncentrationsförmåga, t ex läsning av komplicerad text, lätt tidningstext och TV-tittande.

0 Jag har inga koncentrationssvårigheter
1
2 Jag har tillfälligt svårt att hålla tankarna samlade på sådant som normalt skulle fånga min uppmärksamhet (t ex läsning eller TV-tittande).
3
4 Jag har påtagligt svårt att koncentrera mig på sådant som normalt inte kräver någon ansträngning från min sida (t ex läsning eller samtal med andra människor).
5
6 Jag kan överhuvudtaget inte koncentrera mig på någonting.

6. Initiativförmåga

Här ber vi dig försöka värdera din handlingskraft. Frågan gäller om du har lätt eller svårt för dig att komma igång med sådant du tycker du bör göra, och i vilken utsträckning du måste övervinna ett inre motstånd när du skall ta itu med något.

0 Jag har inga svårigheter med att ta itu med nya uppgifter.
1
2 När skall jag ta itu med något, tar det emot på ett sätt som inte är normalt för mig.
3
4 Det krävs en stor ansträngning för mig att ens komma igång med enkla uppgifter som jag vanligtvis utför mer eller mindre rutinmässigt.
5
6 Jag kan inte förmå mig att ta itu med de enklaste vardagssysslor.

7. Känslomässigt engagemang

Här ber vi dig ta ställning till hur du upplever ditt intresse för omvärlden och för andra människor, och för sådana aktiviteter som brukar bereda dig nöje och glädje.

0 Jag är intresserad av omvärlden och engagerar mig i den, och det bereder mig både nöje och glädje.
1
2 Jag känner mindre starkt för sådant som brukar engagera mig. Jag har svårare än vanligt att bli glad eller svårare att bli arg när det är befogat.
3
4 Jag kan inte känna något intresse för omvärlden, inte ens för vänner och bekanta.
5
6 Jag har slutat uppleva några känslor. Jag känner mig smärtsamt likgiltig även för mina närmaste.

8. Pessimism

Frågan gäller hur du ser på din egen framtid och hur du uppfattar ditt eget värde. Tänk efter i vilken utsträckning du ger självförebråelser, om du plågas av skuldkänslor, och om du oroat dig oftare än vanligt för t ex din ekonomi eller din hälsa.

0 Jag ser på framtiden med tillförsikt. Jag är på det hela taget ganska nöjd med mig själv.
1
2 Ibland klandrar jag mig själv och tycker jag är mindre värd än andra.
3
4 Jag grubblar ofta över mina misslyckanden och känner mig mindervärdig eller dålig, även om andra tycker annorlunda.
5
6 Jag ser allting i svart och kan inte se någon ljusning. Det känns som om jag var en alltigenom dålig människa, och som om jag aldrig skulle kunna få någon förlåtelse för det hemska jag gjort.

9. Livslust

Frågan gäller din livslust, och om du känt livsleda. Har du tankar på självmord, och i så fall, i vilken utsträckning upplever du detta som en verklig utväg?

0 Jag har normal aptit på livet.
1
2 Livet känns inte särskilt meningsfullt men jag önskar ändå inte att jag vore död.
3
4 Jag tycker ofta det vore bättre att vara död, och trots att jag egentligen inte önskar det, kan självmord ibland kännas som en möjlig väg.
5
6 Jag är egentligen övertygad om att min enda utväg är att dö, och jag tänker mycket på hur jag bäst skall gå tillväga för att ta mitt eget liv.

Lägg samman poängen från *båda sidor* av formuläret och ange summan i rutan

Wyeth AB