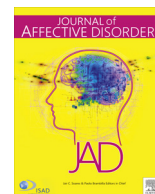




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Research Paper

Pharmacological and psychosocial treatment of depression in primary care: Low intensity and poor adherence and continuity

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ABSTRACT

Background: Primary health care bears the main responsibility for treating depression in most countries. However, few studies have comprehensively investigated provision of pharmacological and psychosocial treatments, their continuity, or patient attitudes and adherence to treatment in primary care.

Methods: In the Vantaa Primary Care Depression Study, 1111 consecutive primary care patients in the City of Vantaa, Finland, were screened for depression with Prime-MD, and 137 were diagnosed with DSM-IV depressive disorders via SCID-I/P and SCID-II interviews. The 100 patients with current major depressive disorder (MDD) or partly remitted MDD at baseline were prospectively followed up to 18 months, and their treatment contacts and the treatments provided were longitudinally followed.

Results: The median number of patients' visits to a general practitioner during the follow-up was five; of those due to depression two. Antidepressant treatment was offered to 82% of patients, but only 50% commenced treatment and adhered to it adequately. Psychosocial support was offered to 49%, but only 29% adhered to the highly variable interventions. Attributed reasons for poor adherence varied, including negative attitude, side effects, practical obstacles, or no perceived need. About one-quarter (23%) of patients were referred to specialized care at some time-point.

Limitations: Moderate sample size. Data collected in 2002–2004.

Conclusions: The majority of depressive patients in primary health care had been offered pharmacotherapy, psychotherapeutic support, or both. However, effectiveness of these efforts may have been limited by lack of systematic follow-up and poor adherence to both pharmacotherapy and psychosocial treatment.

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1. Introduction

Treatment of depression is a major challenge for primary care (PC). Altogether 30 million Europeans are estimated to suffer from depression, and depression is likely to be the most important illness in Europe in terms of disability-adjusted life-years (Wittchen et al., 2011). Marked efforts have been made to improve recognition, treatment, and outcome of depression in PC. These include education of PC doctors (Sikorski et al., 2012), use of depression screens (Thombs et al., 2012), and application of service delivery models such as collaborative (Sighinolfi et al., 2014; Thota et al., 2012) or stepped (Firth et al., 2015) care. Furthermore, a large-scale national initiative to promote psychological treatment in PC in the UK (Clark, 2011) and guidelines produced by national health

care organizations (Leitlinien, 2015; National Board of Health and Welfare, 2010; NICE, 2010) or professional societies (American Psychiatric Association (APA), 2010; Cleare et al., 2015; Kennedy et al., 2009; The Finnish Medical Society Duodecim and Finnish Psychiatric Association, 2014) have been implemented. In addition, over the last 25 years, use of antidepressants (ADs) has risen in Europe, which at least on an ecological level is associated with a decline in suicide mortality (Gusmao et al., 2013). However, evidence for a major positive change in terms of public health is limited and uncertain.

General population studies consistently show that the majority of individuals suffering from depression either do not seek treatment or receive adequate care (Demyttenaere, 2003; Gabilondo et al., 2011; Hamalainen et al., 2009; Kessler et al., 2003; Wang et al., 2005). In epidemiological studies, a significant proportion of individuals with depressive syndromes do not perceive themselves as suffering from a mental disorder (Hamalainen et al., 2004). Both anosognosia and the often somatic complaints in PC (Vuorilehto et al., 2005) are obstacles to recognition of depression.

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The likelihood for recognition increases with depression severity (Thompson et al., 2001). The quality of treatments is central from the point of view of public health. However, limited comprehensive studies exist in PC, mainly focusing on pharmacotherapy and follow-up monitoring (Coyne et al., 1997; Gilchrist and Gunn, 2007; Limosin et al., 2004; Lin et al., 2000; Ronalds et al., 1997; Rost et al., 1995, 1998; Simon et al., 2001, 2004). Besides reports from the UK Improved Access to Psychological Therapies (IAPT) project (Richards and Borglin, 2011), few clinical epidemiological studies exist on the availability, type, and quality of psychological treatments. While national guidelines commonly instruct referral to specialized psychiatric care, the actual patterns of referral have seldom been investigated.

Whatever the treatment modality, patient adherence is crucial for any benefits to materialize (Chong et al., 2011; Lynch et al., 2011; Raue et al., 2009; Thompson et al., 2000a). Depending on their attitudes, patients may immediately decline treatment, ostensibly accept it but not start, discontinue at a later phase, or participate too irregularly for any benefit to be gained (Melartin et al., 2005). Thus, the adherence to treatment is likely to play an important role in the adequacy of treatment (Chong et al., 2011; Lynch et al., 2011; Raue et al., 2009; Thompson et al., 2000a, 2000b). However, most studies address the issue by reporting on the quality of care merely in terms of treatment provision, neglecting the potential shortcomings due to poor adherence. Moreover, not all patients believe that ADs are helpful (Edlund et al., 2008), and some prefer no treatment to an unacceptable treatment modality (Morey et al., 2007). Adherence to the chosen treatment modality may be less than optimal if a patient is obliged to use a modality that he/she does not desire (Raue et al., 2009). The few PC studies investigating adherence mainly focus on pharmacotherapy, although psychological treatments in PC are known to be equally effective for mild or moderate depression (Cuijpers et al., 2009) and are often preferred (Raue et al., 2009; van Schaik et al., 2004; Vuorilehto et al., 2007). Moreover, most reports are based on treatment trials with selected patient populations. Despite chronicity and the recurrent nature of depression necessitating continuity of care, naturalistic studies comprise only short follow-ups of acute depression. According to these studies, a significant proportion of patients fail to start an AD prescribed. Discontinuation is very common at the beginning of pharmacotherapy, especially among young patients, a fact of which the clinician is often unaware (Bambauer et al., 2007; Demyttenaere, 2003; Hunot et al., 2007; Lin et al., 1995; Maddox et al., 1994; Simon et al., 1993). Thus, although patient adherence is a precondition for any treatment benefits, the role of attitudes towards treatments and the types of adherence problems encountered in PC have been relatively poorly studied.

Overall, despite abundant guidance, specific treatments and service delivery models, knowledge of actual treatment provision for depression in PC is fragmentary and crude. In this study, we followed 100 PC patients with MDD for 18 months and observed their treatment. We investigated their contacts with PC doctors, the pharmacological and psychosocial treatments offered, and the factors predicting treatment provision. We also examined treatment attitudes, different types of adherence problems encountered, and factors related to referral to psychiatric services.

2. Methods

The Vantaa Primary Care Depression Study (PC-VDS) is a naturalistic and prospective cohort study on depressive disorders. The study protocol was approved by the pertinent ethics committee in December 2001. The PC-VDS forms a collaborative research project between the Department of Mental and Alcohol Research of the

National Institute of Health and Welfare and the City of Vantaa, Finland. The catchment area comprises a population of 63 400, served by 30 general practitioners with population-based responsibility. The methodology has been described in detail elsewhere (Vuorilehto et al., 2005, 2009).

2.1. Screening and baseline evaluation

In the first stage, between 2 January and 31 December 2002, a total of 1119 consecutive patients aged 20–69 years received the screening questionnaire of PRIME-MD (Spitzer et al., 1994) in general practitioners' waiting rooms. Altogether 375 patients answered "yes" to at least one of the two questions concerning depressed mood or anhedonia during the last month (1. feeling down, depressed, or hopeless or 2. having little interest or pleasure in doing things). Over the telephone, we ensured that at least one core symptom of MDD was present according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I/P) (First et al., 1997). We excluded patients with psychosis (other than depressive) or bipolar or organic mood disorder or those currently receiving treatment in psychiatric care. After the telephone interview altogether 175 patients remained potentially eligible to the study.

In the second stage, after receiving written informed consent, we interviewed all 175 potentially eligible patients face-to-face using the SCID-I/P with psychotic screen. Inclusion criteria were current MDD, subsyndromal MDD with two to four depression symptoms (minimum one core symptom), and lifetime MDD and minor depression. Distress or functional impairment was required for all. The joint diagnostic reliability for current depressive disorders was 100% (kappa 1.0 for depression diagnoses). Patients who refused to participate (15%) did not differ significantly in age or gender from those who consented. Altogether 137 patients were included in the cohort (Vuorilehto et al., 2005).

2.2. Other research instruments

Current and lifetime psychiatric disorders were assessed by using the SCID-I/P and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II) (First et al., 2002). Observer and self-report scales included the Hamilton Depression Rating Scale (Ham) (Hamilton, 1960) and the Occupational Functioning Assessment Scale for DSM-IV (SOFAS) (Goldman et al., 1992). Self-report scales included the 21-item Beck Depression Inventory (BDI) (Beck et al., 1961), the Beck Anxiety Inventory (BAI) (Beck et al., 1988), and the Perceived Social Support Scale – Revised (PSSS-R) (Blumenthal et al., 1987). A self-report questionnaire, medical records, and an interview were used for chronic medical illnesses. In addition, all available data, including medical and psychiatric records, were gathered to reconstruct the lifetime course for depression.

2.3. Attitudes

Attitudes towards ADs and psychotherapeutic treatment were rated with the following items: patient 1) actively approves, 2) passively accepts, 3) has reservations, 4) has definitely negative attitudes, or 5) could not answer. Attitudes were analysed in two groups: 1) favourable attitudes comprising those who actively approve of or passively accept treatment and 2) negative attitudes comprising those who have reservations about or negative attitudes towards treatment.

2.4. Follow-up

After baseline, patients were followed up with a graphic life-

chart to determine the exact duration of the index episode (IE). To ensure accuracy of the life-chart, we gathered information at three different time-points: the BDI was rated at 3, 6, and 18 months, self-report scales were included at 3, 6, and 18 months, and the current diagnosis of depression was investigated by telephone at 6 months, and face-to-face in SCID-I interviews at 18 months. In addition, observer scales were used at the 18-month assessment. We gathered all available data, including medical and psychiatric records, which were then integrated into the life-chart based on DSM-IV definitions. We also used probes related to important life-events to improve the accuracy of the assessment of change points in the psychopathologic states (Melartin et al., 2004; Vuorilehto et al., 2009).

The outcome of IE was divided into full remission or recurrence after at least two consecutive months of partial or full remission. Recurrence followed the DSM-IV definition for “296.3x MDD”. Among those whose IE was still continuing at the 18-month follow-up interview, the state of depression was either MDE (5 or more of the 9 MDD criteria symptoms) or partial remission (1–4 symptoms). Definitions of full remission followed DSM-IV criteria, thus requiring at least two consecutive months in which no MDD criteria symptoms were met.

2.5. Offered treatment

Earlier and ongoing treatments during IE were investigated by interview at baseline and six and 18 months, by a mail questionnaire at three months, and by investigating all clinical information on treatment, including medical and psychiatric records. The offered treatment was assessed 1) retrospectively from the beginning of IE to baseline and 2) prospectively from baseline to the end of IE and, in case of ongoing IE, to the 18-month interview. The minimum criteria for adequate doses of ADs were based on the lower end of adult doses in the APA Guidelines (American Psychiatric Association (APA), 2010).

Psychotherapeutic support (PS) comprised all appointments with a health care professional other than a doctor or with a social worker with the explicit aim of helping the patient by discussing his/her mental problems (weekly psychotherapy included). Weekly psychotherapy was defined as having weekly therapy sessions with a qualified and certified psychotherapist.

Monitoring of depression by a PC doctor was assessed, for feasibility reasons, only for the period from baseline to the end of IE or the 18-month interview. The monitoring comprised all face-to-face visits or telephone contacts where depression-related symptoms or treatment for depression were discussed. We counted the number of contacts with doctors concerning any health problems separately.

2.6. Treatment adherence

Patient adherence was investigated by asking about attending sessions/being on ADs, with response options of 1) regularly, 2) somewhat irregularly (whether this would affect treatment goals was unknown), 3) very irregularly (treatment did not proceed according to plan), and 4) not at all (provided treatment could not be implemented). Premature discontinuation of ADs without discussing it with a doctor was assessed only in patients who took an AD regularly or somewhat irregularly. They were divided into two groups: patients who ceased taking ADs 1) during full criteria of MDD and 2) during partial remission. Poor adherence was considered taking ADs/attending sessions very irregularly or not at all and premature discontinuation without discussing it. Subjective reasons for poor adherence were also sought.

Table 1.

Baseline characteristics of 100 primary care patients with major depressive disorder in the Vantaa Primary Care Depression Study.

Sociodemographic characteristics	N = %	
Gender, male	23	
Married or cohabiting	53	
High level of education	35	
Good or moderate economic situation	51	
Welfare benefits within 6 months	27	
Comorbid disorders	N = %	
Any Axis I disorder	64	
Any anxiety disorder	47	
Any substance use disorder	15	
Any Axis II disorder	55	
Cluster A personality disorder	4	
Cluster B personality disorder	29	
Cluster C personality disorder	33	
Comorbid chronic illness	53	
Depression characteristics	N = %	
Moderate or severe MDD ^a	46	
Mild MDD	36	
Partial remission	18	
Recurrent MDD	65	
Treatment in earlier episodes	N = %	
AD ^b treatment	41	
Psychiatric care	43	
Patient attitudes	N	%
Positive towards ADs	62	65
Positive towards psychotherapeutic methods ^c	65	83
Negative towards ADs	34	35
Negative towards psychotherapeutic methods ^c	12	16
Symptoms, functioning and social support	Mean	S. D.
Hamilton Depression Scale	17.2	5.3
Beck Anxiety Inventory	18.6	13.0
SOFAS ^d	55.7	11.3
Perceived Social Support Scale -Revised	42.1	12.8
Age		
Age at baseline	46.7	12.9
Age at onset of MDD	32.6	13.9

^c Standard deviation

^a Major Depressive Disorder.

^b Antidepressant.

^c Missing information or could not answer (23/100) 23%.

^d Social and Occupational Functioning Assessment Scale.

2.7. Final study cohort

Of the 137 patients initially included in the cohort, three patients (2%) dropped out from all follow-up investigations, two more patients (2%) were missing at 6 months, and altogether 10 patients (7%) at 18 months. The drop-outs did not differ from the study cohort in baseline characteristics. The diagnosis of four patients (3%) switched to bipolar disorder during the 18-month follow-up; they were censored at the time of diagnostic switch. This report includes only patients with MDD (n=82) or MDD in partial remission (n=18) at baseline. Guideline-concordant care was a main focus in this study, and guidelines usually offer recommendations for these disorders. The characteristics of the final cohort of 100 patients are presented in Table 1.

2.8. Statistical analyses

For descriptive statistics, Pearson's Chi-square test, Student's *t*-test, the Mann-Whitney *U* test, and the Kruskal-Wallis test were used as appropriate. The proportion of missing data in each group was less than 5%, unless stated otherwise. For descriptive purposes, we present all *p*-values significant at the <0.05 level, irrespective of the high number of statistical tests and the risk of type I errors. Logistic regression models were used to adjust for

confounding factors. PASW, version 18.0, was used.

3. Results

3.1. Follow-up contacts with PC doctor

During IE after baseline (median duration 16 months), patients contacted their PC doctors for any health reason a median of five times (25–75% percentiles 2–9). Less than one-half (median 2; 25–75% percentiles 1–5) of these contacts included monitoring of depression, and thus, could be regarded as a follow-up contact for depression. The third of patients [38% (38/100)] with three or more follow-up contacts for depression were in univariate analyses younger (43.0 years vs. 48.6 years) and at baseline more depressed (BDI 24.5 vs. 18.6) and had lower level of functioning (SOFAS mean 53 vs. 58). In a logistic regression (LR) model adjusted for age and gender, higher BDI (OR 1.062; $p=0.009$, CI 1.015–1.111) predicted three or more follow-up contacts.

3.2. Pharmacotherapy

3.2.1. Offering antidepressants

ADs were offered at least once to 82% (82/100) of all patients at some point during the IE (Table 2). In univariate analyses, of those who were offered ADs 70% (vs. 40%) had a lower level of education and 27% (vs. 6%) were currently receiving welfare benefits. They also perceived lower social support (PSSS 40.7 vs. 48.8). Of the group offered ADs, 41% (vs. 16%) had used ADs also during a former MDE. Factors relating to the stage of MDD at baseline, such as symptom severity scales, were not associated with being offered ADs. In LR, being offered ADs was associated strongly with lower level of education (OR 4.502; $p=0.016$, CI 1.327–15.271) and having used ADs in a former MDE (OR 6.097; $p=0.013$, CI 1.461–25.000).

3.2.2. Patient adherence to antidepressants

Of the patients who were offered ADs, 61% (50/82) adhered to the medication (started it, took it fairly regularly, and did not discontinue it prematurely without discussing with a doctor). In

Table 2.

Treatment, outcome, and duration of index episode among 100 primary care patients with major depressive disorder in the Vantaa Primary Care Depression Study.

Treatment during index episode	Number of patients
AD prescription offered	82
Before baseline	41
After baseline	41
More than one AD trial	18
Hypnotics or tranquilizers	31
Antipsychotics	6
psychotherapeutic support offered	49
Before baseline	15
After baseline	34
Referral to specialist care and discharge before baseline	20
Referral to specialist care after baseline	8
Follow-up by doctor after baseline (three or more discussions about depression)	38
Depression outcome in 18 months	
Total remission (index episode ended)	42
Recurrence (index episode ended)	11
Full criteria of MDD (index episode continuing)	23
Partial remission (index episode continuing)	24
Duration of index episode, months	median (Percentiles 25–75)
Before baseline	7 (2–24)
After baseline	16 (6–)

Table 3.

Poor adherence to offered antidepressant prescription among 82 primary care patients with major depressive disorder in the Vantaa Primary Care Depression Study.

Forms of poor adherence	N (82)	%
Did not start	9	11
Irregular use	10	12
Discontinuation without informing the doctor	13	16
During full criteria of MDD ^a	5	6
In partial remission	8	10
Poor adherence of any form	32	39

^a Major Depressive Disorder.

univariate analyses of compliant patients, 46% (vs. 19%) had a Cluster C personality disorder and 79% (vs. 50%) had favourable attitudes towards ADs. In LR, both Cluster C personality disorder (OR 4.950; $p=0.11$, CI 1.451–16.950) and favourable attitude towards ADs (OR 5.263; $p=0.005$, CI 1.655–16.666) were significant predictors of adherence.

Those who did not decline ADs but adhered poorly ($n=23$) (Table 3) reported multiple reasons for taking the AD irregularly or not at all. These included fear of side effects ($n=4$), generally negative attitude towards ADs ($n=2$), lack of motivation to take an AD ($n=2$), and high price ($n=2$). Reasons for discontinuation were subjective feeling of recovery ($n=4$), side effects ($n=4$), and not experiencing a response to the AD ($n=1$). Four patients did not give a reason.

3.2.3. Types and number of pharmacotherapy trials

The first prescribed AD among those reportedly taking ADs regularly during IE was an SSRI in 68% (43/63), a newer antidepressant (tetracyclics, NaSSA, SNRI, RIMA) in 24% (15/63), a monoamine oxidase in two, and a tricyclic in three cases. While SSRI and newer antidepressants were prescribed in adequate doses in all but one case, tricyclic doses were inadequate in all three cases.

A non-AD medication was prescribed for one-third (32% [32/100]): benzodiazepines or hypnotics for 31% (31/100) and anti-psychotics 6% (6/100). Prescribing a non-AD medication was not associated with offering an AD.

The pharmacotherapy included only one AD trial for 71% (45/63) of patients (Table 4, Fig. 1). Of the 29% (18/63) who received two or more trials, in univariate analyses 39% (vs. 9%) had a substance use disorder and 72% (vs. 40%) had used an AD during an earlier MDE. They also had more symptoms of depression at baseline (BDI 27.2 vs. 19.6; Ham 20.6 vs. 15.9) and lower perceived social support (PSSS 32.6 vs. 44.5). In LR, multiple trials were associated with comorbid substance use disorder (OR 8.394; $p=0.007$, CI 1.794–39.273), higher symptom severity at baseline (Ham, OR 1.155; $p=0.019$, CI 1.024–1.302), and ADs during an earlier MDE (OR 8.563; $p=0.001$, CI 2.332–31.440).

Table 4.

Intensity of depression treatment in primary care offered to 77 patients with major depressive disorder (patients referred to psychiatric care during the index episode were excluded).

Offered treatment	N	%
No treatment	15	19
Only psychotherapeutic support	3	4
Only AD ^a	24	31
AD ^a plus psychotherapeutic support	7	9
AD ^a plus follow-up	10	13
AD ^a plus psychotherapeutic support and follow-up	18	23
Total	77	100

^a Antidepressant.

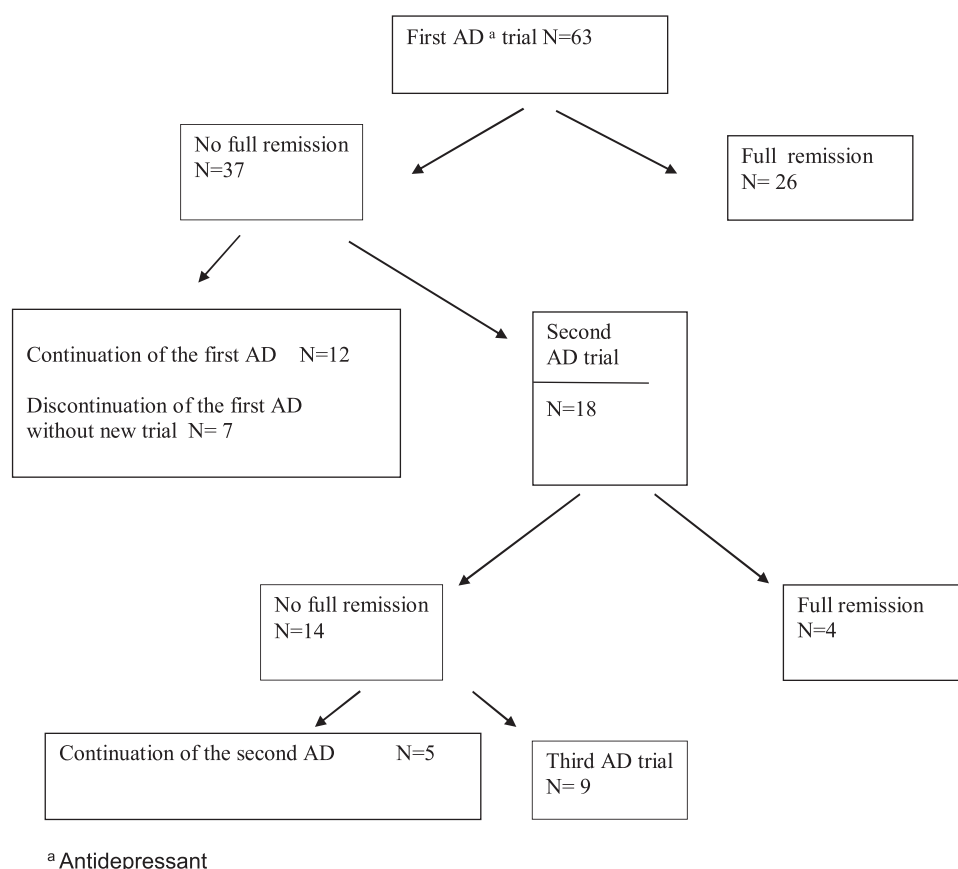


Fig. 1. Flow chart of the first and subsequent antidepressant trials among 63 primary care patients with major depressive disorder who used antidepressants regularly. ^a Antidepressant.

3.3. Psychotherapeutic support

3.3.1. Offered psychotherapeutic support

In IE, some type of psychotherapeutic support (PS) (as defined in the Methods section) was offered to one-half [49% (49/100)] of patients (Table 2). In univariate analyses, these patients were younger (42.6 years vs. 50.2 years), 57% (vs. 37%) had a comorbid anxiety disorder, and 53% (vs. 33%) had received specialized mental health care in an earlier MDE. Their onset of MDD had been earlier (at 28.5 years vs. 36.6 years), and at baseline they had more depressive symptoms (BDI 24.6 vs. 17.3; Ham 18.5 vs. 15.9) and a lower level of functioning (SOFAS 53.4 vs. 58.0). In LR, younger age (OR 1.061; $p=0.003$, CI 1.021–1.103), specialized care in a former MDE (OR 2.808; $p=0.034$, CI 1.078–7.299), and higher BDI (OR 1.086; $p=0.002$, CI 1.031–1.144) were significant predictor for being offered PS.

3.3.2. Patient adherence to PS

Of those offered PS, 59% (29/49) adhered to the treatment. A small minority (6% [3/49]) did not start treatment, and one-quarter (27% [13/49]) did not attend the sessions regularly enough to fulfil the purposes of treatment. Self-reported reasons for poor adherence were lack of motivation or laziness ($n=5$), poor personal chemistry ($n=4$), practical obstacles ($n=2$), or no reason provided ($n=2$). No significant predictors for poor adherence were found.

3.3.3. Details of PS

Of PS, one-third (33% [15/46]) was provided in PC and one-fifth (20% [9/46]) in specialized mental health care. Other providers were the social sector, including alcohol and substance abuse

counselling services, and third sector services such as churches or voluntary services. Few patients (3/46) attended weekly psychotherapy. Information about the PS provider was missing in three cases. The intensity of PS varied widely, from a single appointment to years of weekly appointments.

3.4. Clustering and intensity of offered treatment in PC

In the subgroup of patients (77/100) solely visiting PC doctors during the IE (those with referral before or after excluded), the various elements of treatment (pharmacotherapy, PS, follow-up visits) had a tendency to cluster among some patients, while others were offered no treatment at all. One-fifth (15/77) of patients was offered no treatment, three patients were offered only PS, and one-third (24/77) of patients was offered only an AD prescription. None of the above-mentioned patients was offered follow-up by the PC doctor (defined as three or more discussions). Intensity of the offered treatment was somewhat higher for the seven patients offered both ADs and PS, the ten patients offered ADs and follow-up, and the 18 patients offered ADs, PS, and follow-up.

3.5. Referrals to specialized mental health care

Another subgroup consisted of patients (23/100) referred to specialized care during IE. One-fifth (20/100) had been referred and also discharged before baseline. After baseline, of these 20 patients, one-quarter was referred again in addition to three new patients, thus altogether 8% (8/100). In univariate analyses of all referred patients, 70% (vs. 41%) had a poor economic situation and 48% (vs. 21%) had received welfare benefits. They also perceived

poor social support (PSSS-R 34.3 vs. 44.6). More than one-third (35% vs. 9%) suffered from comorbid substance use disorder. They had at baseline more symptoms of depression (BDI 27.9 vs. 18.8; Ham 20.3 vs. 16.3) and anxiety (BAI 26.7 vs. 16.0) and less functional capacity (SOFAS 48.5 vs. 57.9). In LR, higher Ham (OR 1.162; $p=0.011$, CI 1.035–1.304) and comorbid substance use disorder (OR 1.193; $p=0.025$, CI 1.072–4.065) predicted referral to specialized care.

4. Discussion

When observing 100 PC patients with MDD for 18 months we documented that over time the vast majority were offered some type of treatment, mostly an AD (82%), and often only an AD. One-half of the patients were offered some type of psychosocial treatment, guideline-concordant or not. However, a significant proportion of patients who were offered treatment, either never started, discontinued, or did not sufficiently adhere to it for a variety of reasons. Both suboptimal patient adherence and limited treatment monitoring by doctors were common shortcomings in continuity of treatment.

This study involved a representative cohort of carefully diagnosed MDD patients. The recruitment of the cohort was based on stratified sampling of PC services and screening for depression (Vuorilehto et al., 2005). Structured diagnostic interviews were used with excellent reliability ($\kappa=1.0$) for MDD, although the reliability of comorbid diagnoses remains unknown. For the patients – very few of whom dropped out – prospective longitudinal information was gathered over an 18-month period. By combining prospective data with the retrospective data gathered at baseline, we achieved a comprehensive picture of each patient's treatment process during the whole IE, irrespective of its length. Thus, we were able to assess various components of adherence, although not with formally validated methods, from patients' acceptance of an offered treatment modality to possible premature discontinuation. We could also assess the treatment process among patients with a chronic course of MDD, a group often neglected in treatment studies.

Some methodological choices need to be clarified and some limitations noted. Firstly, our cohort represents the cross-sectional prevalence of MDD in PC, with each patient entering the study in a variable phase of their IE, either with full criteria of MDD or in partial remission (with subthreshold symptoms). Therefore, the significance of the baseline severity as a predictor may be an underestimation, as it not always represents the worst point of a patient's MDD. Secondly, although both retrospective and prospective information was obtained from multiple sources, some inaccuracy concerning the onset of IE may exist among those with a long course of MDD (over 24 months before baseline among 25%). However, this would not have influenced the assessment of offered treatments, as this information could be quite reliably traced in medical records. In addition, patients may have embellished their adherence to the treatments provided, thus providing an overestimate. The number of contacts due to depression did not differ between patients whose depression had been detected already before baseline and patients with acute or undetected MDE whose contacts all occurred after baseline. Thus, our results may be considered an estimate of offered depression monitoring contacts per time unit. Thirdly, in this naturalistic study the treatment was not under our control. It is possible that for a short period after the baseline research interviews, the treatment was more intensive than in usual care, as the doctors in some cases became aware of their patients' MDD. At the same time, also education about depression was provided in health centres in the catchment area. A study involving follow-up interviews also might enhance

treatment. Moreover, patient adherence to treatment may have been boosted by the moderately low treatment costs for patients in Finland (Simon et al., 2004). Fourthly, generalizability of our findings from PC for the City of Vantaa, Finland in 2002–2004 to other PC settings remains unknown. As provision of both AD treatment as well as psychotherapies has increased in Finland since the study period, the findings may be underestimates of the treatments currently provided in PC. In our view, however, our findings are concordant with the few comparable PC studies available and extend previous findings.

4.1. Management of depression in primary care

In this study, the management of mild and moderate depression failed to follow expert guidelines in several crucial aspects (American Psychiatric Association (APA), 2010; Clark, 2011; Cleare et al., 2015; Kennedy et al., 2009; Leitlinien, 2015; National Board of Health and Welfare, 2010; NICE, 2010; The Finnish Medical Society Duodecim and Finnish Psychiatric Association, 2014). First of all, active monitoring, even if regarded as crucial for patient adherence (Bull et al., 2002), was offered to only for those who also received ADs. There clearly had been possibilities for monitoring most patients' depression, as the patients frequently consulted their doctors for other health problems. The doctors' responsibility to ensure monitoring has perhaps not been stressed enough in depression management in PC, where patients' decision-making is highly autonomous.

Moreover, NICE (NICE, 2010) recommends interventions other than pharmacotherapy as the frontline treatment for mild depression with no history of severe symptoms, e.g. low-intensity PS that includes guided self-help with problem-solving techniques and behavioural activation (Bee et al., 2008; Bower et al., 2001; Richards and Borglin, 2011) or computer psychotherapy (Andrews et al., 2010). In our study, only three patients out of 100 received PS without pharmacotherapy.

Guidelines recommend provision of education and support for all patients. In our study, only one-half of the patients were offered some type of PS. Although research evidence supports collaboration in PC depression management (Sighinolfi et al., 2014; Thota et al., 2012), only one-sixth of all of the patients here were provided PS in a PC context, which might have represented some kind of collaboration between doctors and other professionals with a shared aim in treatment.

Moreover, the collaboration between PC and specialist care appeared suboptimal, with some of the patients repeatedly referred. The patients referred, however, were severely depressed and suffered from comorbid psychiatric problems known to influence their recovery (Johnson et al., 2005; Mattisson et al., 2009) such as comorbid substance use disorders; this subgroup of patients has earlier been reported to be a neglected group concerning referrals (Wells and Sherbourne, 1999). Finally, a small group of patients with MDD was totally ignored. As noted by the first author (MV), most of this group appeared to attribute their symptoms to illnesses other than depression at the baseline interview. This kind of patients' resistance to diagnosis and treatment has been described the most challenging barrier to depression care (Nutting et al., 2002; Van Voorhees et al., 2003, 2005). In our study, a larger group of patients received suboptimal care or dropped out of care. These shortcomings could better be addressed in the organization by enhancing multifaceted care with active monitoring and clearly defined PS (Katon et al., 1995, 1996).

4.2. Antidepressant treatment and adherence to treatment

We found that PC doctors offered the first AD trial comprehensively and at adequate doses, but unfortunately adherence to it

was suboptimal, and further trials, even if needed, were neglected. Up to 80% of patients were given an opportunity to start ADs at some point during their MDE, which is nearly double the LIDO study's rate of detected depressive disorders (Simon et al., 2004). The higher detection rate in our study might be partly due to the longer follow-up and also PC doctors might have been encouraged by enhanced education in pharmacotherapy and the ongoing depression research project in the catchment area. In general, however, education alone is unlikely to change practice (Thompson et al., 2000a). Patients who had received AD treatment during a former episode were offered the same for the current episode. This finding is concordant with Klinkman's report on former treatments being relevant factors in PC doctors' clinical decisions (Klinkman et al., 2010). On the other hand, we also found that patients' lower education predicted being offered ADs. The intensity of AD treatment declined after the first prescription, and only one-half of those who failed to recover during the first trial were provided a second trial. More intensive AD treatment clustered among patients with more symptoms of depression, comorbid substance use, and recurrent MDD with a treatment history.

As suggested in earlier studies (Bambauer et al., 2007; Demyttenaere, 2003; Hunot et al., 2007; Lin et al., 1995; Maddox et al., 1994), non-adherence to ADs was common and the patients often discontinued ADs prematurely without consulting their doctor. The patients provided widely variable subjective reasons for discontinuation, as also reported elsewhere (Demyttenaere, 2003). In our study, the relatively low adherence may partly be related to the number of follow-up visits, as it is known that fewer than three follow-up visits would predict discontinuation of pharmacotherapy (Bull et al., 2002). Somewhat surprisingly, better adherence was found among patients with cluster C personality disorder, and expectedly, among those with a positive attitude towards pharmacotherapy. This has earlier been reported in specialist care patients (Melartin et al., 2005). We did not, however, replicate Bambauer's finding in a shorter follow-up of better adherence by young patients (Bambauer et al., 2007).

4.3. Psychosocial support and adherence to the regimen

Some kind of PS was offered to one-half of patients, mainly to those with more severe illness and pharmacotherapy. Although psychological treatment in PC is considered equally effective for mild or moderate depression (Cuijpers et al., 2009) and is often preferred by patients (Raue et al., 2009; van Schaik et al., 2004), in our study it did not appear to be a serious alternative to AD treatment. Neither did it appear to be guidelines concordant collaborative care (Coventry et al., 2014; Sighinolfi et al., 2014; Thota et al., 2012). Moreover, weekly psychotherapy provided by a trained therapist was very rare, although known effective (Cuijpers et al., 2008, 2009; Cuijpers et al., 2011).

Apart from more severe depression and ongoing AD treatment, patients offered PS differed from other patients by more often having a treatment history in specialist care for earlier episodes, thus perhaps being more able to demand PS also in the IE. Moreover, these patients were younger, and thus, perhaps more flexible and capable of psychological changes and also more in need of active treatment due to having a long life ahead. The rate of adherence in this study was less than two-thirds, about the same as in pharmacotherapy.

5. Conclusions

In this PC study, we found several foci of improvement in treating depression. While pharmacotherapy was offered to most

patients, monitoring of outcome and support for adherence were suboptimal, with patients making their own decisions about continuing with the offered treatment. Also the available forms of PS failed to form an integral part of the treatment process. Finally, collaboration between PC and specialist care failed to form genuine steps in the intensity of treatment).

Conflict of interest

The authors have no conflicts of interest to report.

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References

- American Psychiatric Association (APA), 2010. Practice Guideline for the Treatment of Patients with Major Depressive Disorder. psychiatryonline.org.
- Andrews, G., Cuijpers, P., Craske, M.G., McEvoy, P., Titov, N., 2010. Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PLoS One* 5, e13196.
- Bambauer, K.Z., Soumerai, S.B., Adams, A.S., Zhang, F., Ross-Degnan, D., 2007. Provider and patient characteristics associated with antidepressant nonadherence: the impact of provider specialty. *J. Clin. Psychiatry* 68, 867–873.
- Beck, A.T., Ward, C., Mendelson, M., Mock, J., Erbaugh, J., 1961. An inventory for measuring depression. *Arch. Gen. Psychiatry* 4, 561–571.
- Beck, A.T., Epstein, N., Brown, G., Steer, R.A., 1988. An inventory for measuring clinical anxiety: psychometric properties. *J. Consult. Clin. Psychol.* 56, 893–897.
- Bee, P.E., Bower, P., Lovell, K., Gilbody, S., Richards, D., Gask, L., Roach, P., 2008. Psychotherapy mediated by remote communication technologies: a meta-analytic review. *BMC Psychiatry* 8, 60–244X–8–60.
- Blumenthal, J.A., Burg, M.M., Barefoot, J., Williams, R.B., Haney, T., Zimet, G., 1987. Social support, type A behavior, and coronary artery disease. *Psychosom. Med.* 49, 331–340.
- Bower, P., Richards, D., Lovell, K., 2001. The clinical and cost-effectiveness of self-help treatments for anxiety and depressive disorders in primary care: a systematic review. *Br. J. Gen. Pract.* 51, 838–845.
- Bull, S.A., Hu, X.H., Hunkeler, E.M., Lee, J.Y., Ming, E.E., Markson, L.E., Fireman, B., 2002. Discontinuation of use and switching of antidepressants: influence of patient-physician communication. *J. Am. Med. Assoc.* 288, 1403–1409.
- Chong, W.W., Aslani, P., Chen, T.F., 2011. Effectiveness of interventions to improve antidepressant medication adherence: a systematic review. *Int. J. Clin. Pract.* 65, 954–975.
- Clark, D.M., 2011. Implementing NICE guidelines for the psychological treatment of depression and anxiety disorders: the IAPT experience. *Int. Rev. Psychiatry* 23, 318–327.
- Cleare, A., Pariante, C.M., Young, A.H., 2015. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association. *J. Psychopharmacol. (Oxf. Engl.)* 29, 459–525.
- Coventry, P.A., Hudson, J.L., Kontopantelis, E., Archer, J., Richards, D.A., Gilbody, S., Lovell, K., Dickens, C., Gask, L., Waheed, W., Bower, P., 2014. Characteristics of effective collaborative care for treatment of depression: a systematic review and meta-regression of 74 randomised controlled trials. *PLoS One* 9, e108114.
- Coyne, J.C., Klinkman, M.S., Gallo, S.M., Schwenk, T.L., 1997. Short-term outcomes of detected and undetected depressed primary care patients and depressed psychiatric patients. *Gen. Hosp. Psychiatry* 19, 333–343.
- Cuijpers, P., van Straten, A., van Oppen, P., Andersson, G., 2008. Are psychological and pharmacologic interventions equally effective in the treatment of adult depressive disorders? A meta-analysis of comparative studies. *J. Clin. Psychiatry*, 1839–1841.
- Cuijpers, P., van Straten, A., van Schaik, A., Andersson, G., 2009. Psychological treatment of depression in primary care: a meta-analysis. *Br. J. Gen. Pract.* 59, e51–e60.
- Cuijpers, P., Andersson, G., Donker, T., van Straten, A., 2011. Psychological treatment of depression: results of a series of meta-analyses. *Nord. J. Psychiatry* 65, 354–364.
- Demyttenaere, K., 2003. Risk factors and predictors of compliance in depression. *Eur. Neuropsychopharmacol.* 13 (Suppl 3), S69–S75.
- Edlund, M.J., Fortney, J.C., Reaves, C.M., Pyne, J.M., Mittal, D., 2008. Beliefs about depression and depression treatment among depressed veterans. *Med. Care* 46, 581–589.
- M.B., First, M., Gibbon, R.L., Spitzer, J.B.W., Williams, L.S., Benjamin, 1997. Structured Clinical Interview for DSM-IV Axis I Personality Disorders, (SCID-I).
- M.B., First, R.L., Spitzer, M., Gibbon, J.B.W., Williams, 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition with Psychotic Screen.
- Firth, N., Barkham, M., Kelleth, S., 2015. The clinical effectiveness of stepped care

- systems for depression in working age adults: a systematic review. *J. Affect. Disord.* 170, 119–130.
- Gabilondo, A., Rojas-Farreras, S., Rodriguez, A., Fernandez, A., Pinto-Meza, A., Vilagut, G., Haro, J.M., Alonso, J., 2011. Use of primary and specialized mental health care for a major depressive episode in Spain by ESEMeD respondents. *Psychiatr. Serv.* 62, 152–161.
- Gilchrist, G., Gunn, J., 2007. Observational studies of depression in primary care: what do we know? *BMC Fam. Pract.* 8, 28.
- Goldman, H.H., Skodol, A.E., Lave, T.R., 1992. Revising axis V for DSM-IV: a review of measures of social functioning. *Am. J. Psychiatry* 149, 1148–1156.
- Gusmao, R., Quintao, S., McDaid, D., Arensman, E., Van Audenhove, C., Coffey, C., Varnik, A., Varnik, P., Coyne, J., Hegerl, U., 2013. Antidepressant utilization and suicide in Europe: an ecological multi-national study. *PLoS One* 8, e66455.
- Hamalainen, J., Isometsa, E., Laukkala, T., Kaprio, J., Poikolainen, K., Heikkinen, M., Lindeman, S., Aro, H., 2004. Use of health services for major depressive episode in Finland. *J. Affect. Disord.* 79, 105–112.
- Hamalainen, J., Isometsa, E., Sihvo, S., Kiviruusu, O., Pirkola, S., Lonnqvist, J., 2009. Treatment of major depressive disorder in the Finnish general population. *Depress Anxiety* 26, 1049–1059.
- Hamilton, M., 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry* 23, 56–62.
- Hunot, V.M., Horne, R., Leese, M.N., Churchill, R.C., 2007. A cohort study of adherence to antidepressants in primary care: the influence of antidepressant concerns and treatment preferences. *Prim. Care Companion J. Clin. Psychiatry* 9, 91–99.
- Johnson, J.G., Cohen, P., Kasen, S., Brook, J.S., 2005. Personality disorder traits associated with risk for unipolar depression during middle adulthood. *Psychiatry Res.* 136, 113–121.
- Katon, W., Von Korff, M., Lin, E., Walker, E., Simon, G.E., Bush, T., Robinson, P., Russo, J., 1995. Collaborative management to achieve treatment guidelines. Impact on depression in primary care. *J. Am. Med. Assoc.* 273, 1026–1031.
- Katon, W., Robinson, P., Von Korff, M., Lin, E., Bush, T., Ludman, E., Simon, G., Walker, E., 1996. A multifaceted intervention to improve treatment of depression in primary care. *Arch. Gen. Psychiatry* 53, 924–932.
- Kennedy, S.H., Lam, R.W., Parikh, S.V., Patten, S.B., Ravindran, A.V., 2009. Canadian Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. Introduction. *J. Affect. Disord.* 117 (Suppl 1), S1–S2.
- Kessler, R.C., Berglund, P., Demler, O., Jin, R., Koretz, D., Merikangas, K.R., Rush, A.J., Walters, E.E., Wang, P.S., National Comorbidity Survey Replication, 2003. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *J. Am. Med. Assoc.* 289, 3095–3105.
- Klinkman, M.S., Buroth, S., Fedewa, S., Kerber, K., Kuebler, J., Adman, T., Sen, A., 2010. Long-term clinical outcomes of care management for chronically depressed primary care patients: a report from the depression in primary care project. *Ann. Fam. Med.* 8, 387–396.
- Leitlinien, N., 2015. S3-Guideline/NVL Unipolar Depression.
- Limosin, F., Loze, J.Y., Zylberman-Bouhassira, M., Schmidt, M.E., Perrin, E., Rouillon, F., 2004. The course of depressive illness in general practice. *Can. J. Psychiatry* 49, 119–123.
- Lin, E.H., Von Korff, M., Katon, W., Bush, T., Simon, G.E., Walker, E., Robinson, P., 1995. The role of the primary care physician in patients' adherence to antidepressant therapy. *Med. Care* 33, 67–74.
- Lin, E.H., Katon, W.J., Simon, G.E., Von Korff, M., Bush, T.M., Walker, E.A., Unutzer, J., Ludman, E.J., 2000. Low-intensity treatment of depression in primary care: is it problematic? *Gen. Hosp. Psychiatry* 22, 78–83.
- Lynch, J., Moore, M., Moss-Morris, R., Kendrick, T., 2011. Are patient beliefs important in determining adherence to treatment and outcome for depression? Development of the beliefs about depression questionnaire. *J. Affect. Disord.* 133, 29–41.
- Maddox, J.C., Levi, M., Thompson, C., 1994. The compliance with antidepressants in general practice. *J. Psychopharmacol.* 8, 48–52.
- Mattisson, C., Bogren, M., Horstmann, V., Tambs, K., Munk-Jorgensen, P., Nettelbladt, P., 2009. Risk factors for depressive disorders in the Lundby cohort—a 50 year prospective clinical follow-up. *J. Affect. Disord.* 113, 203–215.
- Melartin, T.K., Rytsala, H.J., Leskela, U.S., Lestela-Mielonen, P.S., Sokero, T.P., Isometsa, E.T., 2004. Severity and comorbidity predict episode duration and recurrence of DSM-IV major depressive disorder. *J. Clin. Psychiatry* 65, 810–819.
- Melartin, T.K., Rytsala, H.J., Leskela, U.S., Lestela-Mielonen, P.S., Sokero, T.P., Isometsa, E.T., 2005. Continuity is the main challenge in treating major depressive disorder in psychiatric care. *J. Clin. Psychiatry* 66, 220–227.
- Morey, E., Thacher, J.A., Craighead, W.E., 2007. Patient preferences for depression treatment programs and willingness to pay for treatment. *J. Ment. Health Policy Econ.* 10, 73–85.
- National Board of Health and Welfare, 2010. National Guidelines for Care in cases of Depression and Anxiety Disorders. 2010.
- NICE, 2010. Depression: The NICE Guideline on the Treatment and Management of Depression In Adults (Updated edition).
- Nutting, P.A., Rost, K., Dickinson, M., Werner, J.J., Dickinson, P., Smith, J.L., Gallovic, B., 2002. Barriers to initiating depression treatment in primary care practice. *J. Gen. Intern. Med.* 17, 103–111.
- Raue, P.J., Schulberg, H.C., Heo, M., Klimstra, S., Bruce, M.L., 2009. Patients' depression treatment preferences and initiation, adherence, and outcome: a randomized primary care study. *Psychiatr. Serv.* 60, 337–343.
- Richards, D.A., Borglin, G., 2011. Implementation of psychological therapies for anxiety and depression in routine practice: two year prospective cohort study. *J. Affect. Disord.* 133, 51–60.
- Ronalds, C., Creed, F., Stone, K., Webb, S., Tomenson, B., 1997. Outcome of anxiety and depressive disorders in primary care. *Br. J. Psychiatry* 171, 427–433.
- Rost, K., Williams, C., Wherry, J., Smith Jr, G.R., 1995. The process and outcomes of care for major depression in rural family practice settings. *J. Rural Health* 11, 114–121.
- Rost, K., Zhang, M., Fortney, J., Smith, J., Coyne, J., Smith Jr, G.R., 1998. Persistently poor outcomes of undetected major depression in primary care. *Gen. Hosp. Psychiatry* 20, 12–20.
- Sighinolfi, C., Nespeca, C., Menchetti, M., Levantesi, P., Belvederi Murri, M., Berardi, D., 2014. Collaborative care for depression in European countries: a systematic review and meta-analysis. *J. Psychosom. Res.* 77, 247–263.
- Sikorski, C., Lupp, M., Konig, H.H., van den Bussche, H., Riedel-Heller, S.G., 2012. Does GP training in depression care affect patient outcome? - A systematic review and meta-analysis. *BMC Health Serv. Res.* 12, 10–6963–12–10.
- Simon, G.E., VonKorff, M., Wagner, E.H., Barlow, W., 1993. Patterns of anti-depressant use in community practice. *Gen. Hosp. Psychiatry* 15, 399–408.
- Simon, G.E., Von Korff, M., Rutter, C.M., Peterson, D.A., 2001. Treatment process and outcomes for managed care patients receiving new antidepressant prescriptions from psychiatrists and primary care physicians. *Arch. Gen. Psychiatry* 58, 395–401.
- Simon, G.E., Fleck, M., Lucas, R., Bushnell, D.M., (LIDO Group), 2004. Prevalence and predictors of depression treatment in an international primary care study. *Am. J. Psychiatry* 161, 1626–1634.
- Spitzer, R.L., Williams, J.B., Kroenke, K., Linzer, M., deGruy 3rd, F.V., Hahn, S.R., Brody, D., Johnson, J.G., 1994. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. *J. Am. Med. Assoc.* 272, 1749–1756.
- The Finnish Medical Society Duodecim and Finnish Psychiatric Association, 2014. Current Care Guideline (Käypä hoito -suositus): Depressio. Suomalaisen Lääkäriseuran Duodecimin ja Suomen Psykiatriyhdistys Ry:n asettama työryhmä.
- Thombs, B.D., Coyne, J.C., Cuijpers, P., de Jonge, P., Gilbody, S., Ioannidis, J.P., Johnson, B.T., Patten, S.B., Turner, E.H., Ziegelstein, R.C., 2012. Rethinking recommendations for screening for depression in primary care. *Can. Med. Assoc. J.* 184, 413–418.
- Thompson, C., Kinmonth, A.L., Stevens, L., Peveler, R.C., Stevens, A., Ostler, K.J., Pickering, R.M., Baker, N.G., Henson, A., Preece, J., Cooper, D., Campbell, M.J., 2000a. Effects of a clinical-practice guideline and practice-based education on detection and outcome of depression in primary care: Hampshire Depression Project randomised controlled trial. *Lancet* 355, 185–191.
- Thompson, C., Peveler, R.C., Stephenson, D., McKendrick, J., 2000b. Compliance with antidepressant medication in the treatment of major depressive disorder in primary care: a randomized comparison of fluoxetine and a tricyclic antidepressant. *Am. J. Psychiatry* 157, 338–343.
- Thompson, C., Ostler, K., Peveler, R.C., Baker, N., Kinmonth, A.L., 2001. Dimensional perspective on the recognition of depressive symptoms in primary care: The Hampshire Depression Project 3. *Br. J. Psychiatry* 179, 317–323.
- Thota, A.B., Sipe, T.A., Byard, G.J., Zometa, C.S., Hahn, R.A., McKnight-Eily, L.R., Chapman, D.P., Abraido-Lanza, A.F., Pearson, J.L., Anderson, C.W., Gelenberg, A.J., Hennessy, K.D., Duffy, F.F., Vernon-Smile, M.E., Nease Jr, D.E., Williams, S.P., 2012. Community Preventive Services Task Force, 2012. Collaborative care to improve the management of depressive disorders: a community guide systematic review and meta-analysis. *Am. J. Prev. Med.* 42, 525–538.
- van Schaik, D.J., Klijn, A.F., van Hout, H.P., van Marwijk, H.W., Beekman, A.T., de Haan, M., van Dyck, R., 2004. Patients' preferences in the treatment of depressive disorder in primary care. *Gen. Hosp. Psychiatry* 26, 184–189.
- Van Voorhees, B.W., Cooper, L.A., Rost, K.M., Nutting, P., Rubenstein, L.V., Meredith, L., Wang, N.Y., Ford, D.E., 2003. Primary care patients with depression are less accepting of treatment than those seen by mental health specialists. *J. Gen. Intern. Med.* 18, 991–1000.
- Van Voorhees, B.W., Fogel, J., Houston, T.K., Cooper, L.A., Wang, N.Y., Ford, D.E., 2005. Beliefs and attitudes associated with the intention to not accept the diagnosis of depression among young adults. *Ann. Fam. Med.* 3, 38–46.
- Vuorilehto, M., Melartin, T., Isometsa, E., 2005. Depressive disorders in primary care: recurrent, chronic, and co-morbid. *Psychol. Med.* 35, 673–682.
- Vuorilehto, M.S., Melartin, T.K., Rytsala, H.J., Isometsa, E.T., 2007. Do characteristics of patients with major depressive disorder differ between primary and psychiatric care? *Psychol. Med.* 37, 893–904.
- Vuorilehto, M.S., Melartin, T.K., Isometsa, E.T., 2009. Course and outcome of depressive disorders in primary care: a prospective 18-month study. *Psychol. Med.* 39, 1697–1707.
- Wang, P.S., Lane, M., Olfson, M., Pincus, H.A., Wells, K.B., Kessler, R.C., 2005. Twelve-month use of mental health services in the United States: results from the National Comorbidity Survey Replication. *Arch. Gen. Psychiatry* 62, 629–640.
- Wells, K.B., Sherbourne, C.D., 1999. Functioning and utility for current health of patients with depression or chronic medical conditions in managed, primary care practices. *Arch. Gen. Psychiatry* 56, 897–904.
- Wittchen, H.U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jonsson, B., Olesen, J., Allgulander, C., Alonso, J., Faravelli, C., Fratiglioni, L., Jennum, P., Lieb, R., Maercker, A., van Os, J., Preisig, M., Salvadori-Cardulla, L., Simon, R., Steinhausen, H.C., 2011. The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur. Neuropsychopharmacol.* 21, 655–679.