## **ORIGINAL ARTICLE**

# Course, risk factors, and prognostic factors in elderly primary care patients with mild depression: A two-year observational study

# MARIA MAGNIL<sup>1,2</sup>, LENA JANMARKER<sup>2</sup>, RONNY GUNNARSSON<sup>1,3,4</sup> & CECILIA BJÖRKELUND<sup>1,5</sup>

<sup>1</sup>Department of Primary Health Care, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden, <sup>2</sup>Primary Care Gothenburg, Sweden, <sup>3</sup>Research and Development Unit, Primary Health Care and Dental Care, Södra Älvsborg County, Region Västra Götaland, Sweden, <sup>4</sup>Cairns Clinical School, School of Medicine and Dentistry, James Cook University, Australia, and <sup>5</sup>The Sahlgrenska Academy, University of Gothenburg, Sweden

#### Abstract

Objective. The aim of this study was to observe course, risk factors, and prognostic factors in a primary care cohort aged > 60 with mild to moderate depression during two-year follow-up. Design. Observational study. Setting. Primary care. Subjects and method. During an 11-month period all (n = 302) consecutive patients aged 60 and above attending a primary care centre in Gothenburg, Sweden were screened by a nurse for depressive symptoms with the Primary Care Evaluation of Mental Disorders, Patient Questionnaire (PRIME-MD PQ) and the Montgomery-Åsberg Depression Rating Scale, selfrated version (MADRS-S) and by a GP with a patient-centred consultation model. In the second step, the GPs diagnosed depression in screen-positives by use of the PRIME-MD Clinical Evaluation Guide (PRIME-MD CEG). All patients with mild to moderate depression were followed up for two years to assess course with several MADRS-S score assessments. Main outcome measures. Risk factors, prognostic factors, and symptoms at baseline and after two years were tested with logistic regression, using the DSM-IV and MADRS-S (cut-off  $\geq$  13) respectively. Course patterns were observed and described. Results. A total of 54 patients were diagnosed with depression. Follow-up revealed declining median MADRS-S scores and three course patterns: remitting, stable, and fluctuating. History of depression, significant life events, lacking leisure activities, and use of sedatives were risk factors for depression, all previously known. An important finding was that lacking leisure activities also increased the risk of depressive symptoms after two years (odds ratio 12, confidence interval 1.1-136). Conclusion. It is desirable to identify elderly individuals with less severe depression. Three course patterns were observed; this finding requires further study of the clinical characteristics related to the different patterns. Awareness of risk factors may facilitate identification of those at highest risk of poor prognosis.

Key Words: Depression, elderly, general practice, longitudinal, primary care, prognosis, Sweden

# Introduction

Patients with medically unexplained symptoms are a challenge to general practitioners (GPs). Somatic complaints are the cause of around half of all primary care (PC) consultations [1]. The association between somatization and depression is common at all ages and multiple or unexplained symptoms may signal a mood disorder, especially in the elderly [2–4].

Depression, with a prevalence of 12–14%, is a common disorder in old age [5]. Many patients remain undiagnosed and untreated, leading to considerable

disability, morbidity, and mortality [6–8]. Most depressive elderly patients are diagnosed and treated in PC [9]. Some 35% of elderly patients with major depression recover within one year compared with 76% of adults aged 18–64 with depression [10,11]. The elderly seem to have a higher risk of recurrent depressive episodes. Furthermore, minor depressive conditions in elderly PC patients elevate the risk of major depression [12–14].

Both prognosis and outcome of depression deteriorate with increasing age [15]. Although depressive

ISSN 0281-3432 print/ISSN 1502-7724 online © 2013 Informa Healthcare DOI: 10.3109/02813432.2012.757074

Correspondence: M. Magnil, MD, Department of Primary Health Care, Institute of Medicine, University of Gothenburg, PO Box 454, SE-405 30 Gothenburg, Sweden. E-mail: maria.magnil@vgregion.se

The course and prognosis of depression in the elderly is generally poor and there are several known risk factors.

- In this study of elderly patients with mild to moderate depression, the variable "leisure activities" was associated with lower risk of depression and increased chance for recovery.
- While median MADRS-S scores declined during the two-year follow-up, three course patterns emerged: remitting, stable, and fluctuating. This finding requires further study of the clinical characteristics related to the three course patterns.
- A majority of elderly depressed patients reported other reasons for the initial encounter than depressive symptoms.

symptoms increase with age, factors other than age must be taken into consideration when assessing prognosis [12,16]. Known factors associated with poor outcomes are severity of depression at baseline, family history of depression, poor physical function, impaired psychiatric function, and perception of low social support [10,11,13,14]. Medical comorbidity and a history of depressive episodes are also strong predictors of poor outcome and, if combined, the risk of recurrence and relapse increases [12].

The naturalistic outcome of depressive disorders in the elderly in PC is heterogeneous; assessment requires frequent observations over time [14,17]. It is desirable to identify factors associated with poor outcome and risk of a chronic course in order to improve treatment and subsequent prognosis [10].

Older people are at higher risk of relapse than younger patients and remissions are often followed by recurrence [17,12,15]. A review of follow-up studies in the elderly showed that the proportion of chronically depressed patients was smaller in studies with more than two follow-ups, reflecting the fluctuating or chronic intermittent course of depressive symptoms in the elderly [15].

The aim of this study was to observe the course and risk factors in an elderly PC cohort with mild to moderate depression over two years and to investigate whether variables related to social network, lifestyle, socioeconomic status, medication, general health, or somatic symptoms were of prognostic importance.

#### Material and methods

#### Subjects

From February to December 2003 we invited consecutive patients aged > 60, visiting a primary care centre (PCC) in Gothenburg, Sweden, for any reason, to participate in a screening programme for mild/moderate depression. Patients with severe psychiatric disorders were excluded.

Written informed consent was obtained from all subjects. The Ethics Committee at the University of Gothenburg approved the study.

# Screening procedures

All patients were screened for depressive symptoms with three different methods:

- the Primary Care Evaluation of Mental Disorders, Patient Questionnaire (PRIME-MD PQ) [18], a patient screening questionnaire with yes/ no questions. Patients answering yes to any of the questions regarding depression and anxiety (questions 17–21) screened positive;
- the Montgomery-Asberg Depression Rating Scale, self-rated version (MADRS-S) [19], consisting of nine questions yielding a maximum of six points each. The cut-off point was set at ≥ 13 points [20];
- a structured screening consultation with a GP based on a patient-centred consultation model comprising seven open-ended key questions [21,22]. If the patient presented at least two of the criteria-based symptoms for depressive disorders according to Diagnostic and Statistical Manual of Mental Disorders (DSM) IV [23] during this consultation, she/he was assessed as having a "possible depression".

First the patients were screened by the study nurse with PRIME-MD PQ and MADRS-S and interviewed regarding socioeconomic status, social network, lifestyle and health, after which the screening consultation with the GP took place.

All patients screening positive in any of these three screening procedures were given another GP appointment, within two weeks, for a diagnostic interview using the PRIME-MD Clinical Evaluation Guide (PRIME-MD CEG). Mild to moderate depression was defined as a minimum of two depressive symptoms, at least one of which was either *depressed mood* or *decreased interest/pleasure*.

The nurse followed up this baseline screening of patients diagnosed with mild to moderate depression after  $\sim 2, 4, 10, \text{ and } 22 \text{ months}$ . The patient's MADRS-S scores and ongoing treatment were registered. Baseline factors from the initial interview and symptoms reported in the PRIME-MD PQ were in a previous study [24] associated with depressive symptoms and were therefore used as variables in this study (see Table I).

A MADRS-S score  $\geq$  13 at the end of the study was used to study the association between baseline factors and prognosis. The course of depression was described by symptom severity and course types [17]. Symptom severity was defined as the median MADRS-S score in all observations [17]. Based on changes in MADRS-S scores from baseline, we noted three course patterns: remitting, stable, and fluctuating, defined as: a decrease of  $\geq 5$  points at the three last assessments, and any change >5 points at three of four assessments, respectively [25]. A chronic course of depression was defined as MADRS-S scores  $\geq 13$  at 80% or more of the assessments [17].

On inclusion, blood tests were taken to exclude somatic conditions. Mini-Mental Status Examination (MMSE) < 24 points at inclusion defined cognitive impairment [26].

Management of mild to moderate depression followed PC guidelines, i.e. pharmacological treatment, psychological treatment, combinations of both, no treatment, and/or more frequent visits to the GP.

Depressive symptoms were noted as the reason for attending if any symptom included in the DSM-IV criteria was presented [23].

# Statistical methods

Associations between the diagnosis of depression at baseline and different factors and symptoms at baseline were tested with logistic regression using DSM-IV-defined depression as the dependent variable. Association between the number of somatic symptoms presented in the PRIME-MD PQ and depression (DSM-IV) was investigated with logistic regression.

Associations between presence/absence of depressive symptoms after two years and different factors and symptoms at baseline were tested with logistic regression, with dichotomization of MADRS-S scores (cut-off  $\geq 13$ ) as the dependent variable. Adjustment for age and gender was made in all logistic regressions. EPI Info, version 3.3.2 (Centers for Disease Control, Atlanta, GA) was used.

# Results

During the 11-month inclusion period, 302 patients aged 60 years and up attended the PCC. All agreed to participate. A total of 177 patients screened positive with any of the three methods (Figure 1). Two died and two were hospitalized (for somatic ailments shortly after screening), and four declined participation. Thus, 169 carried out a diagnostic interview (Figure 1). Ten patients were excluded due to other psychiatric diagnoses, including dementia. Another three patients assessed as having mild to moderate depression declined further participation in the study, 102 did not have depression, while 54 had mild to moderate depression (PRIME-MD CEG). The depressed patients (41 women, 13 men) were included in the follow-up study and 51 completed all assessments. Three patients died during follow-up (two cancer, one ischaemic heart disease) (Figure 1).

Several factors and symptoms at baseline were associated with baseline prevalence of depressive diagnosis (Table I). One of these factors, "lacking leisure activities", was also a risk factor for depressive symptoms (MADRS-S  $\geq$  13) two years later (Table II).

During the two-year follow-up period there was a reduction in the median MADRS-S scores. Of the 51 patients completing all five assessments, 15 (29%) had a *remitting* course, 25 (49%) had a *stable* course, and 11 (22%) had a *fluctuating* course (Figure 2) (course definition by observational undertaking).

Ten of the 51 patients had a chronic course, defined as MADRS-S scores  $\geq 13$  at 80% or more of the observations [10]. Of the 54 included patients, 23 reported depressive symptoms as the reason for the initial encounter and for the remaining 21 patients: check-up of chronic disease (n = 6), musculo-skeletal



Figure 1. Flow chart of the study.

Item	OR	95% CI	p-value
Variable			
"Having a partner"	0.41	0.20-0.85	0.02
Not widowed during last year	0.11	0.02-0.57	0.009
No leisure activities	3.4	1.4 - 8.2	0.006
No significant life event during the last year	0.32	0.15-0.67	0.0025
No history of depression	0.40	0.19-0.80	0.0099
Perception of good health	1.5	0.94-2.3	0.09
Socio-economic situation	1.0	0.56 - 1.9	0.94
Medication			
Sedatives, benzodiazepines	2.0	1.0 - 4.0	0.051
Sedatives, non-benzodiazepines	3.8	1.9 - 7.8	0.0002
Lipid-lowering medication	0.48	0.17 - 1.4	0.17
Symptoms			
Stomach ache	1.2	0.56 - 2.6	0.65
Back pain	2.1	1.0-4.3	0.041
Chest pain	1.6	0.76-3.2	0.22
Dizziness	1.2	0.61 - 2.4	0.60
Palpitations	1.5	0.72-3.1	0.28
Dyspnoea	1.1	0.53-2.3	0.79
Constipation or diarrhoea	1.4	0.69-2.9	0.35
Fatigue or loss of energy	4.4	1.5-13	0.009
Insomnia/hypersomnia	1.5	0.76 - 2.9	0.25
Change in appetite	2.6	0.65-10	0.18

symptoms (n = 7), gastrointestinal symptoms (n = 4) and "miscellaneous" (n = 14).

For every additional somatic symptom in the PRIME-MD PQ, the odds ratio (OR) for a depressive diagnosis increased (OR 1.4, 95% confidence interval (CI) 1.2-1.6, p < 0.0001).

After the diagnostic interview, 25 patients elected to begin antidepressant medication (median MADRS-S scores 15), while 22 chose more frequent follow-ups by the GPs, four psychological treatment, and three a combination of antidepressants and psychological treatment (median MADRS-S scores 10.5, 11, and 15, respectively).

#### Discussion

The main findings were that there were several identified risk factors for mild to moderate depression; the median MADRS-S scores declined; and three course patterns emerged. Many of the risk factors we found are known from previous studies [27]. As cross-sectional studies on risk factors and prognostic factors limit cause–effect interpretation, this should be considered when interpreting our finding that "leisure activities" was associated with a lower risk for mild to moderate depression. However, a recent systematic review indicated that psychosocial preventive interventions aimed at increasing social networks, contacts, and activities might improve mental

Table II. Factors and symptoms at baseline predicting prevalence of depressive symptoms two years later, defined by MADRS-S score  $\geq$  13 (n = 51).

Item	OR	95% CI	p-value
Variable			
"Having a partner"	1.7	0.30-9.6	0.55
No leisure activities	12	1.1-136	0.041
No significant life event during	0.51	0.05-5.2	0.57
the last year			
No history of depression	0.17	0.02 - 1.6	0.12
Perception of good health	1.9	0.52 - 6.7	0.34
Socio-economic situation	0.43	0.09 - 2.0	0.29
Medication			
Sedatives, benzodiazepines	1.1	0.20-5.6	0.94
Sedatives, non-benzodiazepines	2.8	0.47 - 17	0.26
Lipid-lowering medication	3.8	0.11-133	0.47
Symptoms			
Stomach ache	0.9	0.14-5.7	0.90
Back pain	0.65	0.11-3.9	0.64
Chest pain	0.43	0.07 - 2.6	0.36
Dizziness	1.6	0.32-7.6	0.58
Palpitations	0.98	0.19-5.0	0.98
Dyspnoea	0.80	0.13-4.8	0.81
Constipation or diarrhoea	0.96	0.15-6.1	0.97
Insomnia/hypersomnia	2.0	0.34-12	0.44
Change in appetite	1.3	0.11–15	0.84

well-being in older adults and prevent the onset of depression [28].

More than half of our patients screened positive with any of the three screening methods. Earlier studies confirm that routine screening for depression or screening high-risk groups is not feasible in PC settings [29,30]. Even if the instruments have good properties, their positive predictive values are of crucial clinical importance. In an earlier paper we compared the patient-centred consultation model with the PRIME-MD PQ and found that the GPs failed to identify every fifth patient but the number of required diagnostic interviews decreased



Figure 2. Median MADRS-S scores at baseline and at four followup visits.

by almost 50%, compared with the PRIME-MD PQ [31].

Many authors consider mood disorders in late life to be a continuum of one illness and minor depression to be a variant of major depression [32]. Adhering to this view, we used the terminology mild to moderate depression and used the lowest cut-off point for depression in the PRIME-MD CEG.

The course of mild to moderate depression was observed by following MADRS-S scores over time. By dividing patients into subgroups based on course types over time might help identify those most at risk of persistent depression, as a signal to intervene [33]. A marked remitting course, with median MADRS-S scores above cut-off point at baseline, suggested a low risk of persistent depressive symptoms. Interpretations should be cautious, especially for the stable and fluctuating course types, for which median MADRS-S scores did not reach the pre-set cut-off value at any assessment. Nonetheless, these patients were assessed as having a clinically significant mild to moderate depression at the diagnostic interview. Possible reasons for this discrepancy are that the MADRS-S instrument, originally developed for psychiatric care, is not as valid in this population and that the recommended cut-off value was too high. Patients not reaching the median cut-off level might have had a "depression without sadness" [34], thus not captured by MADRS-S, or persistent sub-threshold symptoms "waxing and waning" within the same spectrum of depressive disorders [32]. The observed change in median MADRS-S scores could be due to the regression towards the mean phenomenon but also to the follow-up encounters and continuity per se [35,36].

Despite the decline in median MADRS-S scores, almost 20% of the patients had MADRS-S scores  $\geq$  13 at 80% or more of the observations, indicating poor prognosis in this subgroup.

The risk of depressive disorders increased for every additional somatic symptom reported in the PRIME-MD PQ. This supports earlier findings [37]. Patients with mental health problems, presenting with exclusively somatic symptoms, are more likely to be overlooked by GPs and remain undiagnosed [38]. Several authors suggest that GPs should consider depression in elderly patients with multiple somatic complaints [3,4].

The majority of patients did not report depressive symptoms as reasons for encounter; there was no obvious reason to suspect depressive diagnosis in these cases. Notwithstanding, patients presenting psychiatric symptoms as the reason for the encounter might have been increased, as screening took place before index consultation, reminding the patient to mention such symptoms to the GPs. The strengths of the study were the initial high participation rate, the use of multiple screening methods, and the repeated assessments during follow-up. Patients seemed positive regarding the follow-up procedure, perhaps reflecting acceptance of the diagnosis, as also seen in other studies [39].

We did not perform diagnostic interviews during follow-up, a weakness of the study, making it difficult to assess remission and recovery. Other prognostic factors might have been revealed. Another limitation of the study is the low number of patients in the follow-up and participating GPs. On the other hand, this is a complete two-year follow-up of all patients aged > 60 years attending a PCC during an 11-month period and diagnosed with mild to moderate depression. To our knowledge, elderly patients with mild to moderate depression have not been followed up for this length of time in PC.

In conclusion, this two-year observation of a cohort of elderly patients with mild to moderate depression showed that while median MADRS-S scores declined, three course patterns could be identified. "Leisure activities" was an important positive prognostic factor and a GP's asking open-ended questions about mood, general health, and social factors in consultation may be of importance in detecting depressive disorders in older patients.

### Acknowledgements

The authors would like to thank the patients and staff at the Lundby-Brämaregården PCC for their cooperation.

#### **Declaration of interest**

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

This study was supported by grants from Region Västra Götaland and from Gothenburg Primary Care.

#### References

- Katon WJ, Walker EA. Medically unexplained symptoms in primary care. J Clin Psychiatry 1998;59(Suppl 20):15–21.
- [2] Sheehan B, Bass C, Briggs R, Jacoby R. Somatization among older primary care attenders. Psychol Med 2003;33:867–77.
- [3] Drayer RA, Mulsant BH, Lenze EJ, Rollman BL, Dew MA, Kelleher K, et al. Somatic symptoms of depression in elderly patients with medical co morbidities. Int J Geriatr Psychiatry 2005;20:973–82.
- [4] Mallen CD, Peat G. Screening older people with musculoskeletal pain for depressive symptoms in primary care. Br J Gen Pract 2008;58:688–93.
- [5] Copeland JR, Beekman AT, Braam AW, Dewey ME, Delespaul P, Fuhrer R, et al. Depression among older people in Europe: The EURODEP studies. World Psychiatry 2004;3:45–9.

- [6] Lebowitz BD, Pearson JL, Schneider LS, Reynolds CF III, Alexopoulos GS, Bruce ML, et al. Diagnosis and treatment of depression in late life. Consensus statement update. JAMA 1997;278:1186–90.
- [7] Penninx BW, Geerlings SW, Deeg DJ, van Eijk JT, van Tilburg W, Beekman AT. Minor and major depression and the risk of death in older persons. Arch Gen Psychiatry 1999;56:889–95.
- [8] Lyness JM, King DA, Cox C, Yoediono Z, Caine ED. The importance of subsyndromal depression in older primary care patients: Prevalence and associated functional disability. J Am GeriatrSoc 1999;47:647–52.
- [9] Karlin BE, Fuller JD. Meeting the mental health needs of older adults. Geriatrics 2007;62:26–35.
- [10] Licht-Strunk E, Van Marwijk HW, Hoekstra T, Twisk JW, De Haan M, Beekman AT. Outcome of depression in later life in primary care: Longitudinal cohort study with three years follow up. BMJ 2009;338:a3079.
- [11] Spijker J, de Graaf R, Bijl RV, Beekman AT, Ormel J, Nolen WA. Duration of major depressive episodes in the general population: Results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Br J Psychiatry 2002;181:208–13.
- [12] Mitchell AJ, Subramaniam H. Prognosis of depression in old age compared to middle age: A systematic review of comparative studies. Am J Psychiatry 2005;162:1588–601.
- [13] Lyness JM, Chapman BP, McGriff J, Drayer R, Duberstein PR. One-year outcomes of minor and subsyndromal depression in older primary care patients. Int Psychogeriatr 2009;21:60–8.
- [14] Cui X, Lyness JM, Tang W, Tu X, Conwell Y. Outcomes and predictors of late-life depression trajectories in older primary care patients. Am J Geriatr Psychiatry 2008;16: 406–15.
- [15] Licht-Strunk E, van der Windt DA, van Marwijk HW, de Haan M, Beekman AT. The prognosis of depression in older patients in general practice and the community: A systematic review. Fam Pract 2007;24:168–80.
- [16] Wu Z, Schimmele CM. Aging and late-life depression. J Aging Health 2012;24:3–28.
- [17] Beekman AT, Geerlings SW, Deeg DJ, Smit JH, Schoevers RS, de Beurs E, et al. The natural history of late-life depression: A 6-year prospective study in the community. Arch Gen Psychiatry 2002;59:605–11.
- [18] Spitzer RL, Williams JB, Kroenke K, Linzer M, deGruy FV III, Hahn SR. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. JAMA 1994;272:1749–56.
- [19] Svanborg P, Åsberg M. A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Asberg Depression Rating Scale (MADRS). J affect Discord 2001;64:203–16.
- [20] Svanborg P, Ekselius L. Self-assessment of DSM-IV criteria for major depression in psychiatric out- and inpatients. Nord J Psychiatry 2003;57:291–6.
- [21] Malterud K. Key questions a strategy for modifying clinical communication. Transforming tacit skills into a clinical method. Scand J Prim Health Care 1994;12:121–7.
- [22] Larsen JH, Risor O, Putnam S. P-R-A-C-T-I-C-A-L: A stepby-step model for conducting the consultation in general practice. Fam Pract 1997;14:295–301.

- [23] Diagnostic and Statistical Manual of Mental Disorders. 4th text revision. Washington, DC: American Psychiatric Association; 2000.
- [24] Magnil M, Gunnarsson R, Björkstedt K, Björkelund C. Prevalence of depressive symptoms and associated factors in elderly primary care patients: A descriptive study. Prim Care Companion J Clin Psychiatry 2008;10:462–8.
- [25] Fantino B, Moore N. The self-reported Montgomery–Asberg depression rating scale is a useful evaluative tool in major depressive disorder. BMC Psychiatry 2009;9:26.
- [26] Folstein MF, Folstein SE, McHugh PR. Mini-mental State: A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.
- [27] Meeks T, Vahia I, Lavretsky H, Kulkarni G, Jeste D. A tune in "A minor" can "B major": A review of epidemiology, illness course, and public health implications of subthreshold depression in older adults. J Affect Disord 2011;129:126–42.
- [28] Forsman AK, Schierenbeck I, Wahlbeck K. Psychosocial interventions for the prevention of depression in older adults: Systematic review and meta-analysis. J Aging Health 2011; 23:387–416.
- [29] Gilbody S, Sheldon T, House A. Screening and case-finding instruments for depression: A meta-analysis. CMAJ 2008; 178:997–1003.
- [30] Christensen KS, Sokolowski I, Olesen F. Case-finding and risk-group screening for depression in primary care. Scand J Prim Health Care. 2011;29:80–4.
- [31] Magnil M, Gunnarsson R, Björkelund C. Using patientcentred consultation when screening for depression in elderly patients: A comparative study. Scand J Prim Health Care 2011;29:51–6.
- [32] Kessler RC, Zhao S, Blazer DG, Swartz M. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. J Affect Disord 1997; 45:19–30.
- [33] Bogner HR, Morales KH, Reynolds CF III, Cary MS, Bruce ML. Prognostic factors, course and outcome of depression among older primary care patients: The PROSPECT study. Aging Ment Health 2012;16:452–61.
- [34] Gallo JJ, Rabins PV. Depression without sadness: Alternative presentations of depression in late life. Am Fam Physician 1999;60:820–6.
- [35] Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: What it is and how to deal with it. Int J Epidemiol 2005;34:215–20.
- [36] Posternak MA, Zimmerman M. Therapeutic effect of follow-up assessments on antidepressant and placebo response rates in antidepressant efficacy trials: Meta-analysis. Br J Psychiatry 2007;190:287–92.
- [37] Kroenke K, Spitzer RL, Williams JB, Linzer M, Hahn SR, deGruy FV III, et al. Physical symptoms in primary care: Predictors of psychiatric disorders and functional impairment. Arch Fam Med 1994;3:774–9.
- [38] Wilhelm K, Finch A, Davenport T, Hickie I. What can alert the general practitioner to people whose common mental problems are unrecognized? Med J Aust 2008;188: S114–18.
- [39] Van Marwijk HW, Ader H, de Haan M, Beekman A. Primary care management of major depression in patients aged > or = 55 years: Outcome of a randomised clinical trial. Br J Gen Pract 2008;58:680–6.