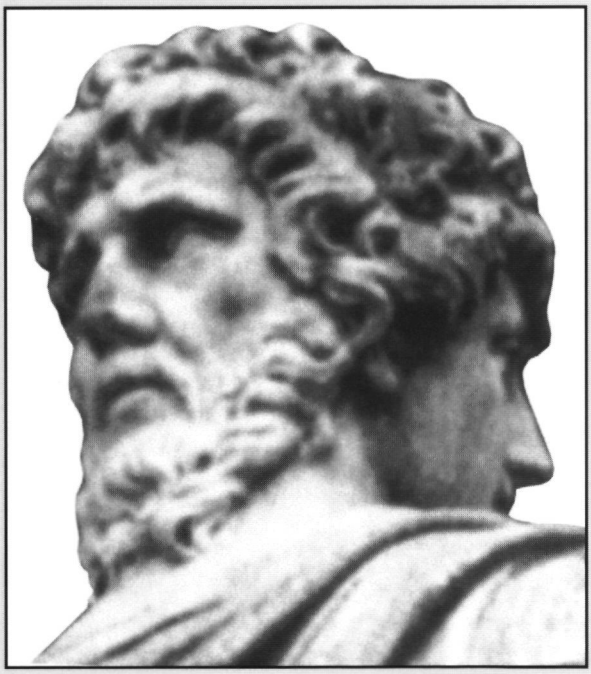
Depression: the long-term perspective

A follow-up study in General Practice



E.M. van Weel-Baumgarten

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Evelyn van Weel-Baumgarten

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Manuscriptcommissie:	Prof. dr. ir. G.A. Zielhuis, voorzitter Prof. dr. C.M.A. Hosman Prof. Sir Denis Pereira Gray, University of Exeter

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Chapter 1

General introduction

BACKGROUND

In every-day general practice one often wonders about the prognosis of depression Some patients have a poor prognosis They present with severe symptoms, suffer a great deal over a long period of time, and have many recurrences or develop a chronic depression On the other hand, every general practitioner also has many patients who pull through severe episodes relatively quickly, sometimes even without medical treatment These patients seem to be functioning quite well again after a while This is in contrast with the current opinion about depression This opinion is based on results of the many studies concerning depression These studies, of which most have been performed with patients referred to psychiatry (only a small part of the depressed population), show that the prognosis is poor [1 7] This is particularly true for patients who have been hospitalised, over 80% of these patients have recurrences [8 9] But if this poor prognosis is also true in general practice is not clear In discussing the long-term outcome of depression there are several issues to consider

Many studies show that depression has a high prevalence and serious, sometimes even life-threatening morbidity [10 13] It causes functional disability and high economic costs as a result [14 16] As the illness has a high prevalence in the general population, a poor prognosis is a matter of concern This is one of the reasons why campaigns have been started to increase the awareness of depression and to draw attention to the importance of detection and treatment [17 18] This implicates that detection and treatment lead to a better outcome, which so far has not been demonstrated in general practice populations [19]

General practitioners are often criticised for their share in poor detection and treatment As far as the diagnosis is concerned there are two main issues, the validity (specificity) and the sensitivity of the diagnosis The validity of the diagnosis of depression made in general practice is not clear, nor are the proportions of minor and major depression in these populations Concerning the sensitivity, many papers show that in general practice the diagnosis is frequently missed [20 25] When patients present with somatic or functional complaints a diagnosis of depression is not always

evident.[26] In particular when patients present frequently with this kind of symptoms and they vary over time, the process of making a diagnosis of depression might take some time and sometimes the diagnosis is overlooked. If the prognosis of these undetected or mislabelled cases is poor, there is reason for concern.

This brings us to the relation between treatment and long-term outcome of depression. General practitioners are often criticised for not treating depressed patients as recommended in current guidelines,[27-29] implying that this guideline concurrent treatment would lead to a better long-term outcome in general practice.[30] So far this relation is much less clear than in selected patients referred to psychiatry. However, to be able to offer good care to every patient with depression, knowledge about the relation between treatment and outcome in these populations is indispensable.

The very long-term perspective is even less clear in general practice. Many studies show that patients with depression have high psychopathology and disability levels during episodes[14] and that with treatment symptoms decrease,[31] and health status improves.[32] If they remain well long-term, and if not presenting with recurrences also means that functioning and wellbeing are unimpaired, is not clear at all.

In this study we tried to find answers to the questions about the diagnosis and a number of aspects of long-term outcome in primary care. How do matters stand with the diagnosis of depression made by general practitioners? Is the long-term outcome of depression as poor in general practice as in psychiatry? How are patients with depression treated in general practice and how is treatment related to the long-term outcome?

THE STUDY

To answer these questions a study was designed consisting of four distinct parts. All patient data in the first three parts of the study were collected through the Continuous Morbidity Registry (CMR) of the University of Nijmegen.[33] This is a unique registry started in 1967 by the late Prof. Dr. Frans Huygen in his single handed practice. In 1971 the registry was extended to three other practices. Since then all morbidity is recorded on an ongoing basis in these four general practices to which the number of

about 12.000 patients have constantly been registered. Criteria for diagnosis are used (a Dutch version of the E-list criteria initially, since 1984 the criteria of the ICHPPC-2 defined)[34,35] and doctors are trained in the use of the classification list and application of criteria. Monthly meetings are held to discuss coding problems and monitor the application of diagnostic criteria. Additional and detailed information is available on the patient's records and can be studied in the practices in which the patient is or was registered.[33] The registry is used for studies on morbidity and morbidity trends on a broad variety of illness, physical as well as mental.[36]

The first part was a historic cohort study. Here we tried to find answers to the question, if the long-term outcome of depression in general practice is as poor in general practice as in psychiatry, and if there is a relation with the prescribed treatment. The population for this part of the study consisted of 222 general practice patients from the registry, classified with a code for depression before 1984, who could be followed up on the records for a full 10 years after the diagnosis of depression was made for the first time. The follow-up concerned recurrences, referral, admission to hospital, suicide attempts and treatment.

The second part of the study was designed to answer the questions about the diagnosis of depression made by general practitioners. With this aim a new study population was selected, consisting of patients from the CMR, equally divided among three categories: patients with depression, controls without a mental disorder and patients with Chronic Nervous Functional Complaints (CNFC) (all diagnoses between October 1996 and Oktober 1997). This population was interviewed with the Composite International Diagnostic Interview (CIDI) -12 month auto version-, which classifies according to criteria of the Diagnostic and Statistical Manual of mental disorders (DSM).[37,38] With this version of the CIDI, diagnoses of current mental illness and that of the previous 12 months are made. Because of the hypothesis that depression is overlooked in patients with varying functional complaints, the patients with CNFC were included in this study population. This is a 'diagnosis' used in the CMR for patients repeatedly presenting with varying functional complaints. It is made when

there is no physical illness and the general practitioner has strong indications that there is a psychosocial or functional basis for the complaints.[39,40]

In the third part of the study we tried to establish if patients with a history of depression had remained well long-term, and if not presenting with recurrences meant, that their functioning and well-being was unimpaired. With this aim, questionnaires were used collecting data about psychopathology, health status, coping behaviour, and social support. The population for this part of the study consisted of all patients with a history of depression from our original historic cohort, who were still registered with the practices and capable of communicating. Their first diagnosis of depression was by then at least 15 years ago. We included equal numbers of normal controls and patients with CNFC from the same practices in this study population. This last group (possibly including a number of undetected cases of depression) was included to study if and how they differed from patients with a history of depression and from normal controls.

The fourth part of the study was a systematic review of the literature. A search of the literature at the start of our study in 1995 had not revealed many studies with long-term outcome data from general practice. We decided to try a more systematic approach and include community studies in the review. Our motivation was that we wanted long-term outcome data of the full spectrum of depression, cases in the community, which had not been identified by any doctor, included. We decided to review studies with a follow-up of at least five years with data about rates of recurrence, depression and health status at follow-up. In these studies we also searched for a relation between long-term outcome and treatment.

OUTLINE OF THE THESIS

Chapter 2 describes the recurrence rates, the number and length of the episodes, referrals, hospitalisation and suicide attempts of the 10 year follow-up of the historic cohort of 222 patients with a diagnosis of depression from the CMR-practices (first study population). Chapter 3 includes a description of the treatment received by the same patients. A description is given of all treatment these patients received during

the follow-up of ten-years. The results of the comparison of first episodes of patients with and without recurrences are also presented and discussed in this chapter.

In chapter 4 results are presented about the validity of the diagnosis of depression made by the general practitioners of the CMR practices and of the accordance with the official criteria of the DSM-IV. This chapter also presents the depression rate, according to DSM-IV criteria, found in the controls and patients with the CNFC. All data in this chapter refer to the second study population.

In chapter 5 results are presented of the comparison of current psychopathology, health status, coping behaviour, and social support of patients with a history of depression (at least 15 years ago) and controls. A distinction is made between patients with and without recurrences.

Chapter 6 also describes results about psychopathology, health status, coping behaviour and social support but in this chapter the attention is focussed on the comparison of patients with CNFC with controls, and with patients with a history of depression. The presented results in chapter 5 and 6 refer to the third study population.

Chapter 7 contains the systematic review of the literature.

Chapter 8 provides a summary and general discussion in English, with recommendations for future study and consequences for general practice.

Chapter 9 contains this summary and general discussion in Dutch.

The quotations between the chapters are from the files with additional information, collected during the patient interviews in the second part of the study (chapter 4).

REFERENCES

1. Angst J. The course of affective disorders. *Psychopathology* 1986,**19(Suppl 2)**:47-52.
2. Burrows GD. Long-term clinical management of depressive disorders. *J Clin Psychiatry* 1992;**53(Suppl)**:32-5
3. Coryell W, Turvey C, Endicott J, et al. Bipolar I affective disorder: predictors of outcome after 15 years. *J Affect Disord* 1998;**50**:109-16.
4 Keller MB. Depression: a long-term illness. *Br J Psychiatry* 1994;Suppl:9-15
5 Kessing LV, Andersen PK, Mortensen PB, et al Recurrence in affective disorder. I. Case register study. *Br J Psychiatry* 1998;**172**:23-8.
6 Paykel ES. Remission and residual symptomatology in major depression. *Psychopathology* 1998;**31**:5-14.
7 Londen L van, Molenaar RP, Goekoop JG, et al. Three- to 5-year prospective follow-up of outcome in major depression. *Psychol Med* 1998;**28**:731-5
8. Angst J, Preisig M. Course of a clinical cohort of unipolar, bipolar and schizoaffective patients: Results of a prospective study from 1959 to 1985. *Schweiz Archiv Neurol Psychiatr* 1995,**146**:5-16.
9. Piccinelli M, Wilkinson G. Outcome of depression in psychiatric settings. *Br J Psychiatry* 1994;**164**:297-304.
10 Williams JW, Kerber CA, Mulrow CD, et al. Depressive disorders in primary care: prevalence, functional disability, and identification *J Gen Intern Med* 1995;**10**:7-12.
11 Froom J, Aoyama H, Hermoni D, et al Depressive disorders in three primary care populations: United States, Israel, Japan. *Fam Pract* 1995;**12**:274-8.
12. Ormel J, van den BW, van der MK, et al. [Prevalence, indication and course of depression in family practice] Prevalentie, signalering en beloop van depressie in de huisartspraktijk. *Ned Tijdschr Geneeskd* 1994;**138**:123-6.
13. Zung WW, Broadhead WE, Roth ME. Prevalence of depressive symptoms in primary care. *J Fam Pract* 1993;**37**:337-44.
14. How disabling is depression? Evidence from a primary care sample. The Counselling Versus Antidepressants In Primary Care Study Group. *Br J Gen Pract* 1999;**49**:95-8.
15 Katon W, Schulberg H. Epidemiology of depression in primary care *Gen Hosp Psychiatry* 1992;**14**:237-47
16 Wells KB, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients. Results from the Medical Outcomes Study *JAMA* 1989;**262**:914-9
17 O'Hara MW, Gorman LL, Wright EJ. Description and evaluation of the Iowa Depression Awareness, Recognition, and Treatment Program. *Am J Psychiatry* 1996;**153**.645-9.

18. Paykel ES, Tylee A, Wright A, et al. The Defeat Depression Campaign. psychiatry in the public arena. *Am J Psychiatry* 1997;**154**:59-65.

19. Edwards JG. Long term pharmacotherapy of depression Can reduce relapses and recurrences in major depression. *Br Med J* 1998;**316**:1180-1

20. Karlsson H, Lehtinen V, Joukamaa M. Psychiatric morbidity among frequent attender patients in primary care. *Gen Hosp Psychiatry* 1995;**17**·19-25.

21. Wright AF. Should general practitioners be testing for depression? *Br J Gen Pract* 1994;**44**:132-5.

22. Ormel J, Koeter MW, van den BW, et al. Recognition, management, and course of anxiety and depression in general practice. *Arch Gen Psychiatry* 1991,**48** 700-6.

23. Kessler D, Lloyd K, Lewis G, et al. Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. *Br Med J* 1999,**318** 436-9.

24. Freeling P, Rao BM, Paykel ES, et al. Unrecognised depression in general practice. *Br Med J Clin Res Ed* 1985;**290**:1880-3

25. Tylee A, Freeling P, Kerry S, et al. How does the content of consultations affect the recognition by general practitioners of major depression in women? *Br J Gen Pract* 1995;**45**:575-8

26. Gulbrandsen P, Fugelli P, Hjortdahl P. Psychosocial problems presented by patients with somatic reasons for encounter: tip of the iceberg? *Fam Pract* 1998;**15**:1-8.

27. Donoghue JM, Tylee A. The treatment of depression. prescribing patterns of antidepressants in primary care in the UK. *Br J Psychiatry* 1996,**168**.164-8.

28. Rosholm JU, Gram LF, Damsbo N, et al. Antidepressant treatment in general practice--an interview study. *Scand J Prim Health Care* 1995;**13**:281-6.

29. Olfson M, Klerman GL. The treatment of depression· prescribing practices of primary care physicians and psychiatrists. *J Fam Pract* 1992;**35**:627-35.

30. Johnson DA Treatment of depression in general practice. *Br Med J* 1973;**2**:18-20.

31. Agosti V, Stewart JW, Quitkin FM, et al How symptomatic do depressed patients remain after benefiting from medication treatment? *Compr Psychiatry* 1993,**34** 182-6.

32. Coulehan JL, Schulberg HC, Block MR, et al. Treating depressed primary care patients improves their physical, mental, and social functioning. *Arch Intern Med* 1997,**157**.1113-20.

33. Weel C van. Validating long term morbidity recording. *J Epidemiol Community Health* 1995;**49(Suppl 1)**:29-32

34. Hodgkin K. *Towards earlier diagnosis in primary care* 2 ed Edinburgh. Chrchill Livingstone; 1966

35. Classification committee of WONCA. *ICHPPC-2-defined (International classification of Health Problems in Primary Care)*. third ed. Oxford: Oxford University Press; 1983

36 Lisdonk EH van de, Weel C van. New referrals, a decreasing phenomenon in 1971-94: analysis of registry data in the Netherlands. *Br Med J* 1996;**313**:602.

37. Andrews G, Peters L The psychometric properties of the Composite International Diagnostic Interview *Soc Psychiatry Psychiatr Epidemiol* 1998;**33**:80-8.

38 Practice guideline for major depressive disorder in adults. American Psychiatric Association. *Am J Psychiatry* 1993,**150**:1-26.

39. Huygen FJ, Hoogen HJ van den, Logt AT van de, et al. [Psychophysiologic disorder in general practice. I. An epidemiologic study] Nerveus-functionele klachten in de huisartsenpraktijk. I Een epidemiologisch onderzoek. *Ned Tijdschr Geneeskd* 1984;**128**:1321-7.

40. Huygen FJ, Hoogen HJ van den, Logt AT van de, et al. [Psychophysiologic disorders in general practice. II. Diagnostic and therapeutic management] Nerveus-functionele klachten in de huisartsenpraktijk II. Diagnostisch en therapeutisch beleid. *Ned Tijdschr Geneeskd* 1984;**128**.1372-6.

'Zeven jaar terug ben ik voor het eerst zwaar depressief geweest. Niks interesseerde me meer en ik had ook een boel andere klachten. Ik ben er zelfs drie maanden voor opgenomen geweest in een herstellingsoord.
Daar kreeg ik medicijnen en psychotherapie en zo ben ik er doorheen gekomen.
Zover zal het nooit weer komen, want ik weet nu dat ik leuke dingen met gaan doen als ik het voel aankomen.
Het afgelopen jaar heb ik het toch weer terug gehad en dat heeft toch ook weer 5 maanden geduurd. Dat kwam door een conflict op het werk, denk ik. Maar toch ben ik niet zo diep weggezakt als de vorige keer. Dat heb ik geleerd. Ik had toch wel weer het gevoel dat ik medicijnen nodig had ter ondersteuning. Na zo'n week of 4 tot 5 merkte ik dat het beter ging.
Nu ben ik weer aan het werk. Ik heb een hele leuke nieuwe baan en dat helpt me er ook meteen overheen, en andere leuke dingen ook.'

'Seven years ago I had my first fit of depression. I wasn't interested in anything anymore, and I had many other problems as well. I was even admitted to a clinic for it.
There I was treated with drugs and psychotherapy, and that helped me pull through.
It will never be that bad again, because I know now, that I must go and do things I enjoy, when I feel it coming on again.
But anyway, this past year it did happen again, and it went on for 5 months.
I think it was probably problems at work that started it off again.
But it wasn't as bad as the first time. I have learnt from that. But I knew I needed medication again. I got better after about 4 or 5 weeks. Now I am back at work. I have a very nice new job and that's really helped me to get over it, and there have been other nice things as well.'

Chapter 2

Ten year follow-up of depression after diagnosis in general practice

E.M. van Weel-Baumgarten

W.J.H.M. van den Bosch

H.J.M. van den Hoogen

F.G. Zitman

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SUMMARY

Background. Depression is a serious illness with a high recurrence rate, mortality, and suicide rate, and a substantial loss of quality of life. Long-term course of depression, in particular of patients not referred to specialist care, is not completely clear. We performed a study in which the course of depression in general practice was studied for 10 years after the first diagnosis.

Aim. To learn more about long-term course and outcome of patients with depressive illness for a full 10 years after diagnosis.

Method. A historic cohort study with 386 patients classified as depressive before January 1984, recruited from four general practices belonging to the Continuous Morbidity Registry of the University of Nijmegen in The Netherlands. This cohort was followed-up for 10 years. Mortality was compared with a control group matched for age, sex, social class, and practice. Of 222 patients out of this cohort who could be followed up for a full 10 years after diagnosis, the case records were studied in detail.

Results. No statistically significant difference was found in mortality between the 386 patients and the control group. Recurrence of depressive episodes did not occur in about 60% of the 222 patients (confidence interval 54% to 67%). Of the depressive patients, 15% were referred to secondary care and 9% were admitted to hospital.

Conclusion. Mortality, suicide, and recurrence rate were lower than expected, taking into account what is known from depression studies in psychiatry. These results stress the importance of long-term prospective follow-up studies of all patients with depression because of the emphasis on case-finding and treatment without exact knowledge of long-term course and outcome of patients who were not referred.

INTRODUCTION

Depression is a serious, potentially life-threatening illness with symptoms that can be severe and persistent and have a great impact on quality of life.[1,2] Most studies on course and outcome of depression have been performed with selected patients referred to secondary care. This research indicates that patients with depressive illness have a poor prognosis. Depression tends to recur, and this tendency increases as patients have more episodes. Mortality and suicide rate are high and the effectiveness of antidepressant drugs diminishes when the illness recurs more often.[3-7] Currently, emphasis is very much on detection and treatment, even though course and outcome of depressive illness is not clear for all patients. To learn more about this long-term course and outcome we followed 222 patients with depressive illness for a full 10 years after diagnosis.

METHOD

The data were collected from the Continuous Morbidity Registry (CMR) of the department of General Practice and Social Medicine of the University of Nijmegen.[8,9] It is a network of four practices in the Nijmegen region that records all morbidity on an ongoing basis since 1971. Together these practices constantly have a practice list of about 12 000 patients. In each practice, no more than one change of doctor has taken place in more than 25 years of CMR. Because, in the Dutch system, the general practitioner has a defined list of patients and is gate-keeper of access to specialist medical care, long-term data are available for nearly all patients, including diagnoses after referral. In the CMR, the following data are recorded: sex, age, social class, and diagnosis of all new episodes of illness (from 1967 to 1984 according to criteria for classification of the Dutch translation of the British E-list[10] since 1984 according to ICHPPC-2 criteria[11]). When a diagnosis is changed after referral, the code is corrected retrospectively. Additional information is available on the patient's records, which can be studied in detail in the practices in which the patient is or was registered.

All patients classified with a code for depressive illness (ICHPPC-2 code for depressive disorder or affective psychosis) before 1 January 1984, were recruited

from the CMR. If patients could not be followed up for 10 years we noted the reasons and the patients were excluded. From the standard registration, mortality and suicide rates were analysed. Patients were compared with a control group matched for age, sex, social class, and practice. To answer questions about recurrence, referral, admission to hospital, and suicide attempts, the case records were studied in detail in the practices. First, age, sex, and social class (based on the occupational index of the Institute for Applied Sociology[9]) at the time depressive illness was diagnosed for the first time, were collected from the standard CMR. Of the patients who, at the time of the case record review were still listed with the CMR-practices (1995-1996), the following data were collected from the case records.

The number and length of each episode of depressive illness

The first or index episode started on the day a diagnosis of depressive illness was made for the first time. It ended on the day the end of the depression was written in the patient's case records. If this statement could not be found in the records as confirmation, the date was noted on which no depressive symptoms (sadness, loss of interest, indecisiveness, forgetfulness, loss of self confidence, feelings of excessive guilt, suicidal thoughts, psychomotor agitation or retardation, loss of energy and fatigue, insomnia or hypersomnia, poor or increased appetite with weight loss or gain, loss of libido) had been written in the case records for a full three months. A recurrent episode of depression was defined as an episode with a renewed code for, or description of, symptoms of depressive illness after at least three months without any description of such symptoms. The end of a new episode is defined in the same way as the end of the index episode.

The number and type of referral, admission to hospital and the number of suicide attempts

These data were collected, as well as the time of all these events in the first 10 years after depression was first diagnosed. Patient confidentiality was guaranteed by anonymous processing of data: the standard CMR data were analysed on a patient

unique number (only traceable in the practice), and the patient identification had been blinded for the review of the case records.

Statistical analysis

Survival curves were calculated with the product-limit method. Differences between survival curves were tested with the log-rank test. Differences between groups were tested with chi-squared statistics. Confidence intervals (all 95%) were calculated using the binomial distribution; for calculation of the confidence interval of the suicide attempts, the poison distribution was used.

RESULTS

Patient characteristics

The cohort of depressive patients consisted of 386 patients, 61% women and 39% men. Of these patients 58% belong to the lower classes, 36% to the middle and 6% to the high social class (total CMR-population = 46% low, 41% middle and 13% high social class). At the time of the review of case records 107 of these 386 patients had left the practices; of whom, six patients were admitted to a psychiatric hospital or nursing home. Significantly fewer patients diagnosed with depression had left the practices compared to the total CMR-population ($P<0.001$). Forty-six patients had died, 41 of natural and 5 of unnatural causes, including two patients who had committed suicide (two suicides in over 6382 patient-years). For one patient, cause of death could not be traced. Comparison of this mortality with that in the control group, though a little higher, showed no statistically significant difference. Since 1971, in the entire CMR population, 13 suicides have been registered (13 suicides in 285 008 patient-years).

There remained 233 patients. Of that group, 11 had to be excluded for administrative related reasons and not depression related ones, leaving 222 patients for the review of the case records.

There was no significant difference in sex and social class between the initial 386 and the 222 remaining patients. The distribution of age did show a statistically significant

difference. As can be seen in Table 2.1, the percentage of patients over 65 years in the sample of 222 is seven, while in the original cohort this was 14%.

Table 2.1. Distribution of age of 222 patients diagnosed with depressive illness in general practice.

Age	Number of patients	Percentage
0-<25	15	7
25-<45	96	43
45-<65	96	43
65-<75	11	5
75+	4	2

Recurrence rate of depressive episodes

In 134 (60%) patients, only one episode of depression had occurred in the 10 years of follow-up, while 12% had more than three episodes. Table 2.2 shows the distribution of the number of depressive episodes of these 222 patients. There was no significant difference between men and women and between the social classes. Mean duration of the first episode was 103 days (range= 14-1266 days). In 11 (5%) patients, this first episode lasted longer than one year. The distribution of the length of the first episode can be seen in Table 2.3.

Table 2.2. Number of episodes with depressive illness (number of patients = 222)

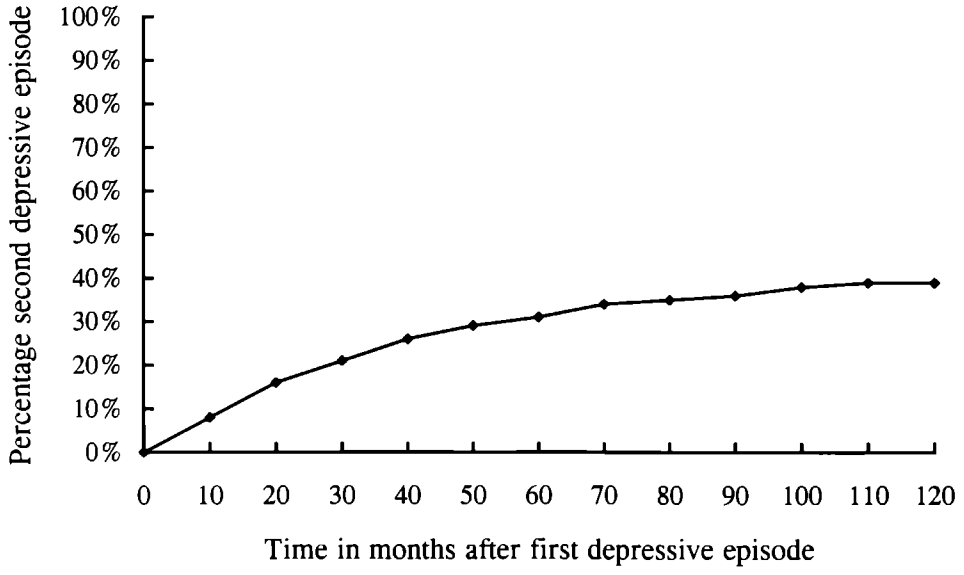
number of episodes	percentage of patients
1	60
2	16
3	12
4	5
5	4
>6	3

Table 2.3. Length of first depressive episode in months (number of patients with depressive illness = 222)

Length in months	number of patients	percentage of patients
0-1	76	34
2-3	71	32
4-6	37	17
7-12	27	12
>12	11	5

As can be seen in Figure 2.1, for half of the patients with more than one episode (88), the interval between first and second depressive episode was two years or less. The same interval was found between second and third episode.

Figure 2.1. Second depressive episode related to time in months after first episode (total number of patients = 222).



Referrals, admission to hospital, and suicide attempts

Forty (18%) patients were referred during their first episode: 28 (12%) to secondary care (23 to a psychiatrist and 5 to a neurologist) and 15 (7%) patients within primary

care (eight to a psychologist, four to a social worker, and three to the ambulatory psychiatric care); three patients being referred within primary care as well as to secondary care.

During following episodes of depression, another five (2%) patients who had not been referred in their first episode were referred to secondary care and 18 (8%) were referred within primary care. Overall, a referral for secondary care was found in 15% of the patients and for primary care this was also 15%. No statistically significant difference was found in referral rate during the first episode of depression of patients with only one episode compared with patients with two or more episodes of depression.

Twelve (5%) patients (confidence interval 2.8% - 9.3%) were admitted to hospital for their depression during their first episode, eight to a general hospital, and four to a psychiatric hospital. The mean length of the admission was 9.7 weeks (range 1-43 weeks). During further episodes, another eight patients were admitted to hospital who had not been admitted during their first episode.

Ten suicide attempts (confidence interval 4.8 – 18.4) were recorded (in 2220 patient-years); six patients made a suicide attempt once and two patients twice. In the entire CMR population, during the whole registration-period (285 008 patient-years), another 118 suicide attempts have been registered.

Discussion

More than 60% of the 222 patients with recognised depression followed up in general practice for as long as 10 years did not have any recurrence of depressive episodes during this period of time. If patients had more than one episode, recurrence occurred relatively shortly after diagnosis. From research published by Angst in 1992,[13] it can be concluded that only 20% of all patients with depression have no recurrence at all.

Available general practice studies show a broad variation in outcome, but are difficult to compare because of differences in method (in particular, of recruitment of patients), definition of 'caseness' and length of follow-up.[14-18]

It is difficult to predict outcome of depression in general practice with any amount of certainty. One of the reasons is that outcome depends largely on the initial diagnosis,

particularly on validity and severity of this diagnosis.[19] The following arguments support our results on outcome, even though, in a study design like ours, the diagnosis can not be assessed retrospectively.

- Though general practitioners possibly miss a large proportion of cases of depression found with screening instruments, they rarely make false positive diagnoses.[20]
- Criteria for diagnosis were used consistently in the CMR practices (E-list, ICHPPC-2) at a time when DSM criteria were not introduced yet. All general practitioners belonging to the CMR practices are trained in the use of the classification list and application of criteria, and monthly meetings are held to discuss coding problems and to monitor the application of diagnostic criteria.
- The chance of detection increases with a longer follow-up and, in the CMR, patients are followed continuously for a very long time. This reduces the chance of a missed diagnosis to a very great extent. If a patient is finally diagnosed with depressive illness, that has gone undetected for a period of time, the previous codes are corrected retrospectively.
- A high validity of morbidity recording in the CMR could be demonstrated in other cases.[9]

Our results on recurrence refer to recognized cases of depression in general practice. They show that the course of illness over the first 10 years after the diagnosis is milder than of selected patients studied in psychiatry.

At the start of the study, the decision was made to include only patients of whom the case records could be studied for the full 10 years. This selection could have introduced a bias. Reasons for this bias could be differences in mortality, suicide rate, and admission to psychiatric hospital between the original (386 patients) and the study population (222 patients). A higher recurrence rate in the age group over 65 could also have introduced a bias because of the lower percentage of the older patients in the case record study.

Mortality and suicide rate were studied in the entire cohort. Though mortality of the patients with depressive illness was a little higher than in a matched control group, no statistically significant difference was found between the two groups. Two suicides

were recorded in the entire cohort of 386 patients in a follow-up of 6382 patient-years (for this calculation, not only the 10-year follow-up after diagnosis was taken into account, but also the longest possible follow-up period of these patients). This suicide-rate, though higher than in the total CMR-population, is still much lower than the 7 to 20% of depressive patients reported in psychiatric literature.[5,13]

The six patients admitted to a psychiatric hospital or nursing home could not have been responsible for a significant higher recurrence rate.

Recurrence rate was not related to age, so the lower percentage of older patients in our case record study cannot cause any bias.

The difference between patients from general practice and patients in (psychiatric) specialist care are usually explained by the fact that only the most 'severe' cases registered by the general practitioner are referred to a psychiatrist, and therefore it is no surprise that their prognosis is poorer than in non-referred cases. In our cohort, 15 % of the depressive patients have been referred to secondary care, and only a small percentage were ever admitted to hospital for their depression.

The referral rate we found during the first episode of patients with only one depressive episode was the same as the referral rate in patients with more episodes, which does not support the hypothesis that only the more severe cases are referred.

The suicide (attempt) rate, which is lower than in psychiatric studies but higher than in the general population, also points to the potential severity of the condition of our patients.

Is the severity by itself the most important reason for referral, and does it determine the course of the illness, or is it the combination of severity with other characteristics? Personality, coping behaviour and (a lack of) social support, for example, are probably also important in this respect.

CONCLUSION

From these study-results, it can be concluded that in general practice many patients with depressive illness do not have any recurrence of depressive episodes in 10 years follow-up. Mortality and suicide risk are lower than in patients receiving psychiatric

care. Since, in this study, 60% of all patients did not have any recurrence in the follow-up, it seems justified to conclude that many of the patients diagnosed as depressive can be helped very well by their general practitioner within primary care, without the need for referral to secondary care. If conclusions about (necessity of) treatment are based largely on studies performed with referred patients, these should not automatically be generalized to patients who have not been referred.

More research is needed of the factors that determine the long-term outcome of depression.

REFERENCES

1 Hays RD, Wells KB, Donald Sherbourne C, et al. Functioning and well-being outcomes of patients with depression compared with chronic general medical illnesses. *Arch Gen Psychiatry* 1995;**52:**11-9

2. Wright AF. *Depression. Recognition and management in general practice.* [RCGP Clinical Series.] London: The Royal College of General Practitioners, 1993.

3. Angst J. The course of affective disorders. *Psychopathology* 1986,**19(2):**47-52.

4. Coryell W, Zimmerman M, Pfohl B. Short-term prognosis in primary and secondary major depression. *J Aff Dis* 1985;**9:**265-70

5. Kiloh LG, Andrews G, Neilson M. The long-term outcome of depressive illness. *Br J Psychiatry* 1988;**153:**752-7.

6. Nystrom S. Depressions Factors related to 10-year prognosis *Acta Psychiatr Scand* 1979;**60:**225-38.

7. Post RM, Roy-Byrne PP, Uhde ThW Graphic representation of the life course of Illness in patients with affective disorder *Am J Psychiatry* 1988;**145(7):**844-8

8. Weel C van. Chronic diseases in general practice: the longitudinal dimension. *Eur J of Gen Pract* 1996;**2(1):**17-21.

9. Weel C van. Validating long term morbidity recording. *Journ of Epidemiol and Commun Health* 1995;**49:**355-8.

10. Hodgkin K. *Towards earlier diagnosis in primary care* (2nd edn.) Edinburgh, London, and New York: Churchill Livingstone, 1966.

11. Classification committee of World Organisation of National Colleges, Academies and Academic Associations of general practitioners/Family Physicians. ICHPPC-2-Defined. *Inclusion criteria for the use of the rubrics of the International Classification of Health Problems in Primary Care.* Oxford: Oxford University Press, 1983.

12. Lisdonk EH van de, Weel C van. New referrals, a decreasing phenomenon in 1971-94. analysis of registry data in the Netherlands. *Br Med J* 1996,**313:**602

13. Angst J. How recurrent and predictable is depressive illness? *Perspectives in psychiatry* 1992,**3:**1-30

14. Parker G, Holmes S, Manicavasagar V Depression in General Practice Attenders. 'caseness', natural History and predictors of outcome *J Aff Dis* 1986;**10:**27-35

15. Tiemens BG, Ormel J, Simon GE. Occurrence, recognition and outcome of psychological disorders in primary care. *Am J Psychiatry* 1996;**153(5):**636-44

16. Dowrick Ch, Buchan I. Twelve month outcome of depression in general practice· does detection or disclosure make a difference? *Br Med J* 1995;**311:**1274-76

17 Blacker CVR, Clare AW Depressive disorder in general practice *Br J Psychiatry* 1987,**150:**737-51

18 Murphy JM, Olivier DC, Sobol AM, et al Diagnosis and outcome depression and anxiety in a general population *Psychol Med* 1986,**16:**117-26

19 Jablensky A Prediction of the course and outcome of depression *Psychol Med* 1987,**17:**1-9

20 Wright AF Should general practitioners be testing for depression? *Br J of Gen Pract* 1994,**44:**132-5

'Nee, het is echt nooit meer terug gekomen. Ik heb veel geleerd van die keer.
Twee jaar geleden kreeg ik kanker. Maar ik werd niet depressief. Het gaat nu ook goed met mij lichamelijk. En ik heb nu een nieuwe, fijne relatie, voor het eerst na al die jaren, lukt ook dat weer. Veertien dagen geleden is zijn vader overleden. Ik ben wel verdrietig, maar gewoon zoals erbij hoort, dat soorten dingen gebeuren nu eenmaal.
Ik werk parttime en dat gaat ook goed.
Ook de zorg voor mijn kinderen kan ik goed aan.'

'No really, it never came back. I have learned a lot from that episode.
Two years ago I got cancer. But I didn't get depressed. I am well now,
physically as well. I am in a new relationship, which for the first time for years, is working out really well.
A fortnight ago his father died. I am sad, but only in a normal way, these things happen.
I work part-time and that's working well.
I am also coping with looking after my two children.'

Chapter 3

Treatment of depression related to recurrence: 10-year follow-up in general practice

E.M. van Weel-Baumgarten

W.J.H.M. van den Bosch

Y.A. Hekster

H.J.M. van den Hoogen

F.G. Zitman

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SUMMARY

Objectives. To study outcomes related to long-term treatment of depression and differences in treatments for first episodes of depression in patients with and without recurrences.

Methods. A historic cohort design study with 222 general practice patients who had been followed up for 10 years after being diagnosed of depression. Prescriptions for antidepressants, psychotropics and references over the period of 10 years following the first diagnosis of depression were studied.

Results. Over the 10-year period, the length of the treatment with antidepressants and the doses prescribed were low compared to what is known to be efficacious in depression. This was also true for treatment during the first episode. Patients with a recurrent type of illness were more often treated with antidepressants and other psychotropics during their first episode than patients with only one episode of depression, but they were not referred any more often.

Conclusions. Even though treatment was not as recommended for depression, the majority of the patients did not have recurrences. Future prospective research is needed to study causal relationships between treatment of depression and long-term outcome.

INTRODUCTION

From literature we know that in general practice, patients with depression often do not get the treatment regarded as therapeutic. Most studies have shown that if antidepressants are prescribed at all, the doses are often too low and the length of the prescriptions too short when compared with what is recommended for depression.[1-4] However, we do not know how patients with depression are treated long-term and the exact relationship between lack of 'adequate medication' and long-term outcome is not clear, particularly in primary care.[5] In a study we performed on course and long-term outcome of depression in general practice, 60% of the patients did not have any recurrence in a follow-up of 10 years after the first diagnosis.[6] Medication and referrals were items that had been checked during the data collection for this study. Therefore, it was possible with the same database to describe all treatment during this 10-year period. The treatment during the first episode of depression was studied with the following questions in mind: how frequently had antidepressants been prescribed? Were dosage and length of treatment prescribed 'adequate' and could differences in treatment of the first episode be found between patients with one, two or more than two episodes of depression?

MATERIAL AND METHODS

Database

The material for this study was collected from the Continuous Morbidity Registry (CMR) of the Department of General Practice and Social Medicine of the University of Nijmegen.[7,8] It is a network of four practices (total of 12 000 patients) in the Nijmegen region, in which all morbidity is recorded on an ongoing basis since 1971. The following demographics are recorded: age, gender, and social class. Diagnoses of all new episodes of illness are registered according to the criteria of the International Classification of Health Problems in Primary Care (ICHPPC-2) (until 1984 according to the criteria for classification of the Dutch translation of the British E-list).[9,10] Although the diagnosis of depression of the patients in this study could not be assessed retrospectively, a recent study showed a high accordance of the diagnosis

of depression by general practitioners in the CMR with the criteria of Major Depressive Disorder (MDD) in psychiatry.[11] Because in the Dutch health care system the general practitioner has a fixed list of patients and is also gate-keeper of access to specialist medical-care, long-term data are available for nearly all patients and it is possible to study treatment related to outcome over a long period of time.

Patient data

For the study on long-term course and outcome of depression mentioned earlier, the charts of 222 patients coded with a first depression (ICHPPC-2 criteria) before 1984 had been studied in detail in the practices. Table 3.1 shows age, gender and social class of the 222 patients, who could be followed up for 10 years starting on the day that the diagnosis of depression was made for the first time. Table 3.2 shows the distribution of the number of depressive episodes of these 222 patients over the10-year follow-up period. In 134 patients (60% of 222) only one episode of depression had occurred in the 10 years of follow-up, while 12% had more than three episodes. For the medication study, 10 full years on the charts were screened for prescriptions with antidepressants and other psychotropic drugs starting on the date of first diagnosis of depression. Referrals within primary care and to secondary care were also registered.

Table 3.1. Demographics of the 222 patients coded for depression

Age	< 45	50%
	45-64	43%
	> 65	6%
Gender	Male	39%
	Female	61%
Social class	Low	63%
	Middle	32%
	High	4%

Table 3.2. Number of episodes with depressive illness. Number of patients = 222

Number of episodes	Percentage of patients
1	60
2	16
3	12
4	5
5	4
> 6	3

Drug data: classification, unit of comparison and episodes

Antidepressant drugs were registered according to the Anatomical Therapeutical Classification methodology as recommended by the WHO Drug Utilization Research Group.[12] As unit of comparison the ratio of Prescribed Daily Dose to Defined Daily Dose (PDD/DDD) was used.[13] To compare the effect of drugs a measure of equipotency must be determined. Therefore all daily doses were standardized by using the PDD, the dose prescribed by the physician for the individual patient. The PDD equals the actual daily dose. The DDD is the assumed average effective daily dose for the drug used for its main indication in adults and is expressed in amount of the active substance. DDD values are assigned by the World Health Organisation (WHO) Collaborating Centre for Drugs Statistics Methodology and Nordic Council on medicines and are published in *Guidelines for Daily Doses*, a publication based on dose documentations per drug as prepared by WHO Oslo, based on international textbooks, journals and documentation approved by drug control authorities. These documentations are available on request from Oslo. Table 3.3 shows the published DDD of antidepressants prescribed to the patients in our study.

A medication-episode was defined as an uninterrupted period with antidepressant medication. Changes in type or dose of the antidepressant drug are allowed in such a medication-episode. The rationale for summating PDD/DDD ratios for different antidepressants is found in the definition of DDD as the average maintenance dose of a particular drug for its main indication in adults.

In these practices a 'first-prescription' was never given for more than 2 weeks, as is the rule nowadays in The Netherlands. Antidepressant medication is not effective within such a short time. Therefore, if only one prescription had been registered on the chart without a clear definition of the length this was considered by us as no medication-episode.

Table 3.3. DDD for antidepressants as published by WHO, 1996[12]

Antidepressants	**DDD (mg)**
Tricyclic derivates	
Desipramine	100
Imipramine	100
Imipramine oxide	100
Clomopramin	100
Opipramol	150
Trimipramine	150
Lofepramine	105
Dibenzepin	300
Amitriptyline	75
Nortriptyline	75
Protriptyline	30
Doxepin	30
Butriptyline	75
Dosulepin	150
Tetracyclic derivates	
Maprotiline	100
Mianserin	60
Modified cyclic derivates	
Nomifensine	150
Trazodone	300

DDD, defined daily dose; WHO, World Health Organisation

Prescriptions for other psychotropic drugs were registered as follows: if they had been prescribed, the type and frequency of the prescription was recorded. A distinction was made between just incidentally (not more than two prescriptions a year), chronically (for more than 6 months a year), or in between.

The first episode of all patients was studied in detail to see if differences could be found in treatment between those patients who eventually had only one, two or more than two episodes of depression.

Statistical analysis

Differences between groups are tested with Chi square (χ^2) statistics and χ^2 for linear trends. The differences in length and ratio of antidepressant medication between the patients with and without recurrent illness were calculated with the Wilcoxon test.

RESULTS

Long-term treatment with antidepressants, other psychotropic medication and referrals.

A total of 441 medication-episodes with antidepressants had been registered on the patient charts during the 10-year follow-up period (148 during the first episode). The doctor's notes allowed the assessment of length of treatment in 80% and dosage in 54% of these medication-episodes (of the first episode 84% and 62%). Sixty-two (28%) patients did not have a medication-episode. Almost all of these patients belonged to the group who had only one episode of depression (57 of 62). Of the 88 patients with recurrences, 94% received prescriptions for antidepressants sometime during the 10-year follow-up period.

The tricyclic antidepressants amitriptyline and imipramine were prescribed most frequently. New generation antidepressant medications did not appear during our study period. Of the 222 patients, 12 received medication with lithium in addition to their medication with antidepressants. Twenty-four percent of the registered medication-episodes for antidepressants were shorter than 28 days, 21% of these episodes had a length of more than 6 months. PDD/DDD ratios were low, 78% of these ratio's had a value of less than 1.

A total of 191 patients (86% of 222) received one or more prescriptions for other psychotropic drugs at a certain point during the 10-year follow-up period, mainly benzodiazepines (175 patients, 79% at least one prescription for a benzodiazepine).

Twenty-six of the 134 patients with single episode depression and five of the 88 patients with recurrent depression never received prescriptions with other psychotropic medication during the 10-year follow-up (19% and 6%, respectively). This difference was significant (P = 0.004).

Other psychotropic drugs were prescribed mostly during the year following the first diagnosis of depression (in 78% of the 222 patients). After this the percentage dropped, but in every subsequent year around 35% of the patients received at least one prescription for these drugs. Thirty-four patients (15%) were referred to secondary care (psychiatrist, neurologist), and 19 patients (9%) within primary care (psychologist, social worker or ambulatory psychiatric care facility).

Relationship between treatment during first episode and recurrence

To compare the management of first episodes of depression, the 222 patients were divided into three categories: patients who during the first 10 years after the diagnosis had experienced just one (n = 134), two (n = 36) or more than two (n = 52) episodes of depression. No significant differences were found in patient demographics between the categories in age, gender and social class. Treatment during the first episode was different for the three categories. Patients who later had recurrences had received more treatment. Table 3.4 shows the differences in treatment between the three categories. A significant trend in treatment approach could be found. Of the 134 patients who did not have any recurrence of depression, 67 (50%) received antidepressant medication during their first and only episode of depression. For the category with two episodes this was 26 (72%) and for the category with more than two episodes 41 (79%). Doses and length of the prescriptions with antidepressants were low, with no significant differences between the three categories. For other psychotropic drugs the percentages in the three groups were 62%, 69% and 79%, respectively. The combination of antidepressants and other psychotropics in the first year after diagnosis also showed a significant trend. Although higher for patients with more episodes, the differences were not significant for referral and other combinations.

Table 3.4. Treatment during first depressive episode related to number of depressive episodes. Percentages of treated patients per episode.

	Number of episodes (number of patients)			
	1 (n = 134)	2 (n = 36)	>2 (n = 52)	Significance (P)
Antidepressants*	50	72	79	<0.001
Psychotropics in first year*	62	69	79	0.03
Referral	16	17	23	0.3
Antidepressants + psychotropics*	33	56	63	<0.001
Antidepressant + referral	9	14	17	0.1
Psychotropics + referral	12	17	21	0.1
Antidepressants + psychotropics+referral	13	14	17	0.07

Referral = referral to primary or secondary care
* significant with Chi square for linear trend

DISCUSSION

The results of this study are consistent with those of other studies, which show that patients prescriptions for antidepressants were for shorter and smaller doses than recommended in guidelines.[14,15] We found differences in treatment of the first episode of depression in patients with one, two or more than two episodes of depression. Although more patients who later had recurrences received prescriptions with antidepressants during their first episode than patients without recurrences, the doses were also low and length of the medication episodes short, with no significant differences between the categories. We also found high prescription rates for minor tranquillisers, mostly benzodiazepines, just as in other studies, for example, a study with depressed outpatients.[16] Although sleep disturbance and comorbidity with anxiety could have been reasons for prescribing this kind of medication, this was not mentioned consistently on the patient records, nor could we find other reasons for the 'lack of adequate medication'. Even though the treatment was 'inadequate by psychiatric standard' the majority of the patients in our study had a favourable outcome without recurrences. With this study design we could not establish a causal relationship between treatment and the outcome. Our results do offer support for a view that depression in primary care may be different from depression seen in psychiatry and may require a different treatment.[17] As has been pointed out in other studies, a diagnosis does not necessarily mean a need for treatment.[18] Even when a diagnosis of Major Depressive Disorder has been made, spontaneous recovery should be considered for a number of cases in general practice and watchful waiting could prove worthwhile. At least one study has demonstrated that patients in general practice receiving antidepressant treatment as recommended in guidelines had higher rates of relapse than those receiving no therapy.[19] Others found patients receiving either placebo or active intervention in mild to moderately severe MDD responding equally.[20] Our results point in the same direction for long-term outcome, no adequate treatment and a low recurrence rate. It could also mean, as has been suggested in other studies, that perhaps antidepressants in a lower dose and with a shorter length of prescriptions are effective for a number of patients with depression in general practice.[21-23]

The strength of this study is the long follow-up period of 10 years and the possibility of relating treatment to outcome. However, a causal relationship cannot be established from our results. Another limitation of this study is that the data on the charts concerning length and doses of the prescriptions for antidepressants were not complete. Even though bias in information recording and retrieval was unlikely, it is still possible and care is required in drawing conclusions from these data. The fact that the results in our study only concern prescriptions with tricyclics could lead to the comment that the value of our conclusions are limited and the results do not reflect the progress made with selective serotonin reuptake inhibitors (SSRIs). There were two obvious reasons for the fact that our results only concern tricyclics: the study period (first depressive episode before 1985) and the fact that in the Dutch guidelines for depression published in 1994, tricyclics are still antidepressants of first choice.[15] Though SSRIs are used more and more frequently, a number of patients still receive prescriptions for tricyclics and for this group our conclusions are still valid. The questions we raised about appropriate treatment for depression in general practice will have to be answered for treatment with SSRIs as well. Lack of knowledge about the severity of the depression, comorbidity and of other confounders is a limitation of this study that should also be mentioned. Finally an aspect that was not taken into account in most studies, including ours, but that should be remembered when discussing treatment related to outcome, is the fact that prescribing medication does not necessarily mean that patients really use these drugs. A study[24] on primary non-compliance with prescribed medication in primary care shows that the percentage of non-redemption of prescriptions is high (14.5%). This should be kept in mind when discussing the results of treatment and should be considered in future studies. Prospective studies concerning long-term course and outcome of depression in general practice, relating treatment to outcome and taking into account other confounders are necessary so that sounder recommendations for treatment of depression in general practice can be made.

REFERENCES

1. Johnson DAW. Treatment of depression in general practice. *Br Med J* 1973;**2:**18-20.
2. Donoghue JM, Tylee A. The treatment of depression: Prescribing patterns of antidepressants in primary care in the U.K. *British Journal of Psychiatry* 1996,**168:**164-8
3. Roshom J-U, Gram LF, Damsbo N, Hallas J. Antidepressant treatment in general practice - An interview study. *Scandinavian Journal of Primary Health Care* 1995;**13**:281-6.
4. Olfson M, Klerman GL. The treatment of depression: prescribing practices of primary care physicians and psychiatrists. *J Fam Pract* 1992,**35**.627-53.
5. Edwards JG Long term pharmacotherapy of depression can reduce relapses and recurrences in major depression. *Br Med J* 1998;**318**:1180-1.
6. Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG. 10-Year Follow-up of depression after diagnosis in General Practice. *Br J Gen Pract* 1998;**48**:1643-1646.
7. Weel C van. Chronic diseases in general practice the longitudinal dimension. *Eur J Gen Pract* 1996;**2**:17-21.
8. Weel C van Validating long-term morbidity recording *J Epid Comm Health,* 1995;**49**:355-8.
9. Hodgkin K. *Towards earlier diagnosis in primary care* 2nd edition. 1966 Edinburgh: Churchill Livingstone, 170-172 and 183-184
10. Classification committee of World Organisation of National Colleges, Academies and Academic Associations of general practitioners/Family Physicians. ICHPPC-2-Defined. (1983) *International Classification of Health Problems in Primary Care*. Oxford: Oxford University Press.
11. Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG. The validity of the diagnosis of depression in General Practice. is using criteria for diagnosis as a routine the answer? *Br J Gen Pract* 2000;**50:**284-7.
12. WHO Collaborating Center for Drugs Statistics Methodology. 1996 *Guidelines for ATC classification and DDD assignment* 1st edn. Oslo WHO/NCM.
13. Lammers MW, Hekster YA, Meinardi H, Renier WO, Lier H van. Monotherapy or polytherapy for epilepsy revisited. A quantitative assessment. *Epilepsia* 199;**36**.440-6.
14. BMA and Pharmaceutical Society of Great Britain (1992) *British National Formulary*. London: BMA and Pharmaceutical Press.
15. NHG. Guideline on depression. *Huisarts en wetenschap* 1994,**11** 482-90.
16. Wells KB, Katon W, Rogers B, Camp P. Use of minor tranquillizers and antidepressant medications by depressed outpatients. results from medical outcomes study. *Am J Psych* 1994;**151**·694-700

17. Klinkman MS, Schwenk TL, Coyne JC. Depression in primary care – more like asthma than appendicitis: the Michigan Depression Project. *Can J Psych* 1997;**42**:966-73.

18. Spitzer RL. Diagnosis and need for treatment are not the same. *Arch Gen Psych* 1998;**55**:120.

19. Rost K, Zhang M, Fortney J, et al. Persistent poor outcomes of undetected major depression in primary care: implications for intervention. *Gen Hosp Psych* 1998;**20**:12-20.

20 Elkin I, Shea MT, Watkins JT, Imber SD, Sotsky SM. National Institute of Mental Health. Treatment of depression collaborative program: general effectiveness of treatments. *Arch Gen Psych* 1989;**46**:971-82.

21 Thompson C, Thompson CM. The prescribing of antidepressants in General practice. II: A placebo-controlled trial of low dose dothiepin. *Human Psychopharmacology* 1989;**4**:191-204

22. Wernicke JF, Dunlop SR, Dornseif BE, Bosomworth JC, Humbert M. Low dose Fluoxetine therapy for depression. *Psychopharmacology Bulletin* 1988;**24**:183-8.

23. Tan RSH, Barlow RJ, Abel C, et al. The effect of low dose lofepramine in depressed elderly patients in general medical wards. *Br J Clin Pharm* 1994;**37**.321-4

24. Beardon PHG, McGilchrist MM, McKendrick AD, McDevitt DG, MacDonald TM. Primary non-compliance with prescribed medication in primary care. *Br Med J* 1993;**307**:846-8.

'Ik was zo somber, had nergens interesse in. Ik sliep ook heel slecht. Ik werd steeds veel te vroeg wakker. Wat voelde ik me waardeloos. Ja schuldgevoel, dat had ik ook en inderdaad ook concentratieproblemen. Wat was ik moe en apathisch.
Maar ja, wat wil je, met zo'n huwelijk. Mishandeling, verkrachting en ook opsluiting. Uiteindelijk ben ik gescheiden. Maar ook toen werd ik nog belaagd door mijn ex-man en ben zelfs zwanger geraakt. Ik heb toen een abortus ondergaan.
Na de scheiding begon ik pas echt last te krijgen, psychisch. Via de huisarts ben ik bij het RIAGG terecht gekomen. Dat klikte niet, dus daar ben ik niet gebleven. Uiteindelijk ben ik naar een paragnost gegaan. Die man heeft me anders leren denken en dat heeft wèl geholpen.
Ik heb nooit medicijnen gehad, daar bewust voor gekozen, samen met mijn huisarts en afgesproken dat ik altijd nog medicijnen kon krijgen. Daar ben ik nog steeds blij mee, vooral ook dat het zo gelukt is! Het is ook nooit meer terug gekomen. Ook het zorgen voor mijn kinderen heeft me er door heen geholpen. En mijn ouders, die hebben mij echt gesteund.'

'I was so depressed, nothing interested me anymore. I had difficulty sleeping. I woke up much too early every day. I felt so worthless. Yes, I also felt very guilty and had problems concentrating. I was so tired and listless....
But what could one expect in a marriage like that. Abuse, rape and often being locked up. Eventually I got divorced. But even then I was still abused by my ex-husband, I even got pregnant. I decided to have an abortion. After the divorce the mental problems really started. My GP sent me to a primary care mental health clinic, but I didn't get on with the psychologist, so I didn't stay. Finally I went to a healer. He taught me to think differently and that really did help. I never took any pills, but that was a deliberate decision I took with my doctor. I could still ask for them if I wanted to. I am still really pleased that I managed without them! The symptoms have never come back.
Having my children to look after really helped me through. And my parents were very supportive.'

Chapter 4

The validity of the diagnosis of depression in general practice: is using criteria for diagnosis as a routine the answer?

E.M. van Weel-Baumgarten

W.J.H.M. van den Bosch

H.J.M. van den Hoogen

F.G. Zitman

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SUMMARY

Background. In general practice, making a diagnosis does not follow the same lines as in secondary care because every new diagnosis is made against 'foreknowledge' and could be coloured by it. This could explain low accordance and differences in diagnoses between primary and secondary care, in particular when mental illness such as depression is concerned. When criteria are used for diagnosis there should be no differences.

Aim. To establish the accordance with Diagnostic and Statistical Manual of mental disorders, 4th edition (DSM-IV) criteria of major depressive disorder when the diagnosis of depression has been made by general practitioners (GPs) for whom coding and using criteria for diagnosis is a daily routine (ICHPPC-2 criteria).

Method. Ninety-nine general practice patients from four general practices belonging to the Continuous Morbidity Registry (CMR) of the University of Nijmegen in The Netherlands were interviewed using the Composite International Diagnostic Interview (auto) 12-month version (DSM-IV criteria). Thirty-three patients had a code for depression; 33 patients a code for chronic nervous functional complaints (CNFC); and 33 had no code for mental illness (the depression and CNFC codes were given in the 12 months prior to the interview). Specificity and accordance with the DSM-IV criteria of major depressive disorder (MDD) were calculated with the results from the interviews.

Results. Of the 33 general practice depression cases (all matching ICHPPC-2 criteria), 28 matched DSM-IV criteria: 26 for MDD and 2 for dysthymia. No cases of DSM-IV MDD were found in the control group without a code for a mental disorder and seven out of 33 were found in the control group with the code for CNFC.

Conclusion. The specificity of diagnosis of depression made by GPs in a continuous morbidity registry and the accordance with DSM-IV criteria are high. Using criteria for diagnosis, which is a trend, could be one of the solutions towards a better diagnosis. As far as the sensitivity is concerned, GPs should not be distracted from using criteria for the diagnosis of depression when a large variety of complaints is presented.

INTRODUCTION

Making a diagnosis in general practice is not the same process as in secondary care. The general practitioner (GP) knows about the patient's background and history, and views the present symptoms against what he/she already knows. From all this, the GP filters the symptoms and either attributes them to a diagnosis already made sometime earlier or makes a new diagnosis. In secondary care, the specialist focuses more on actual symptoms for which the patient has been referred than on previous complaints, history, and context.

These two situations seem like two different worlds, and it is not so surprising that this can lead to a low accordance between diagnoses in primary and secondary care, in particular when mental illness is concerned. When patients present a mixture of many physical as well as mental complaints, we know this filtering and attributing of symptoms to be even more complex. In the literature, these topics of low accordance, low specificity of the diagnosis of depression, and low sensitivity in general practice are discussed in various ways.[1-9] We do not know if this difference in accordance between diagnoses is also found when criteria for diagnosis are used. Does it make a difference to the specificity and the sensitivity of the diagnosis if GPs are used to coding and, therefore, already routinely use criteria for diagnosis? A high validity of diagnoses could be demonstrated for various somatic diagnoses in a general practice morbidity registry, but does this apply for diagnoses of mental illness as well?[10]

Our aim was to study the specificity of the diagnosis of depression made by GPs in a morbidity registry and the accordance with the diagnosis of major depressive disorder (MDD) according to the criteria of the Diagnostic and Statistical Manual of mental disorders, 4th edition (DSM-IV).[11] In the process of doing this we hoped to get some data on the sensitivity as well.

In the Continuous Morbidity Registry (CMR) when patients present a large variety of physical complaints for a certain length of time, with no evident explanation for these complaints by a somatic disease and when no specific code for a mental illness is appropriate, a code is used, called chronic nervous functional complaints (CNFC). By

including patients from this category in our study, we hoped to shed some light on where and why cases of depression are overlooked.

METHOD

A study was designed in which the diagnosis of depression that had been coded in the year before was validated with the Composite International Diagnostic Interview (CIDI) in a recent cohort of patients from the CMR of the Department of General Practice and Social Medicine of the University of Nijmegen in The Netherlands.[12,13] We checked the diagnosis of depression, which in the CMR nowadays is made according to the inclusion criteria for the use of the rubrics of the International Classification of Health Problems in Primary Care (ICHPPC-2), against the criteria of MDD.[14]

Patients and database

The patients for this study were selected from the CMR of the Department of General Practice and Social Medicine of the University of Nijmegen, The Netherlands. The GPs of this registry receive a general training in using the classification list and to learn to apply ICHPPC-2 criteria for all diagnoses in general practice. Monthly meetings are held to discuss coding problems and monitor the application of diagnostic criteria.

Starting from the assumption that about 90% of the patients coded with depression in general practice would also have a depression according to the criteria of the DSM-IV, power calculation showed that, with a total of 35 patients interviewed in the depressive group, percentages of accordance could be estimated with a confidence interval (CI) of $\pm$ 10% (Chronbach's a = 0.05). In the group with the nervous functional complaints, the CI is $\pm$ 15% (Chronbach's a = 0.05), with the assumption that no more than 20% of the patients would have a depression. We estimated that, by inviting all patients in the registry with a new code for depression between October 1996 and October 1997, we would have roughly this number of patients. A new code for depression could either be a first diagnosis or a new episode of depression. Further inclusion criteria were that patients must be aged 18 years or over and capable of communicating. Patients meeting these criteria were invited by their GP to be interviewed. For every patient consenting

to the interview, two controls matched for age, sex, social class, and practice were randomly selected by the registry - one without any code for a mental illness, the other with a code in that same year for CNFC - and were also invited by their GP for interview.

Table 4.1. Criteria for depression according to ICHPPC-2, and for major depression and dysthymia according to DSM-IV.

	ICHPPC-2 defined depression	**DSM-IV MDD**	**DSM-IV Dysthymia**
Number of required symptoms	**≥3**	**≥ 5**	**≥3**
Core symptoms			
Depressed mood	+	+[a]	+[a]
Decrease in interest	+	+[a]	-
Suicidal thoughts	+	+	+
Indecisiveness	+	+	+
Worthlessness/sense of guilt	+	+	+
Insomnia/morning tiredness	+	+	+
Anxiety/irritablility	+	-	-
Psychomotor agitation	+	+	-
Psychomotor retardation	-	+	-
Hypersomnia	-	+	+
Change in appetite/weight	-	+	+
Loss of energy	-	+	+
Concentration problems	-	+	-
Loss of sex drive	-	+	-
Duration	-	≥ 2 weeks	≥ 2 years
Almost daily	-	+	+
Social dysfunctioning	-	+	-

[a] At least one of the core symptoms is obligatory

INTERVIEW

All patients were interviewed with the 12-month computerised version of the CIDI which classifies according to the criteria of the DSM-IV/ICD-10 classification. Table 4.1 shows these criteria as well as the DSM-IV criteria for MDD and dysthymia.

For this article we used results from the following sections:

- demographics (A),
- depressive disorders and dysthymic disorder (E) and
- manic and bipolar affective disorder (F).

We classified according to DSM-IV criteria only. The interviewer had followed a three-day training programme to understand the rules for the administration of the interview. The category to which the patient belonged was blinded for the interviewer by, after consent, offering the interviewer a list of names of patients to invite for the interview without mentioning any category. Patients were interviewed at their home or, if the patient preferred, in the practice of their own GP or in the University.

For every patient, a file was added to the interview containing extra information that the patient gave during or after the interview. With this file the ICHPPC-2 code was validated, and differences between GP and DSM-IV cases could be described. The data were processed anonymously.

RESULTS

Patients

Forty-five patients meeting the inclusion criteria had received a code for depression between 1 October 1996 and 1997: 16 men and 29 women; median age = 46 years (range 19 to 91). Thirteen patients (seven men and five women) declined the interview. Thirty-three (65%) patients consented: nine men and 24 women; median age = 47 years (range = 22 to 91). For every patient, the two controls were invited, resulting in a total of 99 interviews.

Validity of the GP's diagnosis and accordance with the CIDI diagnosis.

All 33 depression codes matched the ICHPPC-2 criteria for depressive disorder as they were gathered with the interview. Of these 33 patients, 26 (79%) met the DSM-IV criteria for diagnosis of MDD (95% CI = 67% to 93%) and another two patients of dysthymia. Together, this adds up to an accordance of 85% (95% CI = 77% to 97%) between general practice and DSM-1V diagnosis. (Table 4.2 shows the cases of MDD in all three groups.)

The cases of the patients who did not match the DSM-1V criteria could be described as brief recurrent depression and minor depression.[15]

Table 4.2. DSM-IV MDD cases in three groups of patients

GP-code	DSM-IV code MDD: no	DSM-IV code MDD: yes	Total
1	7	26	33
2	26	7	33
3	33	0	33
Total	66	33	99

1 = general practice code for depression;
2 = general practice code for nervous functional complaints;
3 = without a general practice code for a mental disorder

DSM-IV diagnosis of depression in the controls

No DSM-IV major depressive disorder was found in the control group without an ICHPPC-2 code for a mental disorder. In the control group with the CNFC, seven (21%) cases of MDD were found (95% CI = 7% to 35%). One of these seven interviews had been marked by the interviewer because there were serious doubts about the validity of the interview owing to language problems and cultural differences.

DISCUSSION

Validity of the GP's diagnosis and accordance with DSM-IV diagnosis of MDD

All diagnoses were made according to ICHPPC-2 criteria. This confirms the idea that GP's rarely make false-positive diagnoses.[16] Even though, in some studies, a low accordance of diagnoses made with official criteria by GPs is found, in the CMR practices the accordance is high. As many as 26 patients, more than three quarters matched the DSM-IV diagnosis of MDD, and another two cases matched that of dysthymia. Dysthymia is a diagnosis not classifiable with ICHPPC-criteria, and is introduced in the DSM to categorise chronic depressions that are of long duration but less severe than major depressive episodes. It is more a diagnosis that is believed to

belong to the wide spectrum of major depressive syndromes than a separate diagnosis, and can cause severe distress.[17] A general training in the use of criteria for diagnosis, including monthly meetings to maintain the standard of this use, also leads to a high validity of the diagnosis when mental illness - in this case depression - is concerned, but it also seems to lead to a high accordance with DSM-IV criteria.

DSM-IV diagnosis of depression in the controls

Although the general practice diagnosis has a very high specificity, doubts about the sensitivity remain. In the control group without an ICHPPC-2 code for mental illness in the previous year, no cases were found. The problem lies in the group with the CNFC. Here, seven patients (out of 33) qualified for a MDD according to the DSM-IV. Even though perhaps one of these interviews was not valid, all patients had many physical and psychological complaints; reasons why the GP chose not to give them a code for depression but for CNFC are described earlier. Nervous complaints as a result of serious physical illness (severe migraine and prolonged complications after a cholecystectomy), physical abuse, incest, and alcohol abuse were found in this group. Though the sensitivity cannot be measured accurately with such small numbers, the fact that about one-fifth of the patients in this control group matched criteria of MDD suggests that this is a group of patients where the GP is distracted by foreknowledge and contextual matters from using criteria for diagnosis.

Limitations and strength

Because of the special nature of the CMR practices in which the GPs are trained to use criteria for diagnoses, care has to be taken not to generalise our results to all general practices and to other countries. In The Netherlands and internationally, an increasing number of GPs use electronic medical records with ICPC codes, and an increasing number of research networks in general practice have been formed that could lead to diagnoses with a high validity.

CONCLUSIONS

In this study we found that using criteria for diagnosis as a routine, as is carried out in morbidity registries, leads to diagnoses with a high validity also when mental illness is concerned, and to a high percentage of accordance between general practice diagnosis of depression and DSM-IV diagnosis of MDD. However, the sensitivity of the diagnosis of depression remains a topic of concern. Perhaps detection can be improved if GPs are aware of the category of patients in which they are likely to overlook cases and in which 'foreknowledge' distracts them from using criteria. The patients with what is called CNFC in the CMR are an example. A high accordance between diagnoses in primary and secondary care would offer great opportunities in the future for good comparative research on outcome and treatment between different groups of patients.

REFERENCES

1 Ormel J, Koeter MW, van den Brink W, Van de Willinge G. Recognition, management and course of anxiety and depression in general practice *Arch Gen Psychiatry* 1991;**48(8):**700-6.

2. Freeling P, Rao BM, Paykel ES, et al. Unrecognised depression in general practice. *Br Med J* 1985;**290:**1880-3

3. Tylee A, Freeling P, Kerry S, Burns T. How does the content of consultations affect recognition by general practitioners of major depression in women? *Br J Gen Pract* 1995;**45:**575-8.

4 Klinkman MS, Coyne JC, Gallo S, Schwenk T. False positives, false negatives, and the validity of the diagnosis of major depression in primary care. *Arch Fam Med* 1998;**7:**451-61.

5. Kessler D, Lloyd K, Lewis G, Pereira Gray D. Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. *Br Med J* 1999,**318:**436-9

6. Heath I Commentary. There must be limits to medicalisation of human distress *Br Med J* 1999;**318:**439-40

7 Wright AF Through a glass darkly: understanding depression. *Br J Gen Pract* 1999,**49:**91-2.

8. UMDS Msc in general practice teaching group. 'You're depressed','No I'm not' GP's and patients' different models of depression. *Br J Gen Pract* 1999;**49:**123-4.

9. Meer K van der, Tiemens BG, Brink W van den. Depression in primary health care: international data on prevalence and treatment, among others from The Netherlands. *Ned Tijdschr Geneeskd* 1996;**140:**2135-9.

10 Weel C van Validating long term morbidity recording. *J Epidemiol and Comm Health* 1995;**49:**355-8.

11. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders.* [4th edition] Washington DC: American Psychiatric Association, 1994

12. Andrews G, Peters L. The psychometric properties of the Composite International Diagnostic Interview *Soc Psychiatry Psychiatric Epidemiol* 1998;**33(2):**80-8

13 Weel C van. Chronic diseases in general practice: the longitudinal dimension. *Eur J of Gen Pract* 1996;**2:**17-21

14. Classification committee of World Organisation of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians *ICHPPC-2-Defined. Inclusion criteria for the use of the rubrics of the International Classification of Health Problems in Primary Care* Oxford: Oxford University Press, 1983

15. Angst J, Merikangas K, Scheidegger P, Wicki W Recurrent brief depression. A new type of affective disorder. *J Affective Dis* 1990,**19:**87-98

16. Wright AF Should general practitioners be testing for depression? *Br J of Gen Pract* 1994;**44:**132-5.

17. Angst J, Wicki W. Is dysthymia a separate form of depression? Results of the Zurich Cohort Study. *Eur Arch Psychiatry Clin Neurosc* 1991;**240**:349-54.

'Ik ben vaak erg somber. Ik heb eigenlijk al heel lang allerlei psychische klachten. Ik heb er nog nooit goed over kunnen praten. Dat zal wel voor een deel komen door de manier waarop ik mijn klachten breng. Maar ja, de 'goeie' vragen zijn ook nog nooit gesteld. Wat moet ik er nu mee, dit leidt echt tot niets?!
Ik zou ze er echt wel eens met iemand over willen praten. Kijken of er echt niets aan te doen is.'

'I often feel very sad. Actually I have had psychological problems for a long time now. I have never been able to talk about it. It's probably because of the way I described my symptoms, but anyway, I never seemed to be asked the 'right' questions. I wish I knew what I could do about it, it doesn't seem to be leading anywhere?!
I really would like to talk about it. Work out if there isn't anything that could be done.'

Chapter 5

The long-term perspective: a study of psychopathology and health status of patients with a history of depression, more than 15 years after the first episode

E.M. van Weel-Baumgarten

W.J.H.M. van den Bosch

H.J.M. van den Hoogen

F.G. Zitman

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SUMMARY

This article examines psychopathology, functioning, well-being, social support, and coping-behavior of family practice patients with a history of depressive illness, both with and without recurrences. Results of depressive patients were compared with each other and with those of "normal" controls. The patients belonged to the four practices of the Continuous Morbidity Registry of the University of Nijmegen, Netherlands. Their first episode of depression for each patient was more than 15 years ago. Data were collected with the Symptom Checklist (SCL-90), the Rand-36, the Social Support List (SSL-12) and the short Utrecht Coping List (UCL-k). Psychopathology scores of patients without recurrences were higher than "normal" controls and lower than patients with recurrences. The same pattern was found concerning health status. No significant differences were found between the groups in social support but patients with recurrences had a lower score of emotional coping than patients without recurrences or normal patients. That even a long time after an episode of depression, patients have higher levels of a variety of psychopathology than controls has implications for every-day practice as it calls for a longer and more critical follow-up of depression by clinicians.

INTRODUCTION

Depression is an illness with a high prevalence and serious morbidity. Many studies both in family practice and psychiatry show that patients with depressive illness experience high levels of disability during episodes.[1-4] Perceived health status is often even worse than that of patients with serious physical illness.[5] With treatment symptoms decrease and health status improves,[6,7] but what is the long-term outlook? Some patients do and yet others do not have recurrences.[8,9] In a follow-up study of depression in family practice we performed, 60% of all patients did not present with any recurrence in 10 years of follow-up. But does the lack of a physician-diagnosed recurrence mean that the functioning and well-being of these patients is also normal? The aim of this study was to test the hypothesis that patients with a history of depression at least 15 years ago, have similar psychopathology and health status to family practice controls. We also expected to show they differed in this respect from patients with a recurrent depressive illness. These results would have consequences for the length of time and the way family physicians follow-up these patients after their recovery. We felt it was likely that social support and individual coping styles could also affect the course of depression, so we studied differences between the groups in this respect as well.

METHOD

Subjects

Our research population for this study, patients who had experienced at least one episode of depression more than 10 years ago, came from the 222 patients involved in our long-term follow-up study mentioned above. This study had a historic cohort design. The patients belonged to the four practices of the Continuous Morbidity Registry (CMR) of the University of Nijmegen in The Netherlands.[10,11] The patients had been coded with depression, initially with E-list criteria, later with the inclusion criteria of the ICHPPC-2.[12-14]

Of the original cohort of 222 (first episode of depression between 1971 and 1985), 42 patients died, among whom two had committed suicide. Forty-one patients had

left the practices Another 13 patients were excluded for various reasons (terminal illness, hospitalization, and dementia) Of these last 13 patients, 4 were younger than 65 The remaining 126 patients were invited for this study The control group was formed by another 126 general practice patients from the CMR stratified for age, gender, social class, and practice who had no code for a mental illness between 1971 and 1999

The patients with a history of depression were divided into two categories, those with and without recurrences In our follow-up study, a recurrence was defined as an episode with a renewed code (ICHPPC-2 criteria) for, or description of, symptoms of depressive illness after at least 3 months without any description of such symptoms Recurrences after completion of the follow-up study were identified with renewed codes for depressive illness A current episode of depression was an exclusion criterion

Instruments

To answer questions about psychopathology we used the Symptom Checklist (SCL-90), a multidimensional self-report symptom inventory that is used to measure psychopathology in medical as well as psychiatric patients [15] In the Dutch version of the SCL-90, scores are tallied in the following eight areas anxiety, agoraphobia, depression, somatization, cognitive-performance deficit, extrapunitivity and paranoid ideation, anger-hostility and sleep disturbance The degree of distress on all 90 items is summarized and presented in the summary score of Psychoneuroticism [16 17] Results of the patients with and without recurrences and controls were compared

To answer questions about health status, a Dutch version of the RAND 36-item Short Form Health Survey (RAND-36) was used, which has a good reliability and validity [18 20] This instrument maps out the following eight health domains physical functioning, role limitation due to physical problems, bodily pain, general health perception, vitality, social functioning, role limitation due to mental problems, and mental health Scores range from 1 to 100 with a higher score meaning better health In addition to these instruments, all patients also received two short validated Dutch

questionnaires, one on social support (Social support list, SSL-12) and one on coping behavior (The short Utrecht Coping List, UCL-k).[21,22]

The SSL-12 is meant to measure the support received in the primary social network and differentiates between every-day social support, social support in problem situations and esteem support. The UCL-k measures the levels of problem-oriented coping, emotional coping and the seeking distraction/stress reduction.

The patient's doctor mailed all questionnaires with an accompanying letter. As with the results on the SCL-90 and RAND-36, social support and coping-behavior were studied in all three groups and differences were tested.

Statistical analysis

An analysis of covariance was performed. All scores were corrected for age and gender (LS means). Differences between groups were tested with t-statistics.

RESULTS

Of all 252 patients invited for this study, 158 (63 %) completed the questionnaires, 74 (59%) in the depressive group and 84 (67%) in the control group. There were no statistically significant differences in age, gender and social class between responding and non-responding patients. In 41 of the 74 patients with a history of depression, no recurrences were recorded (12 were male and 29 female, 1 under and 40 over 50 years of age). Four patients with a current episode of depression patients were excluded because of the possibility their scores could introduce a bias. Of the remaining 29 patients, 11 were male and 18 female, 3 were under, and 26 over 50 years of age. Mean length of time since the first depressive episode was 24 years (15–34). Though not significant there were some small differences in the male/female ratio and age of the responders in the three groups.

Psychopathology

On 3 of the 70 SCL-90 questionnaires of patients in the depressive group, missing data prevented scoring according to the criteria, leaving 67 patients in this group, 40

Table 5 1 SCL-90 Scores of patients with a history of depression and "normal" patients (History of depression with and without recurrences)

	Depression without recurrence *(n=40)*	Normal *(n=75)*	Depression with recurrence *(n=27)*	*P* value without recurrence versus normal	*P* value with recurrence versus normal	*P* value with versus without recurrence
Anxiety, mean and (CI)	15 (13-17)	14 (12-15)	16 (13-18)	0 05	0 02*	0 5
Agoraphobia	8 9 (7 6-10)	8 2 (7 4-9 1)	9 5 (7 9-11)	0 04*	0 03*	0 6
Depression	27 (23-30)	23 (21-25)	28 (24-32)	0 01*	<0 01*	0 7
Somatization	21 (18-23)	19 (17-20)	21 (18-24)	0 1	0 06	0 8
Cognitive performance deficit	16 (14-17)	14 (13-15)	16 (14-18)	0 04*	0 1	0 8
Extrapunitivity and paranoid ideation	29 (25-32)	25 (23-27)	26 (22-30)	0 02*	0 4	0 3
Anger-Hostility	7 6 (6 6-8 5)	7 2 (6 7-7 7)	8 7 (7 7-9 8)	0 2	< 0 01*	0 09
Sleep disturbance	6 5(5 4-7 6)	5 4 (4 7-6 1)	6 8 (5 5-8 1)	0 07	0 03*	0 7
Summary psychoneuroticism	142 (128-157)	126 (117-135)	144 (127-160)	<0 01*	< 0 01*	0 9

Scores are means rounded off and corrected for age and gender
All confidence intervals (CI) 95%
Differences between group were tested with t tests

without and 27 with recurrences. Of the control group 75 questionnaires could be used. The scores on the SCL-90 and *P* values of the differences are presented in Table 5.1. Patients without recurrences of their depression do have more psychopathology than controls. In four of the eight dimensions of the SCL-90 as well as in the summary score of psychoneuroticism, these differences were significant. Patients with recurrences showed higher scores than either patients without recurrences (except the score for Extrapunitivity and Paranoid Ideation) or normal patients.

Health status

The scores on the RAND-36 are presented in Table 5.2. Here, all questionnaires could be used. Patients without recurrences showed scores between those of the normal controls and those of patients with recurrences. In comparison with controls, patients without recurrences only showed significant differences in the mental health score, whereas patients with recurrences had significantly higher scores for bodily pain, vitality and role limitation mental as well.

Social Support and Coping Behavior

No significant differences were found between the groups in social support. As can be seen in Table 5.3, patients with recurrences showed lower scores of emotional coping than the normal control group.

DISCUSSION

It is not clear whether patients who have recovered from an episode of depressive illness experienced many years ago and without recurrences according to their family physician function at a normal level. Previous studies show that symptoms of depressed patients are reduced, sometimes even to normal levels, immediately after treatment and that well-being improves.[6,7] However when we measured the time between 15 and 34 years after the depressive episode, patients had higher levels of psychopathology than controls. Patients with recurrences, although not depressed

Table 5.2. RAND-36. Scores of patients with a history of depression and "normal" patients (History of depression with and without recurrences)

	Depression without recurrence *(n=41)*	Normal *(n=84)*	Depression with recurrence *(n=29)*	*P* values without recurrence versus normal	*P* values with recurrence versus normal	*P* values without versus with recurrence
Physical function, mean (CI)	73 (64-82)	75 (69-82)	66 (56-76)	0.7	0.1	0.3
Role limitation physical	69 (56-86)	72 (61-83)	56 (39-73)	0.7	0.08	0.2
Bodily pain	72 (65-80)	77 (72-82)	64 (55-73)	0.3	0 02*	0.1
General health perception	61 (54-68)	67 (63-72)	59 (50-67)	0.09	0.05	0.6
Vitality	61 (55-68)	67 (62-71)	58 (51-67)	0.1	<0.05*	0.6
Social functioning	69 (63-75)	70 (66-75)	62 (55-69)	0.7	0.08	0.1
Role limitation mental	78 (64-92)	90 (81-99)	74 (57-90)	0.09	0.03*	0.7
Mental health	69 (63-75)	76 (72-80)	62 (55-69)	0.04*	<0.01*	0.1

Scores are means rounded off and corrected for age and gender.
All confidence intervals (CI) 95%.
Differences between group were tested with t tests.

Table 5 3 UCL-k Scores of patients with a history of depression and "normal" patients (History of depression with and without recurrences)

	Depression without recurrence *(n=39)*	Normal *(n=83)*	Depression with recurrence *(n=29)*	*P* values without recurrence versus normal	*P* values with recurrence versus normal	*P* values without versus with recurrence
Problem oriented coping (CI)	12 (11-13)	11 (10-12)	13 (11-14)	0 5	0 1	0 7
Emotional coping	9 5(8 9-10)	9 2 (8 7-9 7)	10 (9 4-11)	0 4	0 04*	0 2
Seeking distraction, stress reducing	8 8(8-9 6)	8 1 (7 6-8 6)	8 7 (7 7-9 6)	0 3	0 3	0 9
Summary score	30 (29-32)	29 (27-30)	31 (29-33)	0 2	0 07	0 7

Scores are means rounded off and corrected for age and gender
All confidence intervals (CI) 95%
Differences between group were tested with t tests

during the study period, showed even higher scores in almost all dimensions of the SCL-90. However the difference between patients with and without recurrences was not very large. In health status, patients without recurrences also present with scores between those of the two other groups. To explain these results, it is important to look longitudinally. When criteria for depression are met, patients have high psychopathology levels, in particular in the depression dimension, and a low health status. Immediately after the episode, these levels improve, although residual symptoms may be present, and treatment of these symptoms may improve long-term outcome.[23,24] It is unlikely that our results can be explained as residual symptoms or the effect of the depressive episode. The period since the depression, certainly for patients without recurrences, is much too long for that and the psychopathology too varied. It is much more likely that our results confirm earlier findings about neurotic illness in family practice.[25] Patients with a history of depression both with and without recurrences form part of a larger group of vulnerable patients with a variety of psychopathology and fluctuating symptoms. Health status varies accordingly. For some patients with depression the downs are lower than for others and they present with recurrences. Others also score lower than normal control patients but do not meet criteria for depression or do not present themselves to their physician.

We found no differences in social support between the groups. The amount of social support varies during a lifetime. As we excluded patients with a current depression from our analysis, we do not have any data on social support during depressive episodes. That patients with a recurrent illness had a social support not discernible from normal, even with the measured levels of psychopathology, could even be part of the reason why they did not have a depression at the time of the study.

Concerning coping behavior, different strategies can develop over time. Patients with recurrences of depression showed larger differences from their normal controls than patients without recurrences in problem-oriented and emotional coping, although only the last difference was significant. A low score of emotional coping is perhaps an indication that a patient is prone to recurrences.

A few limitations of our study should be mentioned. The loss of patients since the original follow-up could have introduced a bias. However, only if more patients with a favorable than with a poor outcome were lost to follow-up, differences with controls in psychopathology and health status would have been smaller and our conclusions different. This does not seem likely, as two of the patients lost to this follow-up had committed suicide. Another matter is that by dividing the patients with a history of depression into two groups, the numbers in these groups were relatively small, and wide confidence intervals can be seen in the tables. However, the strength of this study is the long-term follow-up. In literature, primary care studies about depressive illness with a long-term follow-up (longer than 5 years) can hardly be found even though the illness - often recurrent or chronic - does require this type of study. Our results have implications for everyday practice. They show that patients with a history of depression, even those without recurrences, have higher levels of psychopathology and a lower health status than normal controls even when the first depressive episode is more than 15 years ago. Awareness of our results could serve as a reminder to clinicians that a variety of psychopathology - and not only depression - can be present in these patients. This could accelerate recognition of recurrences of depression in some cases and lead to identification of other diagnoses in others. Appropriate treatment could then be offered. For patients who do not meet criteria for specific diagnoses the offering of support could perhaps prevent recurrences and improve quality of life.

REFERENCES

1. Williams JW, Kerber CA, Mulrow CD, Medina A, Aguilar C Depressive disorders in primary care: prevalence, functional disability, and identification *J Gen Int Med* 1995;**10**:7-12.
2. The Counselling versus Antidepressants in Primary Care Study Group. How disabling is depression? Evidence from a primary care sample *Br J Gen Pract* 1999;**49**:95-8.
3 Wells KB, Stewart A, Hays RD *et al.* The functioning and well-being of depressed patients: results from the Medical Outcomes Study *JAMA* 1989;**262**.914-9.
4 Katon W, Schulberg H. Epidemiology of depression in primary care *Gen Hosp Psychiatry* 1992,**14**:137-247.
5. Lyons RA, Lo SV, Littlepage BNC. Comparative health status of patients with 11 common illnesses in Wales. *J Epidemiol Community Health* 1994;**48**:388-90.
6. Coulehan C, Schulberg HC, Block MR, Madonia MJ, Rodriguez E Treating depressed primary care patients improves their physical, mental and social functioning. *Arch Int Med* 1997;**157**:1113-20.
7. Agosti V, Stewart JW, Quitkin FM, Ocepek-Welikson K. How symptomatic do depressed patients remain after benefiting from medication treatment? *Compr Psychiatry* 1993;**34**:182-6.
8. Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG 10 Year Follow-up of depression after diagnosis in general practice. *Br J Gen Pract* 1998,**48**:1643-6.
9. Angst J. How recurrent and predictable is depressive illness? *Perspectives in psychiatry* 1992;**3**:1-30.
10. Weel C van. Validating long term morbidity recording *J Epidemiol and Community Health* 1995;**49**:355-8.
11 Weel C van. Chronic diseases in general practice: the longitudinal dimension. *Eur J Gen Pract* 1996;**2**:17-21.
12. Hodgkin K. Towards Earlier Diagnosis in Primary Care, Second Edition: Edinburgh, Churchill Livingstone, 1966
13. Classification Committee of World Organisation of National Colleges, Academies and Academic Associations of general practitioners/Family Physicians: ICHPPC-2-Defined. Inclusion Criteria for the Use of the Rubrics of the International Classification of Health Problems in Primary Care. Oxford, Oxford University Press, 1983
14 Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG. The validity of the diagnosis of depression in general practice. is using criteria for diagnosis as a routine the answer? *Br J Gen Pract* 2000;**50**:284-7.

15. Derogatis LR. SCL-90. Administration, Scoring and Procedures Manual-1 for the Revised Version. Baltimore, John Hopkins University School for Medicine, Clinical psychometrics Research Unit, 1977

16 Arrindell WA, Ettema JHM. SCL-90 Handleiding bij een multidemensionele psychopathologie-indicatie. Lisse, Swets & Zeitlinger B V., 1986

17. Arrindell WA, Ettema H. Dimensionele structuur en betrouwbaarheid en validiteit van de Nederlandse bewerking van de Symptom Checklist (SCL-90); gegevens gebaseerd op een fobische en 'normale' populatie. *Med Tijdschr Psychologie* 1998;**36**:77-108.

18 Hays RD, Sherbourne DC, Mazel RM. The Rand 36-item health survey 1.0. *Health Econ* 1993;**2**.217-227.

19 Ware JE, Kosinski M, Gandek B, *et al.* The factor structure of the SF-36 Health Survey in 10 countries· results from the IQOLA project. *J Clin Epidemiol* 1998;**51**:1159-65.

20. Aaronson NK, Acquadro C, Alonso J, *et al.* International quality of life assessment (IQLA) project special communication. *Qual Life Res* 1992;**1** 349-51.

21. Eijk LM van, Kempen GI, Sonderen FL van A short scale for measuring social support in the elderly: the SSL12-I. *Tijdschr Geront Ger* 1994;**25**·192-6.

22. Schreurs PJG, Willige G van de, Brosschot JF, Tellegen B, Gaus GHM. De Utrechtse Copinglijst: UCL. Omgaan met problemen en gebeurtenissen/The Utrecht copinglist: UCL. Dealing with problems and events. Lisse, Swets & Zeitlinger, 1993

23 Paykel ES. Remission and residual symptomatology in major depression. *Psychopathology* 1998,**31**:5-14

24 Fava GA Subclinical symptoms in mood disorders. pathophysiological and therapeutic implications. *Psychol Med* 1999,**29**.47-61

25 Lloyd KR, Jenkins R, Mann A Long term outcome of patients with neurotic illness in general practice. *Br Med J* 1996;**313**:26-8.

'Ik voelde me al een hele tijd niet goed. Er was van alles gebeurd, met mezelf en met de kinderen. Ze kregen de verkeerde mannen, drugs en zo.
Ik werkte toen nog, maar had ook veel huilbuien tijdens het werk, kon het werk niet goed meer aan. Toen kwam ik dus in de WAO terecht.
De hele dag maar huilen, vreselijk. En het duurde maar..... Ook mijn man is een tijd thuis geweest vanwege mijn problemen.
Eerst kreeg ik kalmeringstabletten, een heleboel soorten. Toen het alsmaar niet goed ging, kreeg ik Prozac. Dat heb ik toen een aantal maanden gebruikt. Nu gaat het goed. Ik ben wel niet altijd de vrolijkste, maar kom er nu zelf uit. We kunnen toch ook niet allemaal de vrolijkste zijn!'

'I haven't felt well for sometime. A lot has happened, both to myself and the children. They ended up with the wrong men, you know, drugs and so on .....
Back then I still had my job, but I cried all the time and couldn't cope with the work. I was off sick for a long time.
I was crying all day long, awful. And it stayed like that for a long time..... My husband had to stop working as well at that time, because of my problems.
First I took all sorts of tranquillisers. When that didn't help, I got Prozac. I took it for a few months. Now I am doing o.k. I am still not the most cheerful person in the world, but I can cope. We are not all born to be cheerful, are do we?!'

Chapter 6

Regarding Chronic Nervous Functional Complaints as a 'diagnosis': is the concept useful?

E.M. van Weel-Baumgarten

W.J.H.M. van den Bosch

H.J.M. van den Hoogen

F.G. Zitman

Submitted

SUMMARY

Background. In general practice a specific diagnosis can often not be made when patients present with varying undifferentiated functional complaints In the Continuous Morbidity Registry (CMR) patients with these complaints are regarded as a separate group and coded with a 'diagnosis' of chronic nervous functional complaints (CNFC) What this diagnosis exactly means for patients is not quite clear Are these patients really ill, do they differ from controls in psychopathology, health status, coping behaviour, and social support, or are they just a 'difficult' group of patients

Objectives To investigate patients with the 'diagnosis' of CNFC and to assess their psychopathology, health status, coping behaviour, and social support

Methods Psychopathology, functioning and well being, social support, and coping behaviour of patients with a CNFC-code were compared with a control group of 'normal' general practice patients and with patients with a history of depression Data were collected with the Symptom Checklist (SCL-90), the 36-item short form (Rand-36), the Social Support List (SSL-12) and the short Utrecht Coping list (UCL-k) All patients belonged to the 4 practices of the Continuous Morbidity Registry of the University of Nijmegen in The Netherlands

Results Two hundred and thirty four patients (62% of 378) completed the questionnaires Patients with CNFC and patients with a history of depression both had statistically significant more psychopathology than the control group This difference was not found between the CNFC and patients with a history of depression Patients with CNFC reported a significantly lower health status than the control group Their health status was also lower than of patients with a history of depression, although this difference was not significant No difference in coping behaviour was found Patients with CNFC also reported significantly less daily social support than the other two groups

Conclusions Patients with CNFC are significantly impaired There are strong indications that within this group specific mental illness could be found By regarding chronic nervous functional complaints as a diagnosis a longitudinal follow-up is facilitated Application of diagnostic criteria for mental illness, not only when

the diagnosis is made for the first time but also during the follow-up, might identify a subgroup of patients with diagnoses of specific mental illness who could benefit from appropriate treatment. The remainder might benefit from the kind of treatment that has proved to be efficacious for specific functional somatic syndromes.

INTRODUCTION

In general practice patients frequently present with functional complaints. Sometimes a diagnosis of a specific functional somatic syndrome can be made (for example irritable bowel syndrome, pre-menstrual syndrome and hyperventilation syndrome). A problem arises when patients present with a variety of undifferentiated physical and mental complaints and no specific diagnosis is appropriate. The use of symptom codes would be a solution for classification, but does not offer any solution in how to deal with these patients. In the Continuous Morbidity Registry (CMR),[1] when the general practitioner has strong indications that the complaints have no somatic but a psychosocial or functional basis, a code called nervous functional complaints[2,3] (NFC) is used for registration. In 1998 this code was used in 140 per 1000 patients. As continuity of care is an important issue in general practice, getting a longitudinal picture is important. Therefore when repeatedly presenting with NFC has become a characteristic of the patient, 'chronic' is added to the code. This happens when the NFC-code has been used repeatedly in the same patient over an average of two years and still no code for a specific mental or physical illness seems more appropriate. It now becomes a 'diagnosis' of chronic nervous functional complaints (CNFC). For patients with this diagnosis attention is focused on a policy of holding back on testing and referrals for somatic illness, to prevent somatic fixation. In 1998, 70 per 1000 patients were coded with CNFC. It is not clear that a diagnostic category of 'CNFC' has advantages over variable symptom codes, however the large overlap between the specific functional somatic syndromes and their reasonable response to similar treatment perhaps justifies this more general approach.[4] In both categories specific diagnoses of mental illness such as depression are easily overlooked by the way functional complaints are presented. Overlooking psychiatric morbidity is also a problem among frequent attenders,[5] to which category many patients with CNFC belong. Aim of this study was to investigate if presenting repeatedly with functional complaints has to be considered simply as a behaviour characteristic or as a sign of serious psychopathology and functional impairment. For that purpose, levels of psychopathology and functional status were assessed. These results were compared

with two other groups: general practice patients without any mental illness and patients with a history of depression. The choice of this last group was made because in a long-term follow-up study on depression in general practice, we discovered that in a number of patients with CNFC a diagnosis of depression was missed.[6,7] Because levels of psychopathology and quality of life could be influenced by social support and by individual coping styles we also studied differences between the groups in this respect.

METHOD

Patients

As this study was performed as part of a larger study on the long term follow-up of depression in general practice, our index group consisted of a historic cohort of 222 patients with a history of depression. The initial diagnosis of depression and episodes of recurrence had been been made with E-list criteria, later adapted to the Inclusion Criteria for the use of the rubrics of the International Classification of Health Problems in Primary Care, (ICHPPC-2).[8,9] After 10 years 40% of the patients had experienced at least one recurrence, 60% of the patients had no recurrences. Of the original 222 patients (first episode of depression between 1971 and 1985), 42 had died of whom 2 had committed suicide, and 41 patients had left the practices. Another 13 patients were excluded for various reasons (terminal illness, hospitalization, and dementia). Of these patients 4 were younger than 65. This left 126 patients to answer our questionnaires. The patients with a code for CNFC were matched with these patients for age, gender, social class and practice, and so were the patients without a code for a mental illness. All 378 patients belonged to the 4 practices of to the CMR of the University of Nijmegen in The Netherlands.[10] Results of the three groups (CNFC, history of depression, and without a code for mental illness) were compared with each other.

Instruments

To study levels of psychopathology the 90-item Symptom Checklist (SCL-90) was used, a multidimensional self-report symptom inventory.[11] This list is widely used for screening and to evaluate treatment in studies with general medical as well as psychiatric patients. The Dutch version of this instrument generates scores in the following 8 dimensions: anxiety, agoraphobia, depression, somatization, cognitive-performance deficit, extrapunitivity and paranoid ideation, anger-hostility and sleep disturbance. In addition a summary score of Psychoneuroticism represents the degree of distress on all 90 items.[12,13] All scores were corrected for age and gender. Results of patients with CNFC were compared with scores of patients in the control group and with patients with a history of depression.

Health status was studied with a Dutch version of the 36-item Rand Short Form (RAND-36), which has a good reliability and validity.[14-16] The following 8 health domains can be distinguished: physical functioning, role limitation due to physical problems, bodily pain, general health perception, vitality, social functioning, role limitation due to mental problems and mental health. Scores reach from 1 to 100, a higher score meaning better health.

All patients also received two short validated Dutch questionnaires, one on social support (SSL-12) and one on coping behaviour (UCL-k).

With the 12-item Social Support List (SSL-12), which is meant to measure the support received in the primary social network, the following social support is measured: every-day social support, social support in problem situations and esteem support.[17]

The short Utrecht Coping List (UCL-k) measures the levels of problem-oriented coping, emotional coping and seeking distraction/stress reducing.[18]

As with the results on the SCL-90 and Rand-36, social support and coping behaviour were studied in all three groups and differences between the groups were tested.

Statistical analysis

An analysis of covariance was performed. All scores were corrected for age and gender (LS means). Differences between groups were tested with t-statistics.

RESULTS

Two hundred and thirty four patients (62%) completed the questionnaires, 75 (59%) in the group with the nervous functional complaints, 75 (59%) in the depressive group, and 84 (67%) in the control group. There were no statistically significant differences in age, gender, and social class between responders and non-responders. Of these 234 patients 82 were male, 152 female, 136 under the age of 65, and 98 were 65 or older. In the depressive group 41 patients had experienced only one episode of depressive illness, 33 had a recurrent type of depression and of 1 patient it was not clear. Of the 33 patients with a recurrent illness, 4 were coded as depressive at the time of the data collection. Mean length of time since the first depressive episode of the total group of patients with a history of depression was 23 years (15-34 years).

Levels of psychopathology

On 4 of the 75 returned SCL-90 questionnaires of patients in the depressive group, missing data prevented scoring according to the criteria, leaving 71 patients in this group. In the other categories all questionnaires could be scored. Table 6.1 shows the psychopathology scores of all three groups as well as P-values of the differences. The patients with CNFC as well as the patients with a history of depression had statistically significant more psychopathology than the control group in all dimensions of the SCL-90. In some dimensions the patients with CNFC had higher scores than the patients with a history of depression. In others the opposite was true but these differences were not very large and none of the differences was significant.

Health status

As can be seen in table 6.2, differences in health status were found in all domains between patients with CNFC and patients from the control group, the CNFC patients experiencing a worse health status. Although health status of the depressive patients was lower than of the control group in all domains, these differences were only significant in the following domains: bodily pain, general health perception, vitality, role limitation mental and mental health. All scores of the patients with CNFC were a

Table 6.1. SCL-90 Scores of patients with CNFC, "normal" patients and patients with a history of depression

	CNFC (n=75)	History with depression (n=71)	Normal (n=84)	*P* values CNFC versus normal	*P* values history of depression versus normal	*P* values CNFC versus history of depression
Anxiety, mean and (CI)	17 (16-19)	17 (15-18)	14 (12-15)	<0 01*	<0 01*	0 8
Agoraphobia	9 6 (8 8-10)	10 (8 9-11)	8 2 (7 3-9)	0 04*	<0 01*	0 4
Depression	28 (26-31)	29 (26-31)	23 (21-26)	<0 01*	<0 01*	0 6
Somatization	23 (22-25)	21 (20-23)	19 (17-20)	<0 01*	0 01*	0 3
Cognitive performance deficit	17 (16-18)	16 (15-17)	14 (13-16)	0 01*	0 01*	0 7
Extrapunitivity and paranoid ideation	29 (27-31)	28 (26-31)	25 (23-27)	0 04*	0 02*	0 9
Anger-Hostility	8 4 (7 9-9)	8 3 (7 7-9)	7 2 (6 6-7 8)	<0 01*	<0 01*	0 9
Sleep disturbance	7 1 (6 3-7 9)	6 8 (6 1-7 6)	5 4 (4 7-6 1)	<0 01*	<0 01*	0 9
Summary psychoneuroticism	153 (143-163)	149 (139-159)	126 (116-136)	<0 01*	<0 01*	0 9

Scores are means rounded off and corrected for age and gender
All confidence intervals (CI) 95%
Differences between group were tested with t tests

Table 6 2 Rand-36 Scores of patients with CNFC, "normal" patients and patients with a history of depression

	CNFC (n=75)	History with depression (n=75)	Normal (n=84)	*P* values CNFC versus normal	*P* values history of depression versus normal	*P* values CNFC versus history of depression
Physical function, mean (CI)	67(61-73)	70(64-76)	76(70-82)	0 04*	0 2	0 5
Role limitation physical	54(44-65)	64(54-74)	72(62-81)	0 02*	0 2	0 3
Bodily pain	66(60-71)	69(63-75)	77(72-83)	<0 01*	0 03*	0 5
General health perception	57(52-61)	59(54-64)	67(62-71)	<0 01*	0 02*	0 6
Vitality	53(49-58)	58(54-63)	67(62 71)	<0 01*	0 01*	0 2
Social functioning	58(52-63)	65(60-69)	70(66-75)	<0 01*	0 09	0 07
Role limitation mental	69(60-78)	75(67-84)	90(80-98)	<0 01*	0 02*	0 5
Mental health	62(58-67)	64(60-69)	76(71-80)	<0 01*	<0 01*	0 7

Scores are means rounded off and corrected for age and gender
All confidence intervals (CI) 95%
Differences between group were tested with t tests

little lower than of patients with a history of depression. Although no significant differences were found here it does mean that in any case they are no better off than patients with a history of depression in this respect.

Social support and coping behaviour

As can be seen in table 6.3, patients with CNFC report less social support than the other two groups. In every-day social support this difference was significant, when compared with the control group and with patients with a history of depression. This difference was not found in the comparison between the patients with a history of depression and the control group. No differences in coping behaviour were found between the groups.

DISCUSSION

Literature shows that patients tend to present a somatic reason for encounter, even when they have psychosocial and psychological problems, and that these problems are overlooked because of this.[5,19] In patients presenting with varying functional symptoms this is also likely to happen. Our results show that in the group of patients with these varying functional complaints, coded with a 'diagnosis' of CNFC, there is real illness. We found indications that their functional complaints are not just a characteristic that is annoying for both doctor and patient but these patients have a variety of psychopathology, and really suffer. The high levels of psychopathology in our study suggest that diagnoses of specific mental illness were overlooked. As we know that specific psychopathology such as depressive illness diminishes functioning and well-being, our results on health status strengthen our opinion that mental illness could indeed be present.[20,21] These results show that patients with CNFC not only perceive their well-being as worse than 'normal' patients do, but there is not much difference in this respect with patients with a history of depression. A diagnostic instrument would have to be used to identify the patients in this heterogeneous group who meet criteria for specific diagnoses of mental illness. In this cross-sectional study high levels of psychopathology and a diminished health status were present when the questionnaires

Table 6.3. SSL12- Scores of patients with CNFC, "normal" patients and patients with a history of depression

	CNFC (*n=75*)	Normal (*n=84*)	History with depression (*n=74*)	*P* values CNFC versus normal	*P* values History of depression versus normal	*P* values CNFC versus history of dpression
Sumscore, (CI)	27 (25-28)	29 (27-30)	28 (27-29)	0.02*	0.6	0 09
Every day social support	9.3 (8.9-9.9)	11 (10-11)	10 (9 8-11)	<0.01*	0.1	0.01*
Support in problem situations	8 (7.5-8.6)	8.1(7.5-8.6)	8.2 (7.6-8.7)	0.9	0.8	0 8
Appreciation support	9.1 (8.5-9.6)	9.8 (9.3-10)	9.7 (9.2-10)	0.05	0.8	0 09

Scores are means rounded off and corrected for age and gender.
All confidence intervals (CI) 95%.
Differences between group were tested with t tests.

were gathered. For a number of patients with CNFC a diagnosis of specific mental illness might have been overlooked when the 'diagnosis' was made for the first time. Other patients in this group perhaps did not meet criteria at that time but developed a specific mental illness later. For those patients episodes of specific mental illness could be hidden among the episodes with functional complaints. Therefore a 'diagnosis' of CNFC has advantages over variable symptom codes: an accurate follow-up of patients with the same diagnosis has more chance of success. Every time a patient with CNFC appears for consultation the diagnosis should be reconsidered and diagnostic criteria of mental illness should be used again to check if a specific diagnosis has become more appropriate. Future studies will have to show if by following-up these patients more closely over a period of time, specific diagnoses of mental illness will emerge. If this is the case appropriate treatment could be offered to these patients and they could perhaps manage to improve their health status as a result. For the remainder of the patients with CNFC an approach focused on prevention of somatic fixation could be supplemented with treatment efficacious for a number of specific functional syndromes and the effect studied not only in individual patients but also for all CNFC patients as a group.

An additional finding was that patients with CNFC scored significantly lower than their normal controls on every-day social support in which they also distinguished themselves from patients with a history of depression. Perhaps the more accurate follow-up recommended above, could offer these patients the support they seem to need and add to the improvement of their well-being. The follow-up of patients with CNFC, taking into account our study results and recommendations should be a subject to study in the future.

REFERENCES

1. Weel C van. Validating long-term morbidity recording. *Journ of Epidemiol and Commun Health* 1995;**49:**355-8
2. Huygen FJA, Hoogen HJM van den, Logt ATh van de, Smits AJA. Nerveus functionele klachten in de huisartspraktijk. I. Een epidemiologisch onderzoek. Nervous disorders in general practice/ I An epidemiological investigation. *Ned Tijdschr Geneeskunde* 1984,**28:**1321-7.
3. Huygen FJA, Hoogen HJM van den, Logt ATh van de, Smits AJA. Nerveus functionele klachten in de huisartspraktijk. II. Een epidemiologisch onderzoek/ Nervous disorders in general practice II. Consequences for diagnosis and therapy *Ned Tijdschr Geneeskunde* 1984;**29:**1372-6
4. Wesserly S, Nimnuan C, Sharpe M Functional somatic syndromes one or many? *Lancet* 1999;**354:**936-9.
5. Karlsson H, Lehtinen V, Joukamaa M. Psychiatric Morbidity among gfrequent attender patients in primary care. *Gen Hosp Psychiatry* 1995,**17:**19-25.
6. Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG. 10 Year Follow-up of depression after diagnosis in General Practice *Br J of Gen Pract* 1998;**48:**1643-6.
7. Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG. The validity of the diagnosis of depression in General Practice: is using criteria for diagnosis as a routine the answer? *Br J of Gen Pract* 2000;**50:**284-7.
8. Hodgkin K. *Towards earlier diagnosis in primary care*. second edition; 170-2 and 183-4. Edinburgh: Churchill Livingstone, 1966.
9. Classification committee of World Organisation of National Colleges, Academies and Academic Associations of general practitioners/Family Physicians. ICHPPC-2-Defined. *Inclusion criteria for the use of the rubrics of the International Classification of Health Problems in Primary Care*. Oxford: Oxford University Press, 1983.
10. Weel C van. Validating long term morbidity recording. *Journ of Epidemiol and Commun Health* 1995,**49:**355-8.
11. Derogatis LR SCL-90: Administration, Scoring and Procedures Manual-1 for the revised version. John Hopkins University School for Medicine, Clinical psychometrics Research Unit, Baltimore, 1977.
12. Arrindell WA, Ettema JHM. SCL-90 Handleiding bij een multidimensionele psychopathologie-indicatie. Lisse: Swets & Zeitlinger B V, 1986.

13 Arrindell WA, Ettema H Dimensionele structuur en betrouwbaarheid en validiteit van de Nederlandse bewerking van de Symptom Checklist (SCL 90), gegevens gebaseerd op een fobische en 'normale' populatie *Med Tijdschr Psychol* 1998 **36:**77-108

14 Hays RD, Donald Sherbourne C, Mazel RM The Rand 36-item health survey 1 0 *Health economics* 1993,**2:**217-27

15 Ware JE, Kosinski M, Gandek B, Aaronson NK, Apolone G, Bech P, et al The factor structure of the SF-36 Health Survey in 10 countries Results from the IQOLA project *J Clin Epidemiol* 1998,**51:**1159-65

16 Aaronson NK, Acquadro C, Apolone G, Bullinger M, et al International quality of life assessment (IQLA) project special communication *Quality of life research* 1992,**1:**349-51

17 Eijk LM van, Kempen GI, Sonderen FL van A short scale for measuring social support in the elderly the SSL12-I *Tijdschr Geront Geriatr* 1994,**25:**192-6

18 Schreurs PJG, Willige G van de, Brosschot JF, Tellegen B, Gaus GHM De Utrechtse Copinglijst UCL Omgaan met problemen en gebeurtenissen Lisse Swets & Zeitlinger, 1993

19 Gulbrandsen P, Fugelli P, Hjortdahl P Psuchosocial problems presented by patients with somatic reasons for encounter tip of the iceberg? *Fam Pract* 1998,**15:**1-8

20 Wells KB, Stewart A, Hays RD, et al The functioning and well being of depressed Patients results from the Medical Outcomes Study *JAMA* 1989,**262:**914 9

21 The counselling versus antidepressants in primary care study group How disabling is depression? Evidence from a primary care sample *Br J of Gen Pract* 1999,**49:**95-8

'Ik heb veel klachten. Het gaat niet echt goed met me. De dokter neemt het niet serieus, vind ik.
Het zal ook wel komen door mijn voorgeschiedenis. Mijn moeder was heel 'hardvochtig', ze heeft me nooit geleerd om liefde te voelen, laat staan er mee om te gaan of te geven.
Toen kreeg ik een relatie met een fijne man, maar dat liep mis. Ik dacht, dan heb ik kennelijk een heel ander soort man nodig. Ik leerde mijn 'nu ex-man' kennen. Maar eigenlijk was hij nog erger dan mijn moeder. Hij was van meet af aan gewelddadig, ook tegen mij. Hij had ook echt hallucinaties, bleek echt ziek. Hij is in de psychiatrie terecht gekomen. Na vier jaar ellende, en met twee kinderen waarvan er een ook nog eens geestelijk gehandicapt is, ben ik definitief bij hem weg gegaan.
Ik heb talloze keren in 'blijf van mijn lijf' gezeten na mishandelingen, ben weglopen en weer terugkomen, en alsmaar het idee hebben dat zij er iets aan zouden kunnen doen.
Daarop volgde financiële problemen, uitkering na baanverlies etc. Ik blijf steeds bang dat ik nog eens m'n baan kwijt raak en van een uitkering afhankelijk word.
Dan heb ik weer eens hier last van en dan van dat. Maar wat wil je?!'

'I have many problems. I am not really doing well. The doctor doesn't take me seriously.
I have had a lot of problems in my past which I think are to blame. My mother was very 'cold and hard', she never taught me how to feel love, let alone give it to others.
Then I got involved with a nice man, but that went wrong. I thought I probably needed a very different kind of man. Then I met my now ex-husband. But he was even worse than my mother, violent from the start, with others as well as me. He had hallucinations, turned out to be really ill. He ended up as a psychiatric case. After four years of misery, bringing up two children, one of them is mentally handicapped, I left him. Before that I had been in homes for battered women, I don't know how many times, running away and coming back all the time, hoping they would be able to do something about it.
Then came the financial problems, losing my job, social security etc. Even now I am afraid I'll lose my job again and will have to live on social security.
I am always getting different symptoms. But what would you expect?!'

Chapter 7

Long-term follow-up of depression in community and family practice: a review of the literature

E.M. van Weel-Baumgarten

H.J. Schers

W.J.H.M. van den Bosch

H.J.M. van den Hoogen

F.G. Zitman

Revised version "Long-term follow-up of depression among patients in the community and in family practice settings: a systematic review" *accepted for publication in The Journal of Family Practice. Tentatively scheduled for publication in J Fam Pract 2000;49(12)*

SUMMARY

Background. Current knowledge about the long-term outcome of depression is based mainly on results of studies performed with the small selection of patients referred to psychiatry. However, because of the high prevalence of depression in community and primary care, knowledge about the long-term outcome in these populations is indispensable to be able to offer the best possible care in these settings.

Methods. A literature search was performed to identify relevant papers published between 1970 and 1999 on original long-term follow-up studies of depression in community and primary care populations. Studies of adult populations with a diagnosis made with diagnostic criteria and a follow-up of at least 5 years were included. Data about recurrences, relapses, psychopathology, disability or quality of life at follow-up were studied.

Results. Eight studies fulfilling these criteria were found. Reported rates of recurrence or depression at follow-up were between 30 and 40%. Higher rates were found in the younger and the older age groups. Data about other predictors of outcome, health status and the relation between treatment and outcome did not justify any hard conclusions.

Conclusions. Long-term outcome of depression in community and primary care is studied rarely. The results of available studies are difficult to compare because of the large differences in populations and methods. Nevertheless they suggest that that the long-term prognosis of depression in community and primary care is not as poor as in psychiatry.

INTRODUCTION

Depression is regarded as a chronic illness with a high prevalence and a large impact on quality of life.[1-6] Nevertheless, the long-term outcome of depression in primary care and community is not so clear. Most long-term outcome studies on depression have been performed with study populations of patients referred to psychiatry.[7-11] However, not everyone with depression in the community consults a physician. And usually only the more severe and lasting cases - about 5 to 15% of all patients who do seek medical attention and are subsequently diagnosed with depression in primary care - are referred to secondary care.[12,13] It is unlikely that the outcome in community and primary care is identical to the outcome of referred cases because of the difference in prevalence between these populations of the various severity levels of depression.[14]

As far as studies on depression have been performed in community and primary care, follow-up was relatively short.[15-17] Therefore our knowledge about the naturalistic long-term course of depression in these populations is rather limited, but indispensable to justify a conservative 'wait and see' strategy instead of treatment. From short-term studies we do know that patients experience disability during depressive episodes, but here again we do not have a clear picture of long-term consequences from the patient perspective.[2,4,5]

Concerning treatment, it has been established in many studies, that antidepressants are effective for the treatment of Major Depressive Disorder (MDD)[11,18,19] and perhaps also for minor depression[20-23] (with a high prevalence in community and primary care) but here again, most of these studies had a relatively short follow-up.[24-27]

In analysing long-term outcome of chronic diseases, a number of papers can be found, describing a totally different picture for short-term outcome compared with long-term.[28,29] These demonstrate that short-term effectiveness and safety does not automatically predict long-term outcome. By now the first studies have been published about negative effects of antidepressants[30-33] and some studies even suggest that they might influence the course of depression in a negative way.[34] It is fundamental for good clinical practice, that decisions about treatment are weighed against information about long-term prognosis. Outcome information should be available for all levels of

depression, cases for which no medical attention is sought included, and differences between naturalistic outcome and outcome after treatment should be clear. Therefore we decided to review the literature looking for long-term outcome studies of depression in community and primary care. In these studies we looked for answers to the three following research questions: what is the recurrence rate of depression, can a relation be found between long-term outcome and treatment, and what are the long-term consequences for the health status of the patients involved?

METHODS

Retrieval of the literature

A computerised search was performed in Medline, Psychlit, Current Contents and the Cochrane library (1970-1999). We chose to include studies from 1970 onwards, because about that time modern classification systems were introduced and research diagnostic criteria became available to investigators. Thesaurus and free text words were combined for depression/depressive disorder with general practice/ family practice /primary care or community and follow-up/course/outcome/prognosis.

Selection of the literature

Two reviewers (HS,EvW) made a selection by screening title and abstracts. If an abstract had been selected by one of the reviewers only, it was discussed until consensus was reached.

Inclusion criteria were: original longitudinal follow-up studies (in English) of adult populations in community or primary care with at least 25 patients in the follow-up; criteria for diagnosis were: ICPC or ICHPPC2-defined in general practice studies, DSM-III, III-R or -IV, the Research Diagnostic Criteria (RDC) or immediate predecessor (St Louis), ICD-9-CM or ICD-10.[35,36] As inclusion criteria for outcome of depression we included studies reporting on recurrences, relapses, psychopathology, disability or quality of life at follow-up. We defined long-term as a follow-up of at least 5 years, because recurrences usually occur within this time

frame.[9,13,37] A follow-up of at least five years should give an indication about percentages of single episode depression and recurrence rates.

When abstracts met the inclusion criteria or remained unclear at this point, full articles were retrieved for further evaluation. We retrieved relevant reviews as well. References of all these studies were screened with the ancestry approach. Additionally, a number of experts in the field from The Netherlands, United Kingdom and USA were asked for possible additional references.

Data abstraction and presentation

Because of the wide variation in study designs we limited ourselves to a qualitative evaluation. We abstracted data about design, setting, diagnostic criteria, number and specific diagnosis of depressive patients in the follow-up, age and sex, length of follow-up, treatment and outcomes.

Recurrence rates of minor and major depression were combined because we wanted to be able to compare outcome results of family practice depression, with DSM cases and cases meeting RDC. A total recurrence rate was calculated for all patients still alive and present at the end of the follow-up of each study.

RESULTS

Selection of articles

The computer search supplied 421 potentially relevant articles. Based on the search, the reference lists of 4 review articles, and suggestions of experts, 56 papers were selected. Eight studies met all inclusion criteria: 6 community and 2 primary-care studies. The other studies were excluded for one or more of the following reasons: no longitudinal follow-up study (13), long-term follow-up shorter than 5 years (35), no diagnostic criteria mentioned in the article (4), study population not from community or primary care (5) or to small (1), or outcome results of depression were mixed with other diagnoses (2). Some studies met more than one exclusion criterion.

Table 7.1. Included studies: design, aim and diagnostic criteria

Author, year of publication and country of study	Design	Aim of study	Diagnostic criteria
Community			
Coryell et al[44] 1991, USA	More wave design: cross-sectional screening of *relatives of affectively ill probands*. Structured clinical assessments at follow-up of a defined cohort of depressed subjects.	To describe natural history of Major Depressive Disorder.	RDC
Kua[39] 1993,Singapore	More wave design: cross-sectional screening of *elderly in the community*. Structured clinical assessments at follow-up of a defined cohort of depressed elderly	To study the prognosis of depression in the elderly.	RDC (GMS-AGECAT)
Kivela et al. [40] 1994, Finland	More wave design. cross-sectional screening of *elderly in the community*. Structured clinical assessments at follow-up of a defined cohort of depressed elderly	To study the prognosis of depression in the elderly	DSM-III

Angst et al.[42] 1997, Switzerland	More wave design: cross-sectional screening of a *community sample of young adults*. Structured clinical assessments at follow-up of a defined cohort of depressed young adults.	To study prevalence and treatment-rates, diagnostic overlap and longitudinal stability of subtypes of depression	DSM III, RDC, III-R and IV resp
Eaton et al.[43] 1997, USA	More wave design: cross-sectional screening of a *community sample of adults*. Structured clinical assessments at follow-up of a Defined cohort of depressed adults.	To study outcome of depression.	DSM-IV
Sharma et al.[41] 1998, UK	More wave design: cross-sectional screening of *elderly in the community*. Structured clinical assessments at follow-up of a Defined cohort of depressed elderly	To study nature and outcome of depression in the elderly living in the community and to study predictors of depression.	RDC (GMS-AGECAT)
Primary care			
Widmer et al.[38] 1978, USA	Historic cohort study. Longitudinal follow-up of patients with depression in one solo family practice	To characterize changes in patient behavior associated with a developing depression.	Criteria incorporated in RDC
van Weel et al.[13] 1998, The Netherlands	Historic cohort study. Longitudinal follow-up of patients with depression in 4 primary care practices.	To study outcome of depression in family practice.	E-list, ICHPPC-2

Design of the studies

Table 7 1 gives an overview of the included studies There was only one study from the seventies[38] meeting our criteria, all others were from the last ten years All community studies were cross-sectional in design, three were performed amongst elderly,[39-41] one among young adults living in the community,[42] and the others in community samples in which all ages were represented [43 44] In one of these last two studies the population consisted of family members and relatives of affectively ill probands Both family practice studies had a historic cohort design[13 38] and refer to patients recognized with depression in family practice Data were extracted from patient records and in the second study also from a morbidity registry [13]

The diagnosis of depression and diagnostic criteria

There was only one study using specific family practice criteria (E-list, later ICHPPC-2) [13] In all other studies DSM,[40 42 43] RDC[38 42 44] or criteria derived from the RDC for use in elderly populations[39 41] were used, (obtained with GMS-AGECAT[45]) In the family practice study by Widmer the symptoms on the records were incorporated in the RDC retrospectively

Length of follow-up of depression

Table 7 2 shows length of follow-up, demographics and outcome results as presented in the articles In one study[44] the length of the follow-up since the onset of depression is not clear, because the follow-up concerns community members with a history of depression, without description when the depressive episodes had occurred In all other studies the follow-up length refers to a follow-up starting during a depressive episode One study starts the follow-up at first episodes only [13] This is the only study in which a time relation between the initial diagnosis and recurrences is presented longitudinally One other study starts at initial episodes in the practice,[38] all others start at index and recurrent episodes, but the proportions are not clear

Description of outcomes

Table 7 3 shows the total rates of recurrence, or depression at follow-up These were calculated for all patients available at the end of the follow-up period of each study Recurrence rates of the populations in which no specific age-group was followed-up ranged from 30 to 40% In the two community studies reporting recurrence rates,[43 44] these rates were calculated from data based on retrospective recall of recurrent episodes In these two studies higher recurrence rates were found in the younger age groups The community studies of depression in the elderly and young adults report outcome as depression at follow-up In two of the studies amongst the elderly[39 41] the rates of depression at follow-up were higher than the 30-40% recurrence, found in the follow-up of populations with varying ages One of these studies only reports on major depression at follow-up [41] This is also the case in the study with young adults [42]

In one of the family practice studies the recurrence rates were calculated retrospectively, relying on the symptoms mentioned on the case-records (35% recurrent) In the other study recurrence (40%) was extracted from a morbidity registry and the data checked against symptoms on the patient records [13] Both present the number of recurrences as well In one study 27 % of the followed patients had two, 6 % three and 3 % four or more episodes,[38] in the other the percentages were 16% with two, 12 % with three and 12% with four or more episodes [13]

TREATMENT

Four studies report on treatment, but none of the studies described nature and length of treatment clearly, and treatment was not related to recurrence or depression at follow-up [38 40 42]

Mortality

Results about mortality were given in 4 studies[13 39-41] (rates ranging from 14-44%), but data on suicide attempts and suicide can only be found in one study [13]

Table 7 2 Number of patients, demographics, and outcome of depression

Author and year of publication	Length of follow up in years	Number of patients in follow-up and diagnosis	Age in years	Sex	Outcome results of depression caseness	Treatment
Community						
Coryell et al [44] 1991	6[a]	total 596				
		396 with lifetime history of MDD	39 8 ±14 2 (mean)	33% M	34% recurrent	Not assessed
		200 with lifetime history of mixed MMD[b]	35 7± 11 9 (mean)	46% M	47% recurrent	
Kua [39] 1993	5 after index or recurrent episode	total 56 31, depression 25, subcases	72 4 (mean)	40% M	At follow-up 39 % case + subcase 14% mortality	2 treated[c] 10 treated by traditional healers
Kivela et al [40] 1994	5 after first or recurrent episode	total 264 42, MDD 199, Dysth[d] 21, Atyp[e] 2, Cycl[f]	70 6 (+/- 7 5) (mean)	34% M	At follow-up 25% D (all types) 4% non respon 28% mortality	Treated[g]
Angst et al [42] 1997	7 after first or recurrent episode	160 total 50, MDD 110, sub-cases	20-22 (mean)	M[h]	At follow-up 44% MDD + 24% sub-threshold 29% MDD % subthreshold ?	Treatment rates presented over life-times for subgroups of depression (+ hospitalization rates)

Eaton et al.[43] 1997	Median 12.6 after first or recurrent episode, range 13-15	89 total[i] 54 current depression 35 depression in history	> 18	40% M[j]	26% recurrent 15% lost in follow-up	Not assessed
Sharma et al.[41] 1998	5 after first or recurrent episode	167 total 120, depression	74, (65-93) (mean)	25% M	At follow-up 21% cases 29% dropout 34% mortality	No exact data found but: majority never received appropriate treatment
		47, subcases	73, (65-86) (mean)	34% M	9% cases 21% dropout 25% mortality	
Primary care						
Widmer et al.[38] 1978	median7[1/2] after first or recurrent episode, range 1-24	154, depression	50, (17-86) (mean)	33% M	35% recurrent	88% of episodes treated with Tricyclic Antidepressants, 12% with MAO-inhibitors, ECT and Psychotherapy
Van Weel et al [13] 1998	10 after first episode	222, depression	7% -< 25 43%: 25-<45 43%: 45-<65 15% >65	39%M	40% recurrent	Not assessed

[a] reevaluation 6 years after first interview, time of episode and therefore length of follow-up not clear
[b] history of MDD + nonaffective disorder
[c] nature of treatment and outcome not mentioned
[d] dysthymia
[e] atypical depression
[f] cyclothymic disorder
[g] nature and numbers unknown
[h] percentages not mentioned
[i] depressive syndrome
[j] description for incident cases only

Table 7.3. Recurrence and depression rates at follow-up[a] in community and primary care

Study	Number of patients at follow-up	Length of the follow-up in years	Depression at intake	Outcome
Community				
Coryell et al.[44] 1991	596	6[b]	Major	38% recurrent (MDD)
Kua[39] 1993	48	5	Major + minor	46% depressed at follow-up
Kivela et al.[40] 1994	178	5	Major + minor	38% depressed at follow-up
Angst et al.[42] 1997	160	7	Major + minor	34% depressed at follow-up (MDD) % subthreshold unknown
Eaton et al.[43] 1997	46	12.6	Major + minor	30% recurrent
Sharma et al.[41] 1998	67	5	Major + minor	43% depressed at follow-up % of subcases unknown
Primary care				
Widmer et al.[38] 1978	154	7 5	Major + minor	35% recurrent
Van Weel et al.[13] 1998	222	10	Major + minor	40% recurrent

[a] calculated for all patients available at the end of the follow-up of each study

[b] since intake interview with patients with history of depression

Health status

Two studies reported on health status or disability but in a different way. In one this disability was linked to depressive episodes that occurred during the follow-up.[44] The other study reported on health status at the end of the follow-up. Forty-six percent of the patients (elderly in this case) reported a poor health status at follow-up, but no relation was found between outcome and perceived health status.[40]

DISCUSSION

Studies about long-term outcome of depression in community and primary care are scarce and difficult to compare. Methodological shortcomings hamper their generalizability.

Referring to our research questions, our data suggest that overall recurrence rates in community and family practice vary between 30 and 40%. The relation between treatment and long-term outcome remains unclear as none of the studies looked into this matter. This also applies to the patient perspective. Almost all studies report exclusively on recurrence, or depression at follow-up, and data do not justify conclusions about long-term outcome of quality of life.

Recurrence rates of 30 - 40% indicate that the prognosis of depression in community and family practice is not as poor as in psychiatry. In psychiatric settings much higher recurrence rates are found, with percentages of up to almost 90%, depending on the length of follow-up and the setting.[9,10,37] We found prognosis to be related to age, young adults diagnosed with depression having a poorer prognosis. Between 30 and 40% of the patients were depressed at follow-up but the results did not include minor depression at follow-up. Furthermore, as the results were presented as depression at follow-up, they do not include recurrences between the follow-up interviews. It is therefore likely that recurrence rates were higher. Higher recurrence rates were found in the younger age groups in two of the community studies[43,44] as well. A poor prognosis for the elderly was found in the studies performed with elderly only, which all report on depression at follow-up,[39-41] but was not confirmed in the two community studies with varying ages and one general practice study.[13,43,44]

This might be explained by the fact, that in the studies with elderly, diagnostic instruments were used, specifically meant for detection of depression amongst elderly. Another explanation might be, that differences were not found because of the relatively small numbers of elderly present in the other studies.

Limitations of the studies

In the community studies subjects were identified with screening instruments. Therefore a number of false positive diagnoses may have been included in these studies and biased outcome results.[46] This risk was minimized by using interviews in addition to the screening instruments. Another important limitation is the risk of missing part of the information about recurrences in the intervals between assessments. In two of the included studies, data about the interval were retrieved using information based on patients recall.[40,43] This method is known to introduce bias: recall does not always give sufficient details after longer periods of time.[47] In the family practice studies, where the specificity of the diagnosis is usually high,[48,49] outcome results may have been biased because results of undetected or misdiagnosed patients with depression were missing. In both studies the information was retrieved from the case-records. Accuracy therefore depended on the completeness of doctors notes. In one of the studies the case-records were used in addition to data from a morbidity registry in which doctors are regularly trained regularly to use criteria for diagnosis. Although suicide data can be found in this study, patients who left the practices or died within ten-years were excluded and outcome results should be viewed taking this into consideration. An important shortcoming is that most studies started at first or recurrent episodes, so it is not possible to give an exact percentage of single episode depression versus recurrent illness. A description of the longitudinal course starting at first diagnosis is also not possible. Even in the one study starting at the first episode we can only draw conclusions about recurrence rates after diagnosis, because we have no certainty that the first diagnosis was in fact the first depressive episode. Other shortcomings were the small number of patients in the follow-up in two[39,43] and uncertainty about representativeness of the samples in

one of the community studies.[39,41,42,44] As a family history with depression is a risk-factor for depression in an individual,[50] the population of family members of affectively ill probands can also not be regarded as a representative community sample.

Limitations of the review

Although our choice of inclusion criteria was made to guarantee a good comparability, we realize that 'older' studies were excluded from this review[51,52] and so were studies in which data on depression could not be extracted from a broader variety of mental illness in family practice.[53] We also made the choice to describe a limited number of outcomes, but the small number of studies included, and the variety within the studies did not allow a review of more outcome results.

Although the calculation of a total recurrence rate may be criticized, we believe that the fluctuating nature of depression justifies this procedure.

CONCLUSIONS

We conclude that there are still large gaps in the available knowledge about long-term outcome of depression in primary care and future studies are required to fill-in these gaps. We recommend that

- the outcome of all types of depression is evaluated in prospective studies with a follow-up of at least five years, in representative samples in both community and primary care
- continuous morbidity registration is used preferably
- studies include naturalistic follow-up and relate treatment to outcome.
- quality of life assessment is included as well.

In the mean time, as a consequence of our findings, family practitioners could reassure a patient with depression by telling, that although the long-term outcome of the illness is not completely clear, there are indications that the majority of the patients with depression do not have such a poor prognosis. This might add to their recovery.

REFERENCES

1 Froom J, Aoyama H, Hermoni D, et al Depressive disorders in three primary care populations United States, Israel, Japan *Fam Pract* 1995,**12** 274-8

2 Ormel J, VonKorff M, Ustun TB, et al Common mental disorders and disability across cultures Results from the WHO Collaborative Study on Psychological Problems in General Health Care *JAMA* 1994,**272** 1741-8

3 Robins LN Lifetime prevalence of specific psychiatric disorders in three sites *Arch Genl Psychiatry* 1984,**41** 949-58

4 Williams JW, Kerber CA, Mulrow CD, et al Depressive disorders in primary care prevalence, functional disability, and identification *J Gen Intern Med* 1995,**10** 7-12

5 Wells KB, Stewart A, Hays RD, et al The functioning and well-being of depressed patients Results from the Medical Outcomes Study [see comments] *JAMA* 1989,**262** 914-9

6 Katon W, Schulberg H Epidemiology of depression in primary care *Gen Hosp Psychiatry* 1992,**14** 237-47

7 Coryell W, Turvey C, Endicott J, et al Bipolar I affective disorder predictors of outcome after 15 years *J Affect Disord* 1998,**50** 109-16

8 Paykel ES Historical overview of outcome of depression *Br J Psychiatry* 1994, **Suppl** 6-8

9 Angst J, Preisig M Course of a clinical cohort of unipolar, bipolar and schizoaffective patients Results of a prospective study from 1959 to 1985 *Schweiz Archiv Neurol Psychiatr* 1995,**146** 5-16

10 Piccinelli M, Wilkinson G Outcome of depression in psychiatric settings *Br J Psychiatry* 1994,**164** 297-304

11 Lavori PW, Keller MB, Mueller TI, et al Recurrence after recovery in unipolar MDD An observational follow-up study of clinical predictors and somatic treatment as a mediating factor *Intern J Methods Psych Research* 1994,**4** 211-29

12 Blacker CV, Clare AW Depressive disorder in primary care *Br J Psychiatry* 1987,150 737-51

13 Weel-Baumgarten E van, Bosch W van den, Hoogen H van den, et al Ten year follow-up of depression after diagnosis in general practice *Br J Gen Pract* 1998,**48** 1643 6

14 Watts CA Depressive disorders in the community the scene in Great Britain, 1965 *J Clin Psychiatry* 1984,**45** 70-7

15 Klinkman MS, Schwenk TL, Coyne JC Depression in primary care--more like asthma than appendicitis the Michigan Depression Project *Can J Psychiatry* 1997,**42** 966-73

16. Lin EH, Simon GE, Katon WJ, et al. Can enhanced acute-phase treatment of depression improve long-term outcomes? A report of randomized trials in primary care. *Am J Psychiatry* 1999;**156**:643-5.

17 Ormel J, Oldehinkel T, Brilman E, et al. Outcome of depression and anxiety in primary care. A three-wave 3 1/2-year study of psychopathology and disability. *Arch Gen Psychiatry* 1993;**50**:759-66.

18 Kupfer DJ. Long-term treatment of depression. *J Clin Psychiatry* 1991;**52 Suppl**:28-34.

19. Prien RF Efficacy of continuation drug therapy of depression and anxiety: issues and methodologies. *J Clin Psychopharmacol* 1990;**10**:86S-90S

20 Tan RS, Barlow RJ, Abel C, et al The effect of low dose lofepramine in depressed elderly patients in general medical wards. *Br J Clin Pharmacol* 1994;**37**:321-4.

21. Thompson C, Thompson CM. The prescribing of antidepressants in general practice: II. A placebo-controlled trial of low-dose dothiepin. 1989;

22. Wernicke JF, Dunlop SR, Dornseif BE, et al. Low-dose fluoxetine therapy for depression. *Psychopharmacol Bull* 1988;**24**:183-8

23 Paykel ES, Freeling P, Hollyman JA. Are tricyclic antidepressants useful for mild depression? A placebo controlled trial. *Pharmacopsychiatry* 1988;**21** 15-8.

24. Hollyman JA, Freeling P, Paykel ES, et al Double-blind placebo-controlled trial of amitriptyline among depressed patients in general practice *J R Coll Gen Pract* 1988;**38**:393-7

25 Mynors WL, Gath D. Predictors of treatment outcome for major depression in primary care. *Psychol Med* 1997,**27**:731-6

26. Scott AI, Freeman CP Edinburgh primary care depression study: treatment outcome, patient satisfaction, and cost after 16 weeks [see comments]. *Br Med J* 1992,**304**:883-7.

27. Schulberg HC, Block MR, Madonia MJ, et al Treating major depression in primary care practice Eight-month clinical outcomes. *Arch Gen Psychiatry* 1996,**53**:913-9.

28 Pincus T, Stein CM. Why randomized controlled clinical trials do not depict accurately long-term outcomes in rheumatoid arthritis. some explanations and suggestions for future studies. *Clin Exp Rheumatol* 1997,**15 Suppl 17**:S27-S38

29. Wolfe F, Hawley DJ, Cathey MA Clinical and health status measures over time: prognosis and outcome assessment in rheumatoid arthritis. *J Rheumatol* 1991,**18**:1290-7.

30 Abajo FJ de, Rodriguez LA, Montero D. Association between selective serotonin reuptake inhibitors and upper gastrointestinal bleeding: population based case-control study [see comments]. *Br Med J* 1999,**319**:1106-9.

31. Po AL. Antidepressants and upper gastrointestinal bleeding [editorial; comment]. Br Med J 1999;**319**:1081-2.

32. Mackay FR, Dunn NR, Martin RM, et al. Newer antidepressants· a comparison of tolerability in general practice. *Br J Gen Pract* 1999;**49**:892-6.

33. Sampson E, Warner JP. Serotonin syndrome:potentially fatal but difficult to recognize. *Br J Gen Pract* 1999;**49**:867-8.

34. Tondo L, Laddomada P, Serra G, et al. Rapid cyclers and antidepressants. *Int Pharmacopsychiatry* 1981;**16**:119-23.

35. Classification committee of WONCA. *ICHPPC-2-defined (International classification of Health Problems in Primary Care)*. third ed. Oxford. Oxford University Press; 1983

36 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. [4th edition.] Washington DC: American Psychiatric Association, 1994

37. Londen L van, Molenaar RP, Goekoop JG, et al. Three- to 5-year prospective follow-up of outcome in major depression. *Psychol Med* 1998;28:731-5.

38. Widmer RB, Cadoret RJ. Depression in primary care: changes in pattern of patient visits and complaints during a developing depression. *J Fam Pract* 1978;**7**:293-302.

39. Kua EH. The depressed elderly Chinese living in the community. A five-year follow-up study. *International Journal of Geriatric Psychiatry* 1993;**8**:427-30.

40. Kivela SL, Kongas SP, Kesti E, et al Five-year prognosis for depression in old age. *Int Psychogeriatr* 1994;**6**:69-78.

41. Sharma VK, Copeland JR, Dewey ME, et al. Outcome of the depressed elderly living in the community in Liverpool: a 5-year follow-up. *Psychol Med* 1998;**28**:1329-37.

42. Angst J, Merikangas K. The depressive spectrum: diagnostic classification and course. *J Affect Disord* 1997;**45**:31-9.

43. Eaton WW, Anthony JC, Gallo J, et al. Natural history of Diagnostic Interview Schedule/DSM-IV major depression. The Baltimore Epidemiologic Catchment Area follow-up. *Arch Gen Psychiatry* 1997;**54**:993-9.

44 Coryell W, Endicott J, Keller MB. Predictors of relapse into major depressive disorder in a nonclinical population. *Am J Psychiatry* 1991,**148** 1353-8

45. Copeland JR, Dewey ME, Griffiths-Jones HM A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. *Psychol Med* 1986;**16**:89-9.

46. Nagel R, Lynch D, Tamburrino M. Validity of the medical outcomes study depression screener in family practice training centers and community settings. *Fam Med* 1998;**30**:362-5.

47. Andrews G, Anstey K, Brodaty H, et al. Recall of depressive episode 25 years previously. *Psychol Med* 1999;**29**:787-91

48 Wright AF. Should general practitioners be testing for depression? *Br J Gen Pract* 1994;**44**:132-5.

49. Weel C van. Validating long term morbidity recording. *J Epidemiol Community Health* 1995;**49 Suppl 1**:29-32.

50. Merikangas KR, Wicki W, Angst J. Heterogeneity of depression. Classification of depressive subtypes by longitudinal course. *Br J Psychiatry* 1994;**164**:342-8.

51. Murphy JM, Olivier DC, Sobol AM, et al. Diagnosis and outcome· depression and anxiety in a general population. *Psychol Med* 1986;**16**:117-26.

52. Hagnell O, Lanke J, Rorsman B Suicide and depression in the male part of the Lundby study. Changes over time during a 25-year observation period *Neuropsychobiology* 1982;**8**:182-7.

53. Lloyd KR, Jenkins R, Mann A. Long-term outcome of patients with neurotic illness in general practice. *Br Med J* 1996;**313**.26-8.

'Ik ben 92 en woon nog steeds zelfstandig. Maar ik voel me vaak eenzaam en somber. Ik ben vaak erg moe en heb dan ook veel andere klachten. Maar als ik bezoek heb, dan voel ik ze niet. Ik zou graag naar een verzorgingshuis willen, maar ze vonden me te goed. Ik denk dat ik me veel beter zou voelen als ik meer aanspraak had. Ik mag wel naar een dagopvang, maar dat gedoe met vervoer daar word ik juist zo moe van. Mijn kinderen wonen verder weg, ik wil ze niet tot last zijn. Ik denk wel veel over de dood. Mijn geloof verbiedt zelfmoord, maar ik denk wel vaak: Onze Lieve Heer mag me nu wel komen halen, er is niet veel lol meer aan.'

'I am 92 and still live on my own. But I often feel lonely and sad. And also very tired and then I have a lot of other problems as well. But when I have company, I don't have any problems. I would really like to move to a home for the elderly, but they told me I couldn't because I appear to manage so well. I think I would feel much better if I had more company. They cán offer me day-care, but transport is such a problem.
My children don't live very near, and I don't want to be a burden on them.
I think a lot about death. I would never commit suicide because of my faith, but I often think: I wish the Good Lord would come and take me now, there isn't much fun left.'

Chapter 8

Summary and general discussion

The aim of this study was to obtain a broader knowledge of the long-term outcome of depression in general practice. With the extensive longitudinal data of the Continuous Morbidity Registry (CMR), we were able to follow-up a historic cohort of 222 patients for ten years after the first diagnosis. We established how often these patients had recurrences (definition of recurrence: a new episode meeting ICHPPC-2 criteria after at least three months without presenting with depressive symptoms). We also established their rates of referral, admission to hospital, suicide attempts and treatment. Of these 222 patients (with a first depressive episode before 1984), 126 were still registered with the practices by the end of 1998. Current psychopathology, health status, coping behaviour and social support was studied in these patients. Because in the CMR, data are available of the total populations registered with the 4 practices, we were not only able to identify patients with depression, but control groups and patients with chronic nervous functional complaints (CNFC) as well. These populations were used for the comparison with patients with depression in studying the diagnosis of depression, and the psychopathology, health status, coping behaviour and social support.

OUTCOMES AFTER 10 YEARS OF FOLLOW-UP

In chapter 2 we described recurrence rates, number and length of episodes, referrals, admission to hospital, and data on suicide of patients with depression in the general practices of the CMR. Of our historic cohort of 222 patients, about 60% experienced only one episode of depression in a follow-up of as long as ten years after the index episode. Mean length of the first episodes was 103 days. Of all patients, 15% were referred within primary care (to a psychologist or social worker). Also 15% were referred to psychiatry, and 9% (of 222) were admitted to hospital for depression in the 10-year period of the follow-up. Of our research population, 4% made a suicide attempt. Because we had excluded patients who had died within the study period and therefore were not able to get data about death by suicide in this cohort, we used a different method. We calculated the suicide rate by using data of all patients with a

code for depression before 1984, for as long as they were registered in the CMR. Death by suicide had occurred in about 0.5% of these patients.

Our results seem to indicate that the long-term outcome of depression is more favourable than in psychiatry, where much higher recurrence rates have been found, sometimes even as high as almost 90% in patients admitted to hospital for depression.[1] Suicide rates confirm this better prognosis, as in psychiatry suicide rates of between 7 and 20% have been reported.[2,3] Our decision to include only the 222 patients who could be followed up for ten years, excluding patients, who had left or died before the end of the study period, could have introduced a bias. We studied the mortality of the patients lost to follow-up. Although 2 patients had committed suicide, the overall mortality was not significantly higher than of a control group matched for age, sex and practice. Nevertheless in interpreting our results, the method we used should be kept in mind.

TREATMENT

In chapter 3, where we deal with the questions about treatment, we show that about 70% of all 222 patients had been treated with antidepressants, at some time during the follow-up, of patients with recurrences this was even 94%. In 78% of the medication episodes the PDD/DDD ratios of the prescriptions with antidepressants had a value of less than 1 (the assumed average effective daily dose).[4] The length of the medication episodes was short, in 24% even shorter than 28 days. Furthermore, the majority (86%) of the patients had received other psychotropics as well, mainly benzodiazepines.

When we focussed on the first episode of patients with and without recurrences, we discovered that although more patients with than without recurrences had received prescriptions for antidepressants, in both groups the doses were too low and length on the prescriptions too short. The patients with recurrences had received significantly more prescriptions for minor tranquillisers. They were not referred more often.

We concluded that the treatment received by the 222 patients in our historic cohort did not meet the standard of current guidelines on depression. But

nevertheless, the majority of these patients had no recurrences. The results in chapter 2 together with these results on treatment offer support for a view that outcomes of depression in primary care and secondary care are not identical. They add to a more balanced view about the long-term outcome of depression. That the majority of the patients did not have recurrences in spite of the 'inadequate treatment' might indicate that depression in primary care is self-limiting in many cases, or that lower doses might be effective in general practice.

Because usually only the more severe and persistent cases of depression are referred to secondary care, finding a better prognosis in general practice is not unexpected.
But how large the proportions of the various levels of severity of depression are in general practice, and if it mainly concerns the less serious cases, is not clear. This leads to questions about the diagnosis.

THE DIAGNOSIS

In chapter 4 we focussed on this diagnosis. We studied the specificity of the diagnosis of depression, made by the general practitioners in the CMR, in a second study population and also looked for 'missed depression' cases in two patient categories. A total of 99 patients were interviewed with the 12-month computerised version of the CIDI, a validated instrument classifying diagnoses of mental illness which have occurred in the past 12 months, according to DSM-IV criteria. Patients were interviewed by a clinician, trained in the rules of this instrument. One third of the 99 patients (for the interviews) had a general practice code for depression, one third for chronic nervous functional complaints (testing our hypothesis that in this category depression was likely to be overlooked) and one third did not have a code for a mental illness (for all three categories referring to the previous 12 months).
We showed that when a diagnosis of depression had been made, the validity of the general practice diagnosis was very high. Our results confirm earlier findings that when general practitioners make a diagnosis the specificity is high.[5] There was also a high accordance with the criteria of the DSM-IV for Major Depressive Disorder (79%).

These results show, that most patients diagnosed with depression in the general practices in our study also met criteria for a 'major' depression. The general practitioners seemed to detect the more serious cases. This puts our long-term outcome results in a new light. Finding a more favourable outcome is remarkable because in major depression the expected outcome is worse and the patients in our historic cohort had not received guideline concurrent treatment.

We have to make a restriction here. The interviews in this part of the study were held recently. Recurrence rates were calculated in a historic cohort of patients of whom the diagnoses of depression were made years ago and could not be validated anymore. However, we have no reason to believe that the validity of diagnoses made in the same registry years ago was lower. The doctors were using the same criteria as today (E-list, ICHPPC-2[6,7]), monthly quality assurance meetings were routine already, and only very few changes of doctors have occurred since the start of the registry. The high reliability of CMR data recording has been demonstrated in many studies about a variety of subjects over the years.[8 12]

Concerning the matter of general practitioners missing the diagnosis: no depression was found in the controls, but about 20% of the patients presenting with chronic nervous functional complaints met criteria for a diagnosis of MDD. These results can only give an indication of where depression might have been overlooked, as the number of patients was small and therefore the sensitivity could not be measured accurately. Although this confirms results of other studies about underdetection of depression by general practitioners, it is also conceivable that in a number of patients there might be reasons, of doctors as well as patients, why symptoms are labelled otherwise. For doctors these reasons might include doubts whether making a diagnosis of depression has advantages for every patient, in particular when they believe there is no immediate need for treatment. For patients these reasons might include resistance to be labelled as depressive out of fear to be stigmatised by a diagnosis of depression, but also dislike of treatment, in particular medication. Having different beliefs about their symptoms than their doctor, might also be a

reason for patients to influence doctors to label the symptoms otherwise and not to make a diagnosis of depression [13]

Earlier we concluded that the long-term prognosis of patients with depression diagnosed in general practice is not so poor as in psychiatry, including many patients with major depression What remains unclear is the long-term outcome of the 'unidentified cases' and if labelling otherwise has adverse effects on their long-term outcome We pointed out that a number of these unidentified cases might be found among patients with CNFC

OUTCOMES MORE THAN 15 YEARS AFTER THE FIRST DEPRESSIVE EPISODE

Pursuing questions about the long-term outcome of depression in general practice, we focussed on doctor and patient perspective even longer after the depression Chapter 5 reports the results of psychopathology, health status, coping behaviour, and social support of patients with a history of depression at least 15 years ago (divided up into with and without recurrences) Questionnaires were sent to the 126 patients from our historic cohort of 222, who were still registered with the practices at the time this part of the study was performed We discovered that patients without recurrences had higher psychopathology levels than controls (patients without any diagnosis of a mental disorder) and did not differ significantly from patients with recurrences This included higher levels of depression, but the variety was broader Furthermore, patients with recurrences reported lower health status scores than the controls In the domains bodily pain, vitality, role limitation due to mental problems and mental health these differences were significant For patients without recurrences the difference with normal controls was only significant where mental health was concerned

These higher levels of psychopathology and lower mental health status scores of the patients without recurrences might seem to contradict our earlier conclusions about a more favourable outcome of depression, for most patients in general practice But having higher levels of psychopathology does not necessarily mean having a mental disorder Among normally functioning people in the community there are also psychological complaints and their mood has a broad variety In stead of explaining the

psychopathology of patients without recurrences as residual symptoms of depression and therefore as a result of their depression, this psychopathology might just as well have been present already before the depression, and characteristic for these patients. Perhaps this was even the reason why they were vulnerable. It is the question if this vulnerability originated from the depressive episode or the depression from the vulnerability. That in almost all domains, patients without recurrences reported normal functioning, even with higher levels of psychopathology than normal controls, might be in support of the view that some of the symptoms were characteristic for them and that they were back to 'normal'. For patients with recurrences this was not the case, they were more impaired than controls. As we did not have any data of before the first depressive episode this theory remains a hypothesis.

In this part of the study we also found that patients with recurrences did worse on emotional coping than controls. Because patients without recurrences did not, we concluded that difficulty with emotional coping might make patients susceptible for recurrences of depression. Although we had expected to find differences in social support, we did not.

We concluded that awareness of these higher psychopathology levels and lower health status of patients with a history of depression, should lead to an attentive follow-up over a long period of time.

OUTCOMES OF PATIENTS WITH CNFC

In chapter 6 the results can be found of extending our questions about long-term outcome from doctor and patient perspective to a broader population. Patients with chronic nervous functional complaints were included in this part of the study because we had already discovered that a number of cases of missed depression were 'hidden' in this category. We therefore tried to establish more characteristics of these patients. With this aim we studied their psychopathology, health status, coping behaviour, and social support and looked, in particular, if and how they differed from patients with a history of depression and normal controls. Our results show that these patients had more psychopathology and a lower health status than normal controls and they did not

differ significantly from patients with a history of depression in this respect. They also reported significantly lower scores of daily social support, contrary to the patients with a history of depression. As patients with depression have high psychopathology and low health status levels, our results in the CNFC patients seem to confirm our earlier findings that depression might be hidden behind the functional complaints. Most likely not only depression, but other specific mental disorders as well. The results on health status also seem to indicate that these patients do not just have a characteristic that is annoying for both doctor and patient, but they are ill and perceive disability. Making a 'diagnosis' of chronic nervous functional complaints might open the possibility of a more accurate follow-up with, in the course of time in a number of patients with these complaints, more specific diagnoses of mental disorders as a result. As the low health status concerned the total group of patients with CNFC and we were particularly interested in the long-term outcome of depression, these results make us wonder about the outcome of the subgroup of patients with depression, who are probably hidden in this category.

LONG-TERM FOLLOW-UP STUDIES IN COMMUNITY AND PRIMARY CARE

After having studied a number of long-term outcomes of depression in general practice we conducted a systematic review of the literature on long-term follow-up studies in community and primary care, with the aim to compare our results with those of other studies. Only very few studies could be found with a follow-up of more than five years in these populations, and meeting previously determined criteria. The recurrence rates mentioned in these studies were comparable with our findings. Recurrence rates of between 30 and 40% were reported in the studies with populations in which varying ages were represented. Three community studies, one specifically on young adults, and two with populations of various ages showed higher recurrence rates in the younger age groups. Higher recurrence rates were also found in studies specifically looking at depression in the elderly. In both general practice studies, in which all ages were represented, these higher recurrence rates for young adults and elderly had not been found. This might have been due to the small percentages of younger and elderly

patients in these studies. Concerning the elderly, it is also conceivable that general practitioners overlooked recurrences in patients presenting with physical illness or anxiety symptoms, where in community studies screening for depression with specific diagnostic instruments these recurrences were identified. General practitioners might also attribute depressive symptoms to 'normal' sadness due to loneliness or recent losses. If they believe treatment for depression, with antidepressants, is not the best solution for the problems, they might choose not to make a diagnosis of (first or recurrent) depressive illness.

There were only two long-term studies with results on health status, both with a very different method, and no studies with results about the relation between treatments and long-term outcome. Therefore no further hard conclusions seemed justified about these outcomes.

MAIN CONCLUSIONS FROM OUR OWN STUDY RESULTS

Concerning the diagnosis

When the general practitioners in our study, using criteria for diagnosis, made a diagnosis of depression, it had a high validity and a high accordance with criteria for major depression. They seemed to be detecting the more serious cases. If criteria are the golden standard for a diagnosis of depression, there was also underdetection. Cases meeting the criteria for depression could be found particularly in a category of patients, defined in the CMR as chronic nervous functional complaints.

Concerning the prognosis

In the identified cases of depression in the CMR, (with a high proportion of major depression), about 60% of patients did not have any recurrences in the ten years following the first diagnosis. The general practitioners did not always follow the recommendations in guidelines concerning treatment for depression. Of the majority of the prescriptions with antidepressants, the doses were too low and the length of the prescriptions too short. That the majority of the patients in our study did not have

recurrences in spite of the 'inappropriate' treatment, supports the view that depression in general practice is mainly self-limiting.

Concerning the long-term outcome from the patient perspective

Patients with a history of depression and no recurrences, reported normal functioning in most domains, long after their first and only episode of depression. They only reported problems concerning their mental health. Patients with recurrences reported a lower health status in a broader variety of domains. Among patients with chronic nervous functional complaints a broad variety of psychopathology was found, and they were really bothered by their symptoms. They did not only rate the quality of their mental health as low, but their quality of life as a whole.

This study answered a number of questions but also generated many others. Therefore we have the following recommendations.

RECOMMENDATIONS FOR FUTURE STUDIES

First of all, as our results were obtained in the Dutch health-care system, in the specific situation of the CMR practices, we realise that our results can not automatically be generalised. Long-term follow-up studies should therefore be performed in a broad variety of general practices and in other countries and cultures as well. As mentioned earlier, our results may have been biased by the decision to include only patients who could be followed up for the full ten-years. Therefore we recommend to include as many patients with depression as possible and study outcome longitudinally, for example with a survival method. In that way data of the longest possible follow-up for every patient can be included, starting at the first diagnosis. Mortality data should also be included in these studies.

Prospective studies with a longitudinal follow-up and continuous data collection will also create the opportunity to study the relation between various treatments and long-term outcome, and look for reasons why doctors do not follow the guidelines.

We did not look for possible predictors of long-term outcome, for example co-morbidity with physical and mental illness, which is a limitation of our study. We recommend that this subject will be included in future studies as well.

Another challenge is research about the outcome of cases, not identified in general practice as depression, up to now only possible in the community. With this aim we recommend to study patients with chronic nervous functional complaints, or however patients with this type of complaints are labelled in other general practices, more in depth. It would be interesting to find out what motives general practitioners have for this label and for not diagnosing depression in a number of these patients. Outcome of these complaints should be followed up longitudinally. However, as we found high psychopathology levels among these patients, diagnostic instruments should be used to identify cases of specific mental illness. Next, outcomes can be studied in patients with and without a diagnosis of a specific mental disorder. These outcomes should include quality of life and changes due to detection and treatment.

CONSEQUENCES FOR GENERAL PRACTICE

As long as long-term outcome of depression is not completely clear, general practitioners could inform patients, consulting with them for depression, that there are strong indications that many patients with depression in general practice do not have recurrences. This message might add to their recovery and perhaps take away some of the fear for this diagnosis and resistance to be labelled as such.

We also recommend an accurate follow-up of patients with a history of depression. If higher psychopathology levels are identified and 'treated', perhaps a number of recurrences can be prevented.

Recommendations about treatment are more difficult to make. As our study results demonstrated that many patients had no recurrences in spite of the 'inadequate' treatment, a 'wait and see' policy might be an option. We then recommend an accurate follow-up. On the other hand, because treatment lacked adequacy, we could not establish if treatment according to guidelines might have contributed to a better long-term outcome in a number of cases. Therefore it is also defendable to

recommend following the current guidelines, if a decision is made that treatment with antidepressants is necessary. Short-term as well as long-term effects should then be studied and registered accurately. By clearly explaining what is to be expected of medication, improvement of the symptoms (and the length of time this usually takes), but expected side effects as well, compliance might increase. This also might add to the effectiveness.

We also want to draw attention to a special category of patients in general practice. In the CMR they are called patients with chronic nervous functional complaints, in other practices for example frequent complainers, frequent attenders or somatizing patients. In consultations with these patients, general practitioners should be aware that they are easily distracted by these complaints, and might overlook diagnoses of specific mental disorders. We recommend using criteria for diagnosis, in particular when presenting with this kind of symptoms becomes a pattern for a patient. This approach might change this type of consultations from a repeatedly annoying into a rewarding experience for both doctor and patient. In cases where a specific diagnosis is made, specific treatment comes within reach. For the other patients in this category treatment efficacious for a number of specific functional syndromes, as for example cognitive behavioural therapy, might be an option.

REFERENCES

1. Angst J, Preisig M. Course of a clinical cohort of unipolar, bipolar and schizoaffective patients: Results of a prospective study from 1959 to 1985 *Schweiz Archiv Neurol Psychiatr* 1995;**146**:5-16
2. Kiloh LG, Andrews G, Neilson M. The long-term outcome of depressive illness. *Br J Psychiatry* 1988,153.752-7
3. Angst J. The course of affective disorders. *Psychopathology* 1986,**19 Suppl 2**:47-52.
4. WHO Collaborating Center for Drugs Statistics Methodology. *Guidelines for ATC classification and DDD assignment.* 1st edn ed. Oslo: 1996
5. Wright AF. Should general practitioners be testing for depression? *Br J Gen Pract* 1994;**44**:132-5.
6. Hodgkin K. *Towards earlier diagnosis in primary care.* 2 ed. Edinburgh: Chrchill Livingstone, 1966
7. Classification committee of WONCA. *ICHPPC-2-defined (International classification of Health Problems in Primary Care).* third ed. Oxford· Oxford University Press; 1983
8. Weel C van, Bosch WJ van den, Hoogen van den, et al Development of respiratory illness in childhood--a longitudinal study in general practice. *J R Coll Gen Pract* 1987;**37**:404-8.
9. Boogaard C van den, Hoogen HJ van den, Huygen FJ, et al. The relationship between breast-feeding and early childhood morbidity in a general population. *Fam Med* 1991;**23**:510-5.
10. Bosch WJ van den, Hoogen HJ van den, Huygen FJ, et al. Morbidity from childhood to adulthood. The medical life history of 103 patients *Fam Pract* 1992,**9**:290-4.
11. Gijsbers-van-Wijk CM, Kolk AM, Bosch WJ van den, et al. Male and female health problems in general practice: the differential impact of social position and social roles. *Soc Sci Med* 1995;**40**:597-611
12. Kolnaar B, Beissel E, Bosch WJ van den, et al. Asthma in adolescents and young adults: screening outcome versus diagnosis in general practice. *Fam Pract* 1994,**11**:133-40.
13. 'You're depressed'; 'no I'm not': GPs' and patients' different models of depression. UMDS MSc in General Practice Teaching Group. *Br J Gen P*ract 1999;**49**·123-4

Chapter 9

Samenvatting en algemene discussie

Deze studie had als doel meer te weten te komen over het lange termijn beloop van depressie bij patiënten in de huisartspraktijk.

Door gebruik te maken van Continue Morbiditeits Registratie (CMR), bleek het mogelijk een historisch cohort van 222 patiënten met de diagnose depressie gedurende 10 jaar vanaf de datum dat de diagnose bij hen voor het eerst werd gesteld longitudinaal te volgen. Bij deze patiënten bestudeerden wij recidief frequenties (definitie van een recidief: een nieuwe episode die voldeed aan ICHPPC-2 criteria, na tenminste drie maanden zonder presentatie van depressie symptomen), gegevens over verwijzing en opname in verband met de depressie, zelfmoordpogingen en behandeling. Van de 222 patiënten (met een eerste episode van depressie voor 1984), bleken er 126 eind 1998 nog in de praktijken te zijn ingeschreven. Bij hen deden wij onderzoek naar psychische klachten, algemene gezondheidstoestand, coping gedrag en sociale steun. Via de CMR, waarin gegevens beschikbaar zijn van de totale populatie die bij de vier praktijken staat ingeschreven, werden ook controle groepen van patiënten zonder psychische klachten en met chronisch nerveus functionele klachten (CNFK) geïdentificeerd. Gegevens over de diagnose, psychopathologie, algemene gezondheidstoestand, coping gedrag en sociale steun van deze patiënten werden vergeleken met die van patiënten met een depressie.

GEGEVENS OVER HET BELOOP GEDURENDE DE EERSTE 10 JAAR

In hoofdstuk 2 worden de resultaten gepresenteerd van het onderzoek bij een historisch cohort van 222 patiënten met een depressie, uit de CMR praktijken. In dit deel van de studie werd gekeken naar recidief percentages, aantal en lengte van depressie episodes, verwijzingen, opnames in het ziekenhuis en gegevens over suïcidepogingen. Ongeveer 60% van deze patiënten bleek gedurende de eerste tien jaar vanaf de diagnosedatum slechts één depressie episode te hebben doorgemaakt. De eerste depressie episode duurde gemiddeld 103 dagen. Vijftien procent van de 222 patiënten bleek in de periode van 10 jaar vanaf de eerste diagnose verwezen te zijn binnen de eerste lijn (naar een psycholoog, RIAGG of het maatschappelijk werk), ook 15% naar de tweede lijn en 9% (van de 222) werd in het ziekenhuis opgenomen in verband met

de depressie. Vier procent van onze onderzoekspopulatie had een zelfmoordpoging gedaan. Omdat we vanwege de gekozen studieopzet bij het cohort geen gegevens over geslaagde suïcides konden krijgen, gebruikten we hiervoor een andere methode. We bestudeerden de suïcidegegevens van alle patiënten met een code voor depressie voor 1984 gedurende de hele periode dat zij in de CMR geregistreerd stonden. Daaruit bleek dat ongeveer 0.5% van deze patiënten was overleden als gevolg van suïcide.

Onze gegevens over het lange termijn beloop van depressie lijken te wijzen op een gunstiger beloop in de huisartspraktijk dan in de psychiatrie. Bij onderzoek in de tweede lijn werden veel hogere recidiefpercentages gevonden, oplopend tot bijna 90% bij patiënten die wegens depressie in het ziekenhuis waren opgenomen.[1] Ook onze suïcidegegevens wijzen op deze gunstigere prognose. In de tweede lijn wordt bij patiënten met een depressie melding gedaan van suïcide percentages van tussen 7 en 20%.[2,3]

Door de gekozen studieopzet, waarbij alleen de 222 patiënten waarvan de volle tien jaar op de patiëntenkaart gevolgd konden worden in de studiepopulatie werden opgenomen, werden patiënten uitgesloten die binnen deze periode waren overleden of vertrokken. Hierdoor kan vertekening van de resultaten zijn opgetreden. Wij bestudeerden de doodsoorzaken van patiënten die waren afgevallen. Twee van deze patiënten waren overleden ten gevolge van zelfmoord maar de totale mortaliteit van de uitgesloten patiënten bleek niet significant hoger te zijn dan van een voor leeftijd, geslacht en praktijk 'gematchte' controlegroep.

BEHANDELING

In hoofdstuk 3 worden resultaten van het onderzoek naar de behandeling van depressie aan de orde gesteld. Deze gegevens betreffen hetzelfde historisch cohort van 222 patiënten uit de CMR als in hoofdstuk 2. Van hen werd ongeveer 70% op een of ander tijdstip gedurende de onderzoeksperiode van 10 jaar behandeld met antidepressiva. Van patiënten met recidieven was dit zelfs 94%. In 78% van de medicatie episodes waren de PDD/DDD ratio's van de voorgeschreven antidepressiva lager dan 1 (de veronderstelde gemiddelde effectieve dagelijkse

dosis).[4] De duur van de medicatie episodes was kort, in 24% van de gevallen zelfs korter dan 28 dagen. De meeste patiënten (86%) kregen bovendien ook andere psychofarmaca, vooral benzodiazepines.

Bij het bestuderen van de behandeling tijdens de eerste episode van depressie bleek dat weliswaar meer patiënten mét dan zonder recidieven antidepressiva hadden gekregen, maar dat voor beide groepen patiënten de doseringen te laag waren en dat voor een te korte periode werd voorgeschreven. De patiënten met recidieven bleken bovendien ook significant meer tranquillizers te hebben gekregen. Ze werden overigens niet vaker verwezen.

We concludeerden dat onze onderzoekspopulatie niet was behandeld zoals wordt aanbevolen in richtlijnen voor behandeling van depressie. Desondanks had de meerderheid van deze patiënten geen recidieven doorgemaakt in de tien jaar, die wij bestudeerden.

De resultaten uit hoofdstuk 2 en 3 over beloop en behandeling ondersteunen de visie dat de prognose van depressie in eerste lijn, verschilt van die in de tweede lijn. Deze gegevens kunnen bijdragen aan een grotere nuancering van gedachten over de prognose van depressie. Het feit dat de depressie bij de meeste patiënten niet recidiveerde ondanks de 'inadequate' behandeling, zou kunnen betekenen dat depressie in de eerste lijn in veel gevallen spontaan geneest. Een andere mogelijkheid is dat lagere doses antidepressiva wellicht effectief zijn in de huisartspraktijk.

Omdat meestal alleen de ernstigere en langdurige gevallen van depressie naar de tweede lijn worden verwezen, is het wel te verwachten dat een betere prognose wordt gevonden in de huisartspraktijk. Niet bekend is echter hoe groot het aandeel van de verschillende ernstgraden van depressie in de huisartspraktijk is, en of het hier vooral om de minder ernstige vormen gaat. Dit roept vragen op over die diagnose.

In hoofdstuk 4 richtten we onze aandacht op deze diagnose. In een tweede onderzoekspopulatie bestudeerden wij de specificiteit van de diagnose depressie, zoals deze werd gesteld door de CMR artsen en bekeken in twee patiëntencategorieën of de diagnose depressie daar over het hoofd was gezien. Met dit doel werden 99 CMR-patiënten geïnterviewd met de 'CIDI-auto-12 maanden', een gevalideerd meetinstrument, waarmee psychische ziekten die zich in de afgelopen 12 maanden hebben voorgedaan, worden geclassificeerd volgens DSM-IV criteria. Deze interviews werden door een clinicus afgenomen die een speciale training had gevolgd om de CIDI volgens de regels te kunnen afnemen. Een derde van de te ondervragen 99 patiënten had een huisarts-code voor depressie, een derde voor chronisch nerveus functionele klachten (om onze hypothese te toetsen dat de diagnose depressie in deze categorie waarschijnlijk in een aantal gevallen over het hoofd wordt gezien) en een derde had geen code voor een psychische stoornis (in alle categorieën met betrekking tot de laatste 12 maanden). We toonden aan dat wanneer er een diagnose depressie gesteld was, de validiteit van de huisarts diagnose zeer hoog was. Dit bevestigt gegevens uit eerder onderzoek, n.l. dat als huisartsen de diagnose stellen, de specificiteit hoog is.[5]

Bovendien bleek deze diagnose in 79% van de gevallen overeen te komen met een diagnose van depressie in engere zin (Major Depressive Disorder, MDD) volgens criteria van de DSM-IV. De huisartsen in ons onderzoek leken vooral de ernstigere gevallen op te sporen.

Door deze gegevens wordt het door ons gevonden, relatief gunstige lange termijn beloop in een ander daglicht gesteld. Dit beloop is vooral opmerkelijk omdat de te verwachten prognose van depressie in engere zin (MDD) ongunstig is en omdat de behandeling van de patiënten uit ons historisch cohort niet had voldaan aan aanbevelingen uit depressie richtlijnen.

Wij moeten hier wel voorzichtig zijn met het trekken van conclusies. De interviews voor het valideren van de diagnose werden recent afgenomen. Recidief percentages werden berekend in een historisch cohort patiënten, waarbij de diagnose lang geleden was gesteld. Het was ook niet meer mogelijk de validiteit van die diagnose nog vast te

stellen. Er zijn echter geen redenen om aan te nemen dat de validiteit van diagnoses die destijds in de CMR werden gesteld, lager is geweest. De artsen gebruikten dezelfde criteria als tegenwoordig (E-list, ICHPPC-2[6,7]), ook toen al werden routinematig maandelijkse kwaliteits bewakings bijeenkomsten gehouden en sinds het begin van CMR is er slechts heel weinig wisseling in artsen geweest. De grote betrouwbaarheid van de CMR werd in de afgelopen jaren al vaak aangetoond in vele studies met een groot aantal verschillende onderwerpen.[8-12]

Wat betreft de door de huisartsen 'gemiste diagnose': er werden geen gevallen van depressie gevonden in de controlegroep patiënten zonder bekende psychische klachten, maar ongeveer 20% van de patiënten met chronisch nerveus functionele klachten (CNFK) bleek te voldoen aan de criteria voor een diagnose van MDD. Vanwege het kleine aantal patiënten was de sensitiviteit niet nauwkeurig te bepalen maar deze resultaten geven wel een indicatie over een categorie patiënten waarin depressie waarschijnlijk over het hoofd wordt gezien. Deze gegevens lijken bevindingen uit eerder onderzoek te bevestigen, waarin wordt aangetoond dat depressie door huisartsen vaak niet wordt herkend. Het is ook denkbaar dat zowel huisartsen als patiënten depressieve klachten soms bewust anders dan met een diagnose depressie labellen. Huisartsen betwijfelen wellicht in een aantal gevallen of het stellen van de diagnose depressie wel voordelen heeft voor de patiënt, zeker als zij het idee hebben dat er op dat moment geen dwingende indicatie is voor behandeling. Patiënten verzetten zich soms zelf tegen deze diagnose uit angst hierdoor gestigmatiseerd te worden, maar soms ook omdat zij geen behandeling willen, vooral niet met medicijnen. Ook schrijven zij hun symptomen soms aan heel andere zaken toe dan hun arts en beïnvloeden deze vervolgens om de symptomen anders te benoemen en niet als depressie.[13]

Eerder concludeerden wij dat de lange termijn prognose van depressie in de huisartspraktijk relatief gunstig is en dat het hierbij ook voor een groot deel een depressie in engere zin betreft. De prognose van niet herkende of als zodanig benoemde depressie blijft echter onbekend en daarmee ook of niet herkennen of benoemen een negatieve invloed heeft op de uiteindelijke prognose. Wij wezen er in dit

hoofdstuk op dat een aantal van deze 'niet herkende depressies' gevonden kan worden bij patiënten met CNFK.

GEGEVENS OVER 'OUTCOME' MEER DAN 15 JAAR NA DE EERSTE DEPRESSIE EPISODE

In het volgende deel van de studie onderzochten we het beloop op de nog langere termijn (zowel vanuit het perspectief van de huisarts als van de patiënt).

In hoofdstuk 5 worden de resultaten gepresenteerd van het onderzoek naar psychische klachten, algemene gezondheidstoestand, coping gedrag en sociale steun bij patiënten met een depressie in hun voorgeschiedenis. Dit deel van het onderzoek werd gedaan bij de 126 patiënten uit het historisch cohort van 222 patiënten met een eerste depressie diagnose voor 1984, die ten tijde van dit deel van het onderzoek nog in de praktijken waren ingeschreven. Het gaat daarbij zowel om patiënten met als zonder recidieven.

Patiënten zonder recidieven bleken meer psychische klachten te hebben dan controles (patiënten zonder bekende psychische morbiditeit) en verschilden hierin niet significant van patiënten met recidieven. Het ging daarbij om een veel breder scala dan alleen depressieve klachten. De patiënten mét recidieven gaven bovendien een slechtere algemene gezondheidstoestand aan dan controlepersonen. Op het gebied van pijn, vitaliteit, rolbeperking ten gevolge van emotionele problemen en mentale gezondheid waren deze verschillen ook significant. Bij patiënten zonder recidieven was er alleen wat betreft mentale gezondheid een significant verschil met de controles.

Deze bevinding - lang na een depressie meer psychische klachten en een slechtere algemene gezondheidstoestand - lijkt in tegenspraak met onze eerdere conclusie over een relatief gunstige beloop van depressie voor het merendeel van de patiënten in de huisartspraktijk. Meer psychische klachten betekent echter niet per definitie ook een psychische stoornis. Ook bij goed functionerende personen in de 'gewone' bevolking komen psychische klachten voor en is er een grote spreiding in grondstemming. In plaats van de psychische klachten van de patiënten met een depressie in hun voorgeschiedenis uit te leggen als residusymptomen en daarmee het gevolg van depressie, is het ook denkbaar dat zij deze symptomen al hadden voor hun depressie en dat ze karakteristiek voor hen waren. Misschien waren deze patiënten juist daardoor al

kwetsbaar. Het is de vraag of deze kwetsbaarheid wel het gevolg is van de depressie of de depressie misschien wel van de kwetsbaarheid. Dat patiënten zonder recidieven zeiden in bijna alle domeinen normaal te functioneren, ondanks hun psychische klachten, zou immers kunnen betekenen dat zij deze klachten normaal vonden omdat ze deze al eerder hadden, en dat zij na hun depressie weer op hun oude, 'gewone' niveau functioneerden. Dit was niet het geval bij patiënten met recidieven, zij hadden veel meer moeite met functioneren dan controlepersonen. Omdat wij niet over gegevens beschikten uit de periode van voordat bij hen de depressie werd vastgesteld, kon deze hypothese niet getoetst worden.

In dit deel van de studie kwam ook aan de orde dat patiënten met recidieven een minder goede emotionele coping hadden dan controles. Omdat dit verschil niet werd gevonden bij patiënten zonder recidieven, concludeerden wij dat problemen met emotionele coping, patiënten wellicht vatbaar maakt voor recidieven. Tegen onze verwachting in vonden wij geen verschillen in ervaren sociale steun.

Wij concludeerden dat deze bevinding (meer psychische klachten en slechtere algemene mentale gezondheidstoestand lang na een depressie) in ieder geval aanleiding zou moeten zijn om patiënten na een depressie langdurig en zorgvuldig te blijven volgen.

GEGEVENS OVER 'OUTCOME' BIJ PATIËNTEN MET CNFK

In hoofdstuk 6 worden de resultaten besproken van het onderzoek naar psychische klachten, algemene gezondheidstoestand, coping gedrag en sociale steun in een bredere populatie. Omdat we inmiddels wisten dat in de categorie patiënten met CNFK een aantal 'gemiste depressies' gevonden kon worden, wilden we achterhalen of en hoe deze patiënten verschilden van patiënten met een depressie in hun voorgeschiedenis en van controlepersonen zonder bekende psychische morbiditeit. Patiënten met CNFK bleken meer psychische klachten te hebben en een slechtere algemene gezondheidstoestand dan de controles en zij verschilden hierin niet significant van patiënten met een depressie in hun voorgeschiedenis. Ook scores in ervaren alledaagse sociale steun van patiënten met CNFK waren significant lager dan van

controlepersonen, terwijl de scores van patienten met een depressie in hun voorgeschiedenis in dit opzicht niet van normaal verschilden

Van patienten met een depressie is bekend dat zij veel psychopathologie en een slechte algemene gezondheidstoestand hebben Onze gegevens lijken dan ook de hypothese te bevestigen dat er bij een aantal patienten met deze 'diagnose' een depressie verborgen zit achter dit klachtenpatroon Waarschijnlijk betreft dit zelfs niet alleen depressie maar ook andere specifieke psychische stoornissen De gegevens over hun slechte algemene gezondheidstoestand lijken erop te wijzen dat dit klachtenpatroon niet alleen een lastige gedragskarakteristiek is voor hen zelf en de huisarts, maar dat zij zich echt ziek voelen en door deze klachten beperkt worden in hun functioneren Door in plaats van steeds wisselende klachten te registreren, CNFK als een diagnose te beschouwen wordt de mogelijkheid gecreeerd om patienten met dit soort klachten zorgvuldiger te volgen Misschien kan dit ertoe leiden dat in de loop van de tijd vaker een diagnose van een specifieke psychische stoornis gesteld kan worden met de eventuele consequenties daarvan

Omdat onze gegevens de totale groep patienten met CNFK betreft, en wij vooral geinteresseerd waren in het lange termijn beloop van depressie, roept dit opnieuw vragen op over de prognose van de subgroep patienten met een depressie, die waarschijnlijk verborgen zit in deze patientencategorie

LITERATUURSTUDIE NAAR HET LANGE TERMIJN BELOOP VAN DEPRESSIE IN BEVOLKING EN HUISARTSPRAKTIJK

Na afloop van het hierboven beschreven onderzoek, waarvan de gegevens verkregen waren via de CMR praktijken, werd nog een systematisch literatuur onderzoek gedaan met als doel onze eigen resultaten te vergelijken met resultaten van studies, waarin het beloop van depressie op de lange termijn was onderzocht in bevolking en huisartspraktijk Er bleken in de literatuur maar weinig studies in deze populaties te vinden met een follow-up van 5 jaar of meer De recidieffrequenties die worden genoemd in de volgens tevoren vastgestelde criteria in het literatuur overzicht ingesloten studies, zijn ongeveer dezelfde als in onze eigen studie In studies waarin

meerdere leeftijdsgroepen waren vertegenwoordigd, werd gesproken van een recidief percentage van tussen de 30 en 40%. In drie bevolkingsonderzoeken, één specifiek onder jongvolwassenen en twee met gevarieerde leeftijdscategorieën werden hogere recidief frequenties gevonden in de jongere leeftijdsgroepen. In bevolkings-studies waarin specifiek gekeken werd naar het beloop bij ouderen, vond men ook hogere recidieffrequenties. In beide studies in de huisartspraktijk, waarin alle leeftijdsgroepen waren vertegenwoordigd, werd deze hogere recidief frequentie bij jongere en oudere patiënten niet vastgesteld. Dit zou het gevolg kunnen zijn van de kleine aantallen jongere en oudere patiënten in de onderzoekspopulaties van deze twee studies. Het is ook mogelijk dat huisartsen bij ouderen die wegens lichamelijke ziekten of met angstsymptomen het spreekuur bezoeken depressie over het hoofd zien, terwijl in bevolkingsonderzoek waarin specifiek wordt gescreend op depressie, deze recidieven wel worden geïdentificeerd. Bovendien schrijven huisartsen depressieve symptomen soms eerder toe aan een 'normale' somberheid als gevolg van eenzaamheid of een recent verlies, dan aan een echte depressie. Vooral als zij de overtuiging hebben dat een behandeling met antidepressiva niet de juiste oplossing is voor het probleem, kiezen ze er wellicht voor om de symptomen ook niet als een depressie(recidief) te diagnosticeren.

Slechts in twee van de in ons literatuur onderzoek ingesloten studies werden gegevens gevonden over de gezondheidstoestand op de langere termijn, en de manier waarop dit in de twee studies werd onderzocht, verschilde sterk. De relatie tussen behandeling en beloop op de langere termijn werd in geen van de studies besproken zodat het ook niet mogelijk was hier uitspraken over te doen.

BELANGRIJKSTE CONCLUSIES UIT ONZE EIGEN STUDIERESULTATEN

Ten aanzien van de diagnose

De diagnose depressie die door de huisartsen uit de CMR volgens de voor hen gebruikelijke criteria werd gesteld, had een hoge validiteit en een grote overeenkomst met de criteria voor een DSM-IV diagnose van depressie in engere zin (MDD). Het lijkt erop dat de huisartsen de ernstigere gevallen opspoorden.

Als het voldoen aan diagnostische criteria voor depressie de gouden standaard is, op grond waarvan de diagnose moet worden gesteld, dan was er ook sprake van onderdiagnosticeren. In de CMR kon depressie dan vooral gevonden worden bij patiënten met Chronisch Nerveus Functionele Klachten.

Ten aanzien van de prognose

Van de depressie patiënten in de CMR had ongeveer 60% geen recidieven doorgemaakt gedurende een periode van 10 jaar vanaf de eerste diagnosedatum. De artsen hielden zich voor wat betreft de behandeling met antidepressiva niet steeds aan depressierichtlijnen. Antidepressiva werden meestal te laag gedoseerd en voor een te korte periode voorgeschreven. Dat de meeste patiënten uit ons onderzoek ondanks deze 'niet adequate' behandeling nooit een recidief doormaakten, ondersteunt de visie dat depressie in de huisartspraktijk in een groot aantal gevallen spontaan geneest.

Ten aanzien van het beloop op de lange termijn vanuit het perspectief van de patiënt

Patiënten die lang geleden éénmaal een depressie doormaakten vonden dat zij in bijna alle opzichten goed functioneerden. Alleen wat betreft hun mentale gezondheid gaven zij aan problemen te ervaren. Patiënten met recidiverende depressies rapporteerden veel meer problemen met functioneren. Patiënten met CNFK hadden niet alleen veel psychische klachten maar gaven bovendien aan niet alleen problemen met hun mentale gezondheid te hebben maar met hun totale algemene gezondheidstoestand.

Met dit onderzoek werd een aantal vragen beantwoord, maar er werden vele nieuwe vragen opgeroepen. Daaruit volgen de volgende aanbevelingen.

AANBEVELINGEN VOOR VERDER ONDERZOEK

Onze resultaten kunnen niet zondermeer gegeneraliseerd worden omdat dit onderzoek werd gedaan in het Nederlandse gezondheidszorg systeem en in de zeer specifieke situatie van de CMR praktijken. Daarom lijkt het raadzaam het beloop van depressie op

de langere termijn te bestuderen in een groot aantal huisartspraktijken en ook in andere landen en culturen.

Zoals reeds eerder gezegd, zouden onze resultaten vertekend kunnen zijn door de keuze alleen patiënten in de studie op te nemen, waarvan de volle tien jaar vanaf de diagnose bestudeerd kon worden. Het is daarom aan te bevelen in toekomstig onderzoek zoveel mogelijk patiënten met een depressie te betrekken en het beloop longitudinaal te bestuderen, bijvoorbeeld met een survival methode. Op die manier kan van elke patiënt de langst mogelijke periode waarover gegevens beschikbaar zijn, worden bestudeerd, te beginnen bij de datum waarop de diagnose voor het eerst werd gesteld. Ook gegevens over mortaliteit moeten in dit onderzoek worden meegenomen.

Door het beloop prospectief en longitudinaal te volgen, wordt tevens de mogelijkheid gecreëerd om het verband te bestuderen tussen diverse vormen van behandeling en de prognose op de lange termijn. Het zou daarbij ook interessant zijn te bestuderen welke motieven huisartsen hebben om de richtlijnen voor behandeling niet op te volgen.

In onze studie hebben we de voorspellende waarde van bijvoorbeeld co-morbiditeit met lichamelijke of psychische ziekten op de prognose op de langere termijn niet onderzocht, hetgeen als een beperking van onze studie gezien kan worden. Dit onderwerp kan in toekomstige studies ook worden meegenomen.

Een volgende uitdaging is onderzoek naar de prognose van die gevallen van depressie die niet worden herkend in de huisartspraktijk. Tot op heden was dit alleen mogelijk met bevolkingsonderzoek. Vanuit deze optiek bevelen wij aan patiënten met CNFK, of hoe zij ook in andere praktijken genoemd worden, nauwlettend te volgen. Het zou interessant zijn te achterhalen waarom huisartsen patiënten zo labelen en waarom zij bij een aantal patiënten de diagnose depressie niet stellen. Het is raadzaam het natuurlijk beloop van deze klachten longitudinaal te volgen. Maar omdat uit ons onderzoek bleek dat patiënten uit deze categorie veel psychische klachten hebben, is het ook raadzaam criteria voor diagnose van specifieke psychische stoornissen te hanteren. Vervolgens kan dan bij patiënten met en zonder diagnoses van specifieke psychische stoornissen het beloop worden bestudeerd. Het is belangrijk ook kwaliteit van leven in dit onderzoek te betrekken en veranderingen daarin als gevolg van detectie en behandeling.

CONSEQUENTIES VOOR DE HUISARTSPRAKTIJK

Zolang het lange termijn beloop van depressie in de huisartspraktijk niet bekend is, zouden huisartsen aan patienten met depressie kunnen vertellen dat er sterke aanwijzingen zijn dat depressie voor veel patienten tot een episode beperkt blijft Dit zou aan hun herstel kunnen bijdragen en wellicht ook een deel van de angst of weerstand tegen deze diagnose kunnen wegnemen

Een volgend advies is om patienten met een depressie in hun voorgeschiedenis zorgvuldig te blijven volgen Misschien lukt het om een aantal recidieven te voorkomen, als tijdig wordt onderkend dat bij hen meer psychische klachten voorkomen en hierop kan worden ingesprongen

Aanbevelingen voor behandeling zijn moeilijker te doen Een afwachtende houding zou voor veel patienten wel eens een optie kunnen zijn Uit ons onderzoek bleek immers dat voor veel patienten het lange termijn beloop ondanks inadequate behandeling niet ongunstig was In dat geval is het wel nodig deze patienten nauwlettend te volgen Maar omdat de behandeling van de patienten in onze studie niet voldeed aan de richtlijnen, was het niet mogelijk vast te stellen of een behandeling die daaraan wel voldeed, misschien in een aantal gevallen het beloop gunstig beinvloed zou hebben Daarom is het ook verdedigbaar om, wanneer de beslissing wordt genomen dat behandeling met antidepressiva noodzakelijk is, te adviseren daarvoor de richtlijnen te volgen Vervolgens moet dan wel het effect van behandeling nauwkeurig worden bestudeerd en vastgelegd, ook voor wat betreft de lange termijn Door patienten goed te informeren over wat zij van een behandeling met antidepressiva mogen verwachten, zal wellicht de therapietrouw verhoogd kunnen worden en daarmee ook het gunstig effect van zo'n behandeling Daarbij hoort zowel informatie over welke symptomen met medicatie zullen verminderen (en hoe lang het meestal duurt voor dit merkbaar wordt) als over de te verwachten bijverschijnselen

Voorts willen wij ook nog eens de aandacht vestigen op een bijzondere categorie patienten in de huisartspraktijk, in de CMR worden hun klachten chronisch nerveus functioneel genoemd In andere praktijken worden ze soms als chronische klagers, frequente spreekuurbezoekers of somatiserende patienten bestempeld Als huisartsen,

tijdens consulten met patiënten met dit type klachten, zich niet te laten afleiden door dit klachtenpatroon, lopen zij minder risico een diagnose van een specifieke psychische stoornis over het te hoofd zien. Het zou goed zijn criteria voor diagnose van psychische stoornissen vooral te hanteren bij patiënten waarbij het erop lijkt dat dit klaaggedrag een vast patroon aan het worden is. Misschien zullen consulten met dit soort patiënten, die vaak gepaard gaan met een steeds terugkerende ergernis bij dokter en patiënt, op die manier veel bevredigender verlopen dan nu vaak het geval is. Mocht er een diagnose van een psychische stoornis gesteld kunnen worden dan valt een specifieke behandeling te overwegen. Bij de overige patiënten uit deze categorie zouden vormen van behandelingen te overwegen zijn, (zoals bijvoorbeeld cognitieve gedragstherapie), die al effectief zijn gebleken bij een aantal specifieke functionele syndromen.

REFERENCES

1. Angst J, Preisig M. Course of a clinical cohort of unipolar, bipolar and schizoaffective patients: Results of a prospective study from 1959 to 1985. *Schweiz Archiv Neurol Psychiatr* 1995;**146**:5-16.
2. Kiloh LG, Andrews G, Neilson M. The long-term outcome of depressive illness. *Br J Psychiatry* 1988;**153**:752-7.
3 Angst J. The course of affective disorders *Psychopathology* 1986;**19 Suppl 2**:47-52.
4 WHO Collaborating Center for Drugs Statistics Methodology. *Guidelines for ATC classification and DDD assignment*. 1st edn ed. Oslo. 1996.
5 Wright AF. Should general practitioners be testing for depression? *Br J Gen Pract* 1994;**44**:132-5
6. Hodgkin K *Towards earlier diagnosis in primary care* 2 ed. Edinburgh: Chrchill Livingstone; 1966.
7. Classification committee of WONCA. *ICHPPC-2-defined (International classification of Health Problems in Primary Care)*. third ed Oxford Oxford University Press; 1983.
8. Weel C van, Bosch WJ van den, Hoogen van den, et al. Development of respiratory illness in childhood--a longitudinal study in general practice *J R Coll Gen Pract* 1987,**37** 404-8.
9 Boogaard C van den, Hoogen HJ van den, Huygen FJ, et al. The relationship between breast-feeding and early childhood morbidity in a general population. *Fam Med* 1991;**23**:510-5.
10. Bosch WJ van den, Hoogen HJ van den, Huygen FJ, et al. Morbidity from childhood to adulthood The medical life history of 103 patients. *Fam Pract* 1992,**9**:290-4.
11 Gijsbers-van-Wijk CM, Kolk AM, Bosch WJ van den, et al Male and female health problems in general practice. the differential impact of social position and social roles. *Soc Sci Med* 1995,**40**:597-611
12 Kolnaar B, Beissel E, Bosch WJ van den, et al Asthma in adolescents and young adults: screening outcome versus diagnosis in general practice *Fam Pract* 1994;**11**:133-40.
13 'You're depressed', 'no I'm not': GPs' and patients' different models of depression. UMDS MSc in General Practice Teaching Group *Br J Gen Pract* 1999;**49** 123-4

Spaendonck KPM van, Weel-Baumgarten EM van. *Feedback.* In: Metz JCM, Scherpbier AJJA, Houtkoop E, redactie. Gezond Onderwijs 2. Universitair Publicatiebureau KUN Nijmegen 1993; 62-65.

Weel-Baumgarten EM van. *Heteroanamnese door simulatiemoeders.* In: Houtkoop E, Pols J, Pollemans MC, Scherpbier AJJA, Verwijnen GM, redactie. Gezond Onderwijs 3. Haasbeek, Alpen aan de Rijn 1994; 19-23.

Baumgarten EM. *Decorso a lunga scadenza della depressione in medicina generale.* Atti del IX Congresso Nazionale dello Csermeg 1996 – Qualità in Medicina Generale – Strategie Nazionali ed Europee di Politica Sanitaria.

Vercoulen JHMM, Weel-Baumgarten E van, Samwel J, Crul BJP en Bleijenberg G. *De hulpverlener en de patiënt met chronische benigne pijn. Een inventariserend onderzoek onder psychologen, huisartsen en bedrijfsartsen.* Nederlands Tijdschrift voor Pijn en Pijnbestrijding 1997; 2: 30-32.

Weel-Baumgarten EM van, Spaendonck KPM van. *Feedback door simulatipatiënten ook op inhoud, kan dat wel?* In: Smal JA, Caten THJ ten, Denekens J et al, redactie. Gezond Onderwijs 6. Houten/Diegem 1997; 268-272.

Weel-Baumgarten EM van, Bosch WJHM van den, Hoogen HJM van den, Zitman FG. *10 Year follow-up of depression after diagnosis in General Practice.* Br J Gen Pract 1998; 48: 1643-1646.

Weel-Baumgarten EM van. How reliable is the diagnosis of depression made by the general practitioner? *Wisconsin Medical Journal*, November 1999; 51-52.

Weel-Baumgarten EM van, Spaendonck KPM van. *De communicatietraining in het nieuwe curriculum te Nijmegen: van vraagverheldering naar verkenning van het referentiekader van de patiënt.* In: Spaai GWG, Verweij AMJJ, Remmen R *et al*, redactie. Gezond Onderwijs 8. Bohn Stafleu Van Loghum Houten/Diegem 1999; 341-345.

Spaendonck KPM van, Pék Gy., Johnston B, Molnar P, Weel-Baumgarten EM van. *Comminication Skills.* In: Medical Skills. Resource Book for Teachers. Pécs Medical University 1999; 37-61.

Spaendonck KPM van, Pék Gy., Johnston B, Molnar P, Weel-Baumgarten EM van. *Habilidades de communicación.* In: Recursos Para Profesores en la Ensenanza de las Habilidades Medicas. Pécs Medical University 1999; 39-64.

Weel-Baumgarten EM van, Spaendonck KPM van. *Communicatietraining in het nieuwe curriculum te Nijmegen: van vraagverheldering naar verkenning van het referentiekader.* TMO 2000; 19,16-20.

Weel-Baumgarten EM van, Bosch WJHM van den, Hekster YA, Hoogen HJM van den, Zitman FG. *Treatment of depression related to recurrence: 10 year follow-up in General Practice.* J Clin Pharm Therapeutics 2000; 25, 61-66.

Weel-Baumgarten EM van, Bosch WJHM van den, Hoogen HJM van den, Zitman FG. *The validity of the diagnosis of depression in General Practice: is using criteria for diagnosis as a routine the answer?* Br J Gen Pract 2000; 50: 284-287.

Weel-Baumgarten EM van, Bosch WJHM van den, Hoogen HJM van den, Zitman FG. *The long-term perspective: a study of psychopathology and health status of patients with a history of depression, more than 15 years after the first episode.* Scheduled Nov 2000. Gen Hosp Psychiatry 2000;22:399-404.

DANKWOORD

'The dwarf sees farther than the giant when he has the giants shoulder to mount on '
Samuel Taylor Coleridge (1772-1834)
English poet, critic and philosopher

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- Hans Bor, jij hebt mij bij alle analyses voor dit proefschrift terzijde gestaan Nooit heb ik jou in de afgelopen jaren horen mopperen, ook niet als er de nodige tijdsdruk was, of als een berekening opnieuw moest omdat ik die tussen alle stapels kwijt had gemaakt! Bovendien wist je voor bijna al mijn computerproblemen een oplossing

- Prof. dr. Y. Hekster, beste Chiel, ook jij heb mij 'verder laten kijken'. Jij hebt me ingewijd in de geheimen van de PDD/DDD's en zo nog een paar dingen en die hulp was onmisbaar.
- Henk Schers, beste Henk, jij hebt mijn maatje willen zijn, toen ik heel laat in het onderzoek nog besloot dat een Evidence Based Clinical Review misschien toch te verkiezen was boven het zo maar even doorkijken van de literatuur. En dat allemaal naast je eigen project, je praktijk waar je nog niet zo lang geleden begonnen was en je taak als 'jonge vader' thuis.
- Alle patiënten die aan het onderzoek hebben meegewerkt. De CIDI interviews kostten u veel tijd en de vragen waren vaak indringend. Ik begrijp heel goed dat dit voor U niet altijd makkelijk is geweest. Toch vertelde U mij soms veel meer dan strikt noodzakelijk was en ik heb veel van uw verhalen geleerd. Ook het zorgvuldig invullen van de uitgebreide vragenlijsten heeft u veel energie gekost. Zonder al deze gegevens was het onderzoek echter niet geslaagd. Dank daarvoor.
- De huisartsen van de CMR-praktijken die het veldwerk mogelijk hebben gemaakt: Wil van den Bosch, Ton Serrarens, Charles Verhoeff, Toine en Bert Lagroo, Carel Bakx en Erik Gelpke. Jullie bewaakten het patiëntenkaart onderzoek, motiveerden patienten om mee te werken aan interviews en invullen van vragenlijsten, en vingen vragen en commentaar op. Mede dankzij jullie hulp is het gelukt genoeg gegevens te verzamelen om het onderzoek tot een goed einde te brengen.
- Trudy Dembrok, Yvonne Ernst, Yvonne Irving, Mirjam Lörx, Rian Jansen, Natascha Peeters, Agnes van Sas, Debby Stevens en Bernadette Toonen, allen assistente in de CMR-praktijken en natuurlijk ook Dorothé Bakx. Jullie hebben door de jaren heen een hoop werk voor mij verzet. Mirjam, jij hebt mij ook nog eens geholpen met de 378 vragenlijsten. Ik weet dat dit je niet is meegevallen vanuit een kamer, met 5 'onderzoekers' en met een grote hoeveelheid rommel en weinig werkruimte, en ik heb je hulp daarom dubbel gewaardeerd.

- Emmy van de Ven, jij hebt voor mij het handschrift van prof. Frans Huygen toegankelijk gemaakt. Zonder jouw hulp zouden veel patiëntenkaarten onleesbaar zijn geweest.
- Mijn kamergenoten op HSV, Wil van den Bosch, Carel Bakx, Linelle Deunk en Heert Tigchelaar. Jullie inhoudelijke bijdragen, discussies als onderzoekers onder elkaar, kletspartijen tussendoor en motiverende woorden als ik die nodig had, zullen mij altijd bijblijven. Ik hoop oprecht dat ik nog lang deel mag uitmaken van dit rommelige, warme, extroverte maar vooral inspirerende gezelschap. Hoe staat het met onze plannen voor de elite eetclub?
- Twanny Jeijsman, jij hebt in korte tijd van al mijn losse hoofdstukken en tabellen een echt professioneel manuscript weten te maken, dat was mij zelf vast nooit gelukt.
- Vince Winklerprins, naast je eerste eigen schreden op het pad van onderzoek tijdens je verblijf in Nederland heb jij mij ook nog eens geholpen om in de laatste artikelen van mijn Nederlandse Engels 'Amerikaans' te maken. Tussen neus en lippen door leverde je bovendien ook nog goed bruikbare kritiek op de inhoud van die artikelen!
- Jill Pereira Gray, dear Jill. I will always remember our session at Dehmels in Vienna, when you helped me translating the Dutch patient quotations into real 'patient English'. That was a highlight, I really enjoyed it. I can think of a few more of those highlights, and Exeter was also one of those occasions.
- De wetenschappelijke stagiaires Hedzer Streutker en Gabby van de Heuvel, jullie hebben direct of indirect een bijdrage geleverd aan dit onderzoek.
- Vervolgens wil ik (in alfabetische volgorde) een aantal medewerkers van de afdelingen huisartsgeneeskunde en psychiatrie noemen die mij op weg hebben geholpen met invoerschermen, vragenlijsten, figuren, tabellen, review, reference manager, computervragen en zo meer. Reinier Akkermans, Annemarie Bekker, Jan van Doremalen, Willem van Gerwen, Joliet Hartman, Cees Kan, Miranda Laurant, Tjard Schermer, Waling Tiersma, Caroline van de Ven en Michel

Wensing. Zonder jullie hulp was veel van het bovengenoemde voor mij abacadabra gebleven.

- En 'last but not least' mijn thuisfront. Chris, door jou ben ik aan het onderzoeken geraakt. Jij hebt bovendien de juiste balans gevonden tussen voldoende afstand en steun. Inhoudelijk heb je je niet met dit proefschrift bemoeid, dat leek ons allebei het beste. Maar ik heb natuurlijk wel van jouw 'netwerk' kunnen en mogen profiteren en ook dat heeft geholpen en mij bovendien veel inspiratie gegeven. Je frequente afwezigheid de laatse twee jaar heeft bijgedragen aan het versneld afronden van 'het boekje'. Nu kan ik hopelijk ook vaker met je mee op pad. Nienke, jij hebt me vaak een hart onder de riem gestoken deze afgelopen tijd. Maar vooral van het grote doorzettingsvermogen tijdens die lange en moeilijke periode van ziekte zo vroeg in jouw leven al, heb ik heel veel geleerd. Ook ik heb nu weer een van mijn doelen bereikt! Door jou, Jorrit, ben ik gaan inzien dat het nemen van wat meer afstand soms helpt om die dingen te zien die je niet ziet als je er te dicht met je neus bovenop zit. Deze wetenschap is voor ons allemaal heel belangrijk maar zeker ook voor het doen van onderzoek!

Allemaal nogmaals heel hartelijk dank!

De auteur van dit proefschrift werd op 8 december 1949 geboren te New York in de Verenigde Staten van Noord Amerika. Na de lagere school in Den Haag en gymnasium β te Amersfoort ging zij in 1967 geneeskunde studeren aan de Rijksuniversiteit te Leiden. In 1974 behaalde zij aldaar het artsexamen. Vervolgens werkte zij enige tijd als arts voor de dr. Rutgersstichting in Rotterdam en Schiedam. Daarnaast begon zij in 1975 parttime als huisarts te werken. Tot oktober 1995 werkte zij met enkele korte onderbrekingen in verschillende praktijken achtereenvolgens in Schiedam, Capelle a/d IJssel, Huissen en Bemmel. Vlak na haar verhuizing vanuit het westen van Nederland naar Nijmegen raakte zij in 1987 betrokken bij het vaardigheidsonderwijs aan geneeskunde studenten te Nijmegen. Zij vervulde gedurende een aantal jaren de rol van tutor tijdens het algemeen co-schap. Sindsdien is zij zich steeds meer gaan toeleggen op het onderwijs in communicatieve vaardigheden. In het nieuwe curriculum van de studie Medische Wetenschappen te Nijmegen houdt zij zich vooral bezig met het ontwerpen en verzorgen van allerlei praktische vaardigheidstrainingen op dit gebied. Van februari 1995 tot februari 1998 werkte zij daarnaast ook als huisarts voor het Kenniscentrum Pijnbestrijding te Nijmegen. In april 1995 werd begonnen met de studie naar het lange termijn beloop van depressie bij patiënten in de huisartspraktijk, waarvan het resultaat nu voor u ligt. Naast haar taken op het gebied van onderwijs in communicatieve vaardigheden werkt zij op dit ogenblik aan een subsidieaanvraag voor vervolgonderzoek bij patiënten met chronisch nerveus functionele klachten.

Zij is sinds 1972 getrouwd met Chris van Weel en zij hebben twee kinderen, Nienke en Jorrit (geboren in 1975 en 1978). Naast haar gezin heeft zij enkele andere grote passies, waarvan die voor de 'Italiaanse taal en cultuur' en lezen niet ongenoemd kunnen blijven.

Stellingen behorend bij het proefschrift '*Depression the long-term perspective A follow-up study in General Practice*' door Evelyn van Weel-Baumgarten

1 Depressie heeft voor veel patienten in de eerste lijn een gunstiger lange termijn beloop dan in de tweede lijn *Dit proefschrift*

2 Wanneer huisartsen de diagnose depressie stellen, betreft dit in een groot deel van de gevallen een depressie in engere zin *Dit proefschrift*

3 De manier waarop de klachten gepresenteerd worden, bepaalt in grote mate of huisartsen een depressie herkennen en/of als zodanig benoemen *Dit proefschrift*

4 De vraag in hoeverre niet herkennen of als zodanig benoemen van depressie schadelijk is voor de patient blijft onbeantwoord zolang de lange termijn prognose van deze gevallen nog onbekend is *Dit proefschrift*

5 Welke 'diagnose' patienten met langdurig steeds wisselende functionele klachten ook krijgen, feit blijft dat zij niet goed functioneren *Dit proefschrift*

6 Je depressief voelen is lang niet altijd hetzelfde als een depressie hebben In een moderne en op consumptie ingestelde maatschappij is er steeds meer risico dat beide op dezelfde manier 'behandeld' worden

7 Op vele momenten gedurende het hele leven helpt de wetenschap dat elk half leeg glas ook half vol is, vol te houden

8 The extent to which beliefs are based on evidence is very much less than believers suppose *Bertrand Russel*

9 Wanneer bij een test geen significantie wordt gevonden, moet men zich wel realiseren dat de afwezigheid van bewijs niet hetzelfde is als bewijs van afwezigheid

10 Een diagnose is een abstractie In de geneeskunde is het de kunst niet een abstractie maar een patient te behandelen *Vrij naar Ian Mc Whinney*

11 Ondanks de ongetwijfeld goede bedoelingen van artsen is de compliantie bij patienten vaak bedroevend laag Een training in de techniek van informeren over een voorgestelde behandeling, zoals sinds kort in het nieuwe Nijmeegse Curriculum van de studie Medische Wetenschappen wordt gegeven, moet dan ook overal deel uitmaken van de opleiding tot arts

12. Omdat het uitschrijven van een recept een heel makkelijke manier is om een consult te beëindigen, wordt nog veel te vaak nodeloos medicatie voorgeschreven.

13. In een welvarende maatschappij met goede sociale voorzieningen blijkt de definitie van ziekte "oprekbaar". *Vrij naar A.Dunning*

14. Het schrijven van een proefschrift heeft veel overeenkomsten met zwangerschap en bevalling: het voldragen duurt gevoelsmatig een hele tijd en tegen het einde wordt het steeds zwaarder. Maar als het 'resultaat' er dan eenmaal ligt, overheerst ontegenzeggelijk het gevoel van grote blijdschap, ondanks het besef van kleine onvolkomenheden.

15. 'No vacancy' vertalen met 'geen vakantie' is onjuist. In de praktijk kan het echter wel op hetzelfde neerkomen.

In antiquity the two-faced god Janus was the guardian of roadways and gates. As gatekeeper he could see past, present, and future. Today - in The Netherlands - the General Practitioner is the gatekeeper of our health-care system. Therefore, just as Janus, and in this case referring in particular to depression, the General Practitioner should be attentive, looking in more than one direction, inwards as well as outwards. Taking into account the past, the GP must safeguard the best interests of all patients trusted to his or her care in the present and future.

Just as Janus, depression has more than one face.

In this statue one face can be seen quite clearly, but how the other really looks, for now remains the question.
This in a way symbolises that not all faces of depression - and that includes long-term outcome - are clear yet.