Depressive Disorders and Symptoms in Older Primary Care Patients

One-Year Outcomes

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Syndromically diagnosable and subsyndromal depressions have substantial prevalence and functional morbidity among older persons seen in primary care, but their naturalistic outcome is largely unknown. The authors describe depressive symptoms and syndromes and functional outcomes at 1-year follow-up and examine specific outcome predictors in a cohort study using psychopathological, medical, and functional assessments at intake and 1-year follow-up. Subjects were 247 patients over age 60, recruited from private internal medicine offices and a university-affiliated family medicine clinic. Multiple-regression techniques examined the independent association of intake variables to outcome measures. Of the 63 subjects with an active depression diagnosis at study intake, 36 (57%) still had an active depression diagnosis at 1 year. The outcome for major depression was worse than for minor or subsyndromal depression. Medical illness burden and neuroticism were independent predictors of outcome. Major depression and depressive symptom severity were independently associated with poorer social functioning at follow-up. Depressive conditions had considerable rates of persistence, yet the outcome was not uniformly poor. Longer-term naturalistic study is needed, as are treatment studies targeting those at highest risk of recurrence or chronicity. (Am J Geriatr Psychiatry 2002; 10:275–282)

Depressive symptoms and syndromes in later life are a major public health problem, with substantial prevalence and associated functional disability.[1] Elderly persons with psychiatric disorders are even less likely to be seen in mental health settings than younger patients, yet they are more likely to see their primary care physicians regularly.[2,3] Most older patients who complete suicide have seen their primary care provider shortly before death, and the majority suffered from depressive conditions at the time of their death,[4] Also, the nature of psychopathology seen in primary care elderly patients may differ from that seen in psychiatric or resi-

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dential care settings.[1–3,5,6] Thus, it is particularly important to better understand depressive psychopathology as presented by older people in primary care settings.[7–9]

Major depression is common among older patients seen in primary care, with a point prevalence of 5%–10%.[5,10,11] There is an even greater prevalence of other depressive conditions, including minor depression and "subsyndromal" or "subthreshold" depression, and, to a lesser extent, dysthymic disorder, that are associated with considerable functional morbidity.[6,12–21] Studies of younger or mixed-age groups have demonstrated that major depression in primary care settings has high rates of persistence in both remitting–recurring as well as continuous patterns, broadly comparable to the chronicity seen in psychiatric treatment settings (see Schulberg et al.[22] for a review). Also, minor and subsyndromal depression are powerful risk factors for subsequent new-onset or recurrent diagnosable depressive disorders in mixed-age or younger adults.[23–26] Unfortunately, few longitudinal primary-care studies have focused on older persons. Two prospective studies[27,28] (33 months and 9 months, respectively) found that depression had high rates of persistence but also high rates of remission and recurrence. Both studies assessed depression solely by use of a cut-off on self-report depressive symptom scales and therefore were unable to determine depressive diagnoses. Schulberg et al.,[10] using operationalized measures to establish a research diagnosis of major depression among older patients seen at university-affiliated internal-medicine centers, found that at 6-month follow-up, 38% of subjects with major depression continued to be fully syndromic, and only 11.5% were fully recovered. Kivela et al.[29] found that 15-month and 5-year outcomes of DSM-III depressive disorders ranged from full recovery to chronic depression.

To summarize, there are few data regarding the course of major depression among elderly primary-care patients, and fewer still about minor or subsyndromal depression or the development of depression among those who were formerly asymptomatic. Similarly, examination of specific outcome predictors has been quite limited despite the need to identify risk factors to target those most requiring treatment in primary care settings. It has been previously noted that medical illness burden is associated with the presence or course of depression in later life.[1,30,31] However, most studies of the relationship of medical illness to depression in later life have used psychiatric patient populations or community samples rather than subjects from primary care settings. There have been cross-sectional studies demonstrating an association between medical illness burden and depression in elderly primary-care patients[5,10,32] Three published longitudinal investigations of older primary-care patients[27–29] found that medical illness severity was associated with poorer depression outcome; however, these were limited by the methods used to assess medical comorbidity and by the lack of structured diagnostic interviews for depression outcome. Thus the predictive role of medical illness with regard to major or subsyndromal depression in elderly primary-care patients remains to be better defined. Similarly, other factors that predict depression outcome in younger adults, or in older psychiatric or nursing home patients, including functional disability,[33] personality trait neuroticism,[26] and social support,[34–36] have received scant study in elderly primary-care patients.

Therefore, we used stratification to develop a sample of older individuals in primary care practices who would have a range of depressive symptoms and then examined their naturalistic outcomes at 1 year. We tested the exploratory hypotheses that the minor and subsyndromal depression groups would have outcomes comparable to each other and intermediate outcomes compared with major depression and nondepressed subjects. Using operationalized psychopathological and medical measures, we also tested the hypotheses that initial medical illness burden, functional disability, neuroticism, and social support would be independently associated with depressive disorders and symptoms at follow-up. We chose to examine functional along with symptomatic and syndromic outcomes, given the importance of functional disability associated with depression and its implications for practice and policy.[14–16] We used 1 year as the follow-up time-point in order to allow sufficient time for depressive conditions to remit (given the Structured Clinical Interview for DSM-III-R's definition[37] of Major Depression in full remission requiring 6 months without clinically significant symptoms), and to allow comparability with previous studies.

METHODS

Our subjects and enrollment procedures have been described in detail elsewhere.[5,6] Briefly, subjects were engaged in the study from three internal-medicine private offices and a university-affiliated family medicine clinic.

After receiving a complete description of the study, all patients age ≥60 years who gave informed consent (using formal verbal or written consent procedures approved by the University of Rochester Research Subjects Review Board) were eligible to participate. Patients were screened in the offices with the Center for Epidemiologic Studies Depression Scale (CES-D).[38] Stratified sampling on the CES-D was used to oversample patients with depressive symptoms for further research assessments by purposefully overrepresenting patients scoring above the cutoff of 21; note, however, that the study included patients scoring both above and below the cutoff.

The psychopathological assessment was based on the Structured Clinical Interview for DSM-III-R (SCID)[37] administered by trained raters at study intake and again at 1-year follow-up. At both time-points, each case was presented at a consensus conference of raters and investigators, at which final diagnoses were assigned on the basis of the SCID and record review. Determination of depressive symptoms used an "inclusive" approach, as recommended previously by our group and others.[39] Therefore, the diagnostic category "organic mood disorders" was not used, and no subjects were excluded on the basis of medical comorbidity, given that such heterogeneity was of interest to the study.

The 24-item Hamilton Rating Scale for Depression (Ham-D)[40] measured depressive symptom severity for the week before the interview. Depression diagnosis at intake and 1-year follow-up was defined ordinally as follows: 1) current major depression (based on the SCID); 2) current Minor Depression (using SCID data and applying criteria from the Appendix of DSM-IV;[41] as with Major Depression, these criteria draw upon a symptom list with a "most of the day nearly every day for 2 consecutive weeks" stipulation, but only requiring two to four symptoms, total, including depressed mood or decreased interests, rather than the five to nine symptoms of Major Depression); 3) subsyndromal depression (defined as a score >10 on the Ham-D and not fitting Group 1 or 2 criteria (cf, Lyness et al.[6]); and 4) nondepressed (all others). As necessitated by ethical concerns, the primary care physician was sent a research note indicating each patient's depression status for those diagnosed with Major or Minor depression. It is important to note that the SCID used data from the interview and the chart to assess lifetime as well as current depressive disorders at the intake interview, and interim and current depressive disorders at follow-up. Our group definitions put patients with a partially remitted depressive diagnosis in either the subsyndromal depression or the nondepressed group, depending on their Ham-D score, whereas subjects with a fully remitted diagnosis were categorized in the nondepressed group.

Medical measures were completed on the basis of both patient interview and physician-investigator review of the primary care chart. Overall medical illness burden was rated on the Cumulative Illness Rating Scale (CIRS),[42] a reliable and validated scale that quantifies the amount of pathology in each organ system. Exploratory analyses also examined the predictive roles of the organ system subscales for the CIRS (Cardiovascular, Gastrointestinal, Genitourinary, Musculoskeletal, Neurological [the psychiatric item was scored 0 by convention in this study], and General). Functional level was rated by the Instrumental Activities of Daily Living and Physical Self-Maintenance Scales[43] and by the sum of the two items assessing Social Functioning from the Medical Outcomes Study Short-Form SF-36.[44]

Neuroticism was assessed by the Neuroticism factor (N) from the NEO-Five Factor Inventory (NEO-FFI),[45] a 60-item self-report questionnaire chosen for its demonstrated reliability and long-term stability. The Neuroticism factor was selected because it captures emotional vulnerability to stress and thus would be expected to relate to depression—a notion supported by previous empirical work demonstrating its relationship to depression outcome in other populations.[26] (See also Duberstein et al.'s review.[46]) Social support was measured by the Duke Social Support Inventory (DSSI),[47] using its three subscales that assess social interaction, perceived social support, and instrumental support. Cognition was included as a covariate in secondary analyses and was measured by the Mini-Mental State Exam (MMSE).[48] Treatment also was included as a covariate in secondary analyses, recognizing that in naturalistic studies, treatment is confounded with illness severity and therefore rarely is associated with a better outcome. Because very few subjects were in active treatment with a mental health professional, treatment was defined as prescription of an antidepressant either at study intake or at 1-year follow-up.

Our follow-up group consisted of 247 subjects. Of the 305 subjects from the initial study cohort, 14 had died, and 44 refused or were not available for follow-up interviews. Compared with the living subjects who did not participate in follow-up assessments, subjects in the present study did not differ significantly in age, gender,

CIRS, or initial depression diagnosis, but had more education (mean [±SD]: 13.4 ± 2.8 versus 12.2 ± 3.1 years; $t_{[55.8]} = -2.5$; $p = 0.02$) and had a lower initial Ham-D score (8.1 ± 6.5 versus 10.7 ± 7.3; $t_{[55.7]} = 2.2$; $p = 0.03$). As we described previously,[5] data available for comparison with subjects not enrolled in the study were limited. Those scoring above the CES-D cutoff did not differ on any of the variables compared (age, gender, CES-D score, CIRS score, or office visit type), whereas those scoring below the CES-D cutoff who completed the SCID had a greater proportion of men and a higher score on the CIRS than those not completing the SCID interview.

Statistical analyses used multiple-regression techniques, covarying age, gender, and years of education, to determine the independent association between predictor (intake) and outcome (1-year) variables. Polychotomous logistic (ordinal) regression[49] was used when the dependent variable was categorical (e.g., depression diagnosis as defined above). These analyses thus demonstrated a predictor variable's association with a change in depression diagnosis category toward a more severe group (thus including remitted depressed patients suffering a recurrence). For the other dependent variables (including the Ham-D), which were discrete with skewed distributions, Poisson (log linear) regression was used with an adjustment for extra-Poisson variation. Parameter estimates (coefficients and standard error) are reported for the independent variables of interest; for the categorical predictor of depression diagnosis group, the reference group (i.e., coefficient = 0) was the nondepressed group. For these ordinal regressions, odds ratios (OR) and confidence intervals (CI) are also reported. In the primary regression models, we also conducted overall tests for the eight variables of interest (i.e., excluding the three covariates): Following standard practice, this was done by comparing the fit of the full model (with all predictors) with the model including only the covariates, and performing a likelihood-ratio chi-square test for the omitted variables (the variables of interest). The regressions reported were based on the 225 subjects who completed all study measures, including the NEO and the DSSI; the results regarding the other predictor variables did not differ when regressions were performed using all 247 subjects. Two-tailed p-values were used, establishing a conservative level of significance, given the large number of tests performed, and alpha was set at 0.05.

RESULTS

The 247 study subjects had a mean age of 71.1 ± 7.5 years, with a range of 60 to 94 years. They had a mean of 13.4 ± 2.8 years of education, with a range of 1 to 17 years. Women comprised 59% of the group ($n = 145$). Initial mean scores were the following: Ham-D score: 8.1 ± 6.5, range: 0–34; CIRS score: 6.0 ± 2.8, range: 0–16; IADL score: 1.8 ± 3.8, range: 0–20; PSMS score: 0.9 ± 1.7, range: 0–15.

Table 1 shows the subject distribution by diagnostic group at intake and at follow-up. Initially, 22 subjects had major depression; 14, minor depression; 27, subsyndromal depression; and 184 were nondepressed. Of the 63 subjects with an active depression diagnosis at intake, 36 (57%) had an active depression diagnosis at 1-year follow-up. At the same time, 40 subjects with an active depression diagnosis at study intake (63%) had moved to a less severely depressed group at 1-year follow-up evaluation: 10 subjects with major depression had moved into partial remission (in the subsyndromal depression group), and 7 into full remission (in the nondepressed group); 3 subjects with minor depression were now in the subsyndromal depression group (in effect, "minor depression in partial remission"); 7 were in full remission (nondepressed), and 13 patients with subsyndromal depression had become nondepressed. Note that, overall, 27 of the 63 subjects with an initial depression diagnosis (43%) had moved to the nondepressed category.

The proportion of patients developing major depression at follow-up was not statistically different for those initially suffering minor depression (2/14; 14%) than for those initially in the subsyndromal depression group (2/27; 7%; Fisher's exact test, $p = 0.60$), but the minor and subsyndromal depression groups together were more likely to develop major depression (4/41; 10%) than those initially in the nondepressed group (4/184; 2%; Fisher's exact test, $p = 0.017$).

Table 2 shows results from the regression analysis predicting depression diagnostic group (i.e., major versus minor versus subsyndromal depression versus nondepressed) at follow-up. As hypothesized, initial medical illness burden (CIRS) was independently associated with depression diagnosis at follow-up. Initial functional status, neuroticism, and social support did not have significant independent associations with depression diagnosis outcome. Initial depression diagnosis also was

an independent predictor, with major depression predicting a poorer outcome than minor depression and both predicting a poorer outcome than the nondepressed reference group, whereas the subsyndromal depression group predicted a better outcome than the nondepressed reference group in this model. Of the covariates, independent predictors of depression diagnosis were younger age ($\chi^2_{[1]} = 3.9$; $p = 0.048$) and female gender ($\chi^2_{[1]} = 4.8$; $p = 0.03$), but not education ($\chi^2_{[1]} = 0.03$; $p = 0.87$).

Table 3 presents the regression analysis examining predictors of Ham-D score at follow-up. The initial CIRS and Neuroticism scores, but not initial functional status or social support, were independently associated with higher Ham-D at 1 year. Higher initial Ham-D score also predicted a higher Ham-D at 1 year. Of the covariates, higher Ham-D score was predicted by female gender ($\chi^2_{[1,213]} = 7.2$; $p = 0.008$) but not by age ($\chi^2_{[1,213]} = 0.3$; $p = 0.56$) or education ($\chi^2_{[1,213]} = 1.8$; $p = 0.17$).

Not shown in the tables were the results after adding antidepressant treatment (initial or follow-up) or the MMSE as predictor variables in separate regressions. Neither antidepressant treatment nor the MMSE were independently associated with depression outcome. These additional covariates did not change CIRS or the other intake variables' associations with 1-year depression diagnosis or symptoms, with the sole exception that after adding intake antidepressant treatment as a covariate, the CIRS was no longer significantly associated with depression diagnosis outcome ($\chi^2_{[1]} = 3.7$; $p = 0.056$).

Our exploratory questions about the organ-system CIRS subscales were addressed with two regressions, on 1-year depression diagnosis and on Ham-D score. The six subscale scores were entered as predictors along with initial depression diagnosis or Ham-D score, respectively, and covariates age, gender, and education. Only the Cardiovascular subscale approached statistical significance as a predictor of depression diagnosis outcome ($\chi^2_{[1]} = 3.5$; $p = 0.06$). For 1-year Ham-D score, two subscales approached statistical significance, the Cardiovascular ($F_{[1,236]} = 3.3$; $p = 0.07$) and the Neurological ($F_{[1,236]} = 3.3$; $p = 0.07$).

Turning to functional outcomes, neither initial depression diagnosis nor Ham-D was independently associated with 1-year functional status as measured by the IADL or PSMS; this was so whether or not we controlled for initial IADL or PSMS, respectively. Similarly, neither

TABLE 1. Depression diagnostic group at intake and 1-year follow-up

	Follow-up Diagnostic Group				
Intake Diagnostic Group	**Major Depression**	**Minor Depression**	**Subsyndromal Depression**	**Nondepressed**	**Totals**
Major depression ($n = 22$)	5	0	10	7	22
Minor depression ($n = 14$)	2	2	3	7	14
Subsyndromal depression ($n = 27$)	2	2	10	13	27
Nondepressed ($n = 184$)	4	5	12	163	184
Totals	13	9	35	190	247

TABLE 2. Predictors of 1-year depression diagnosis (major depression vs. minor depression vs. subsyndromal depression vs. no depression)

Predictor Variable (at intake)	Parameter Estimate (±SE)	$\chi^2_{[df]}$	p	Odds Ratio (95% Confidence Interval)
Initial depression diagnosis	Major: −0.80 ± 0.77	$11.9_{[3]}$	0.008	0.5 (0.1–2.1)
	Minor: −0.07 ± 0.68			0.9 (0.3–3.5)
	Subsyndromal: 1.36 ± 0.69			3.9 (1.0–15.0)
CIRS	−0.15 ± 0.07	$4.1_{[1]}$	0.042	0.9 (0.7–0.99)
IADL	−0.06 ± 0.07	$0.7_{[1]}$	0.40	0.9 (0.8–1.1)
PSMS	−0.06 ± 0.18	$0.0_{[1]}$	0.97	1.0 (0.7–1.4)
Neuroticism	−0.04 ± 0.03	$1.7_{[1]}$	0.19	1.0 (0.9–1.0)
DSSI-IS	0.01 ± 0.10	$0.0_{[1]}$	0.91	1.0 (0.8–1.2)
DSSI-SI	0.14 ± 0.14	$1.0_{[1]}$	0.32	1.1 (0.9–1.5)
DSSI-PSS	−0.04 ± 0.09	$0.2_{[1]}$	0.69	1.0 (0.8–1.2)

Note: Covariates: age, gender, education. Overall test for the eight variables of interest: $\chi^2_{[1]} = 97.1$; $p < 0.0001$.

CIRS: Cumulative Illness Rating Scale; IADL: Instrumental Activities of Daily Living; PSMS: Physical Self-Maintenance Scale; DSSI-IS: Duke Social Support Inventory–Instrumental Support; DSSI-SI: Duke Social Support Inventory–Social Interaction; DSSI-PSS: Duke Social Support Inventory–Perceived Social Support.

TABLE 3. Predictors of 1-year depressive symptoms (Ham-D)

Predictor Variable (at intake)	Parameter estimate (±SE)	$F_{[df]}$	p
Initial Ham-D	0.03 ± 0.007	$20.3_{[1,213]}$	<0.0001
CIRS	0.06 ± 0.02	$11.5_{[1,213]}$	0.0008
IADL	0.007 ± 0.02	$0.2_{[1,213]}$	0.66
PSMS	−0.0007 ± 0.04	$0.0_{[1,213]}$	0.99
Neuroticism	0.02 ± 0.006	$5.9_{[1,213]}$	0.017
DSSI-IS	−0.003 ± 0.02	$0.0_{[1,213]}$	0.88
DSSI-SI	−0.04 ± 0.03	$1.4_{[1,213]}$	0.23
DSSI-PSS	−0.001 ± 0.02	$0.0_{[1,213]}$	0.95

Note: Covariates: age, gender, education.

Overall test for the eight variables of interest: $\chi^2_{[1]} = 424.8$; $p < 0.0001$.

Ham-D: Hamilton Rating Scale for Depression; CIRS: Cumulative Illness Rating Scale; IADL: Instrumental Activities of Daily Living; PSMS: Physical Self-Maintenance Scale; DSSI-IS: Duke Social Support Inventory–Instrumental Support; DSSI-SI:–Duke Social Support Inventory–Social Interaction; DSSI-PSS: Duke Social Support Inventory–Perceived Social Support.

initial social functioning nor initial depression diagnosis (i.e., major versus minor versus subsyndromal depression versus nondepressed) was significantly associated with poorer social functioning at follow-up (parameter estimates [±SE]: major depression: –0.004 ± 0.08; minor depression: 0.02 ± 0.08; $F_{[3,231]} = 1.9$; $p = 0.13$). However, major depression alone (i.e., versus nondepressed) was independently associated with poorer social functioning even after covarying initial social functioning (parameter estimate: –0.17 ± 0.07; $F_{[1,191]} = 6.2$; $p = 0.01$). In the whole group, initial Ham-D score also was associated independently with social functioning after controlling for initial social functioning (parameter estimate: –0.01 ± 0.003; $F_{[1,233]} = 8.4$; $p = 0.004$).

DISCUSSION

Our results must be considered in the context of potential study limitations, including the possibility that the findings may not be generalizable to older patients with lower educational attainment or from other geographic regions. We also note that we conducted multiple analyses on a relatively modest sample size, and so our results bear replication.

Nonetheless, these data confirmed the public-health importance of depressive conditions seen in elderly patients in primary care. All the depressive conditions studied had considerable rates of persistence at 1 year. Consistent with our exploratory hypotheses, subsyndromal depression had an outcome generally comparable to that of minor depression, and both had outcomes somewhat more favorable than major depression, but worse than the nondepressed group. It is not clear how to interpret the directional difference of subsyndromal depression as a predictor, although this may be an artifact produced in the context of the other predictors in the model because the unadjusted data indicate that the subsyndromal group had higher rates of worsening than the nondepressed group.

Major depression (versus no depression) and depressive symptom severity predicted poorer social functioning, although overall depression group did not. This suggests that major depression confers significant risk for poorer social functioning outcome, but this risk is "diluted" when considering minor and subsyndromal depression, which did not confer significant risk of poorer outcome in this domain.

At the same time, we note that the 1-year outcome of depressive conditions was not uniformly poor, with more than half the subjects improving and more than one-third becoming free of diagnosable current depression. This improvement was not associated with antidepressant treatment. Such outcome variability may be responsible for depression's general lack of association with poorer functional outcome on the IADL, PSMS, and social functioning scales.

In our study, as with previous findings from other populations, medical illness burden was a significant predictor of poorer depression outcome. Results from our exploratory analyses indicate the need for future work to pay particular attention to cardiovascular disorders and neurological conditions (cf, our review[50] and additional analyses from this data set[51]).

Neuroticism, a powerful predictor of depression outcome in younger psychiatric patient populations, was associated with greater depressive symptoms, albeit not with depression diagnosis at 1 year. It may be that the dimensional outcome of depressive symptoms is more "sensitive" to a dimensional construct of personality than are categorical depression diagnoses,[46] although this result also may be ascribed to differences in statistical power in detecting associations with categorical versus dimensional constructs.

The lack of association of antidepressant treatment with outcome is provocative. It is possible that, in our naturalistic study, selection bias may have contributed; that is, patients who were more ill (and thus have a poorer prognosis) may be more likely to receive treat-

ment. However, the lack of a measure of treatment adequacy is a limitation of this study that should be addressed in future work. Our finding certainly raises the possibility that suboptimal treatment (including inadequate dosing or duration of medication therapy) contributed to the observed outcomes.

We recognize that improvement at 1 year does not indicate sustained wellness. Further naturalistic study is required to determine the rates of subsequent recurrences over longer time periods. There is sufficient outcome variability to question the necessity of treating all patients showing depressive symptoms with uniform treatment approaches. Empirically supported practice guidelines clearly indicate that clinicians should offer treatment to patients with major depression.[22] For patients with minor or subsyndromal depression, evidence for specific treatment efficacy is more limited.[52] However, our data indicate that there is risk sufficient that clinicians may choose to treat those at greatest risk of chronicity or recurrence. For patients with minor or subsyndromal depression, then, clinicians may wish to consider targeting treatment to those with previous episodes, with substantial medical comorbidity (perhaps especially cardiovascular or neurological), or with personality vulnerabilities that lead to difficulty negotiating psychosocial stressors.

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