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## REDUCING SUICIDAL IDEATION AND DEPRESSION IN OLDER PRIMARY CARE PATIENTS: 24-MONTH OUTCOMES OF THE PROSPECT STUDY

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## Abstract

**Objective**—The PROSPECT Study evaluated the impact of a care management intervention on suicidal ideation and depression in older primary care patients. This is the first report of outcomes over a 2-year period.

**Method**—The subjects (N=599) were older (>=60 years) patients with major or minor depression selected after screening 9,072 randomly identified patients of 20 primary care practices randomly assigned to the PROSPECT intervention or usual care. The intervention consisted of services of 15 trained care managers, who offered algorithm-based recommendations to physicians and helped patients with treatment adherence over 24 months.

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**Results**—Intervention patients had a higher likelihood to receive antidepressants and or psychotherapy (84.9–89% vs. 49–59%) and a 2.2 times greater decline in suicidal ideation than usual care patients over 24 months. Treatment response occurred earlier in intervention patients and continued to increase from the 18<sup>th</sup> to the 24<sup>th</sup> month, while there was no appreciable increase in usual care patients during the same period. Among patients with major depression, a greater number achieved remission in the intervention than the usual care group at 4 (26.6 vs. 15.2%), 8 (36% vs. 22.5%), and 24 (45.4% vs. 31.5%) months. Patients with minor depression had favorable outcomes regardless of treatment assignment.

**Conclusions**—Sustained collaborative care maintains high utilization of antidepressant treatment, reduces suicidal ideation, and improves the outcomes of major depression over two years. These observations suggest that sustained collaborative care increases depression-free days.

#### Keywords

Geriatric psychiatry; Outcome Studies; Suicide; Mood Disorders-Unipolar

## INTRODUCTION

The Institute of Medicine has identified prevention of suicide as a national imperative <sup>1</sup>. Despite recent decline in suicides of persons older than 64 years, the suicide rate (14.3/100,000) of older adults remains higher than that of the general population <sup>2</sup>. Suicidal ideation and depression are two major risk factors for late-life suicide and targets for prevention <sup>3</sup>.

Primary care is a strategic setting for treating geriatric depression and for preventing suicide. Major depression has been identified in 6–9% of primary care patients while more than 17% have less severe depressive symptoms <sup>4</sup>. Moreover, 18% of primary care patients with major depression have suicidal ideation <sup>5</sup>.

Care management models offered over one year increase utilization of antidepressant treatment and improve outcomes of depression in primary care patients <sup>6,7</sup>. Depression in old age is a chronic, relapsing illness, and one-year data alone are insufficient for understanding the impact of care management.

This report presents outcomes of a 2-year intervention by the Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT). An early analysis showed greater decline in suicidal ideation and depressive symptomatology and higher response and remission rates in depressed patients receiving the PROSPECT intervention than usual care <sup>6</sup>. However, by 12 months, the advantages of intervention were no longer retained.

This paper focuses on PROSPECT's primary outcomes during the second year of treatment. It tests the hypotheses that depressed patients treated in practices offering the PROSPECT intervention have: 1) greater reduction in suicidal ideation; and 2) better outcomes of depression, i.e. greater decline in depressive symptomatology and higher rates of treatment response and remission than patients of usual care practices over 2 years.

## METHOD

#### Subjects

The study was conducted in 20 primary care practices of urban, suburban, and rural areas. Its procedures were approved by the institutional review boards of participating centers (Cornell, University of Pennsylvania, University of Pittsburgh). The study used a two-stage

#### Randomization

Ten pairs of practices were formed, each consisting of practices with similar academic affiliation, size, setting, patients, and region. The practices of each pair were randomly assigned to intervention or usual care. Randomization by practice was selected to minimize "contamination" of intervention procedures to usual care.

#### Intervention

The intervention was offered for 24 months to patients who presented at baseline with a major depression based on DSM-IV criteria, or a minor depression defined as three to four depressive symptoms, a 24-item Hamilton Depression Rating Scale (HDRS) <sup>8</sup> score of 10 or higher, and a duration of at least one month. It consisted of a composite intervention (further described elsewhere <sup>6</sup>) implemented by 15 practice-based care managers guided by a treatment algorithm. The care managers were social workers, nurses, and psychologists trained in PROSPECT procedures. They helped physicians to recognize depression, offered algorithm-based recommendations, monitored depressive symptoms and side effects, and provided follow-up over 24 months. The care managers also offered interpersonal psychotherapy (IPT) to patients who refused medication. They saw patients at the practices' offices but made house calls to patients unable to travel and addressed patient concerns related to treatment adherence.

The algorithm was based on Agency for Health Care Policy and Research (AHCPR) Practice Guidelines modified for use in elderly patients (described elsewhere) <sup>9</sup>. The first step of the algorithm was use of citalopram at the target daily dose of 30 mg. to avoid undertreatment. Physicians had the option to prescribe other antidepressants or refer subjects for psychotherapy other than IPT. Research funds covered the cost of citalopram and IPT only. Psychiatrist investigators provided weekly group supervision to care managers and were available by telephone.

#### **Usual Care**

Physicians in usual care practices had no assistance but received videotaped and printed material on geriatric depression and its treatment. They were also informed by letter of the patients' depression diagnosis and suicidal ideation when present.

#### Systematic Assessment

Diagnoses were based on the Structured Clinical Interview for DSM-IV (SCID-IV)<sup>10</sup>. Severity of depression was assessed with the HDRS and cognitive impairment with the Mini Mental State Examination (MMSE)<sup>11</sup>. Suicidal ideation was rated with the Scale for Suicide Ideation (SSI)<sup>12</sup>. The SSI has sound psychometric properties in younger psychiatric outpatients <sup>12</sup> and has yielded a factor structure for older adults similar to that for younger adults <sup>13</sup>. The SSI scores were skewed; 80–90% of patients had a score of 0 (no suicidal ideation) at any assessment point. For this reason, the SSI was treated as a dichotomous variable. We also created dichotomous variables of the three SSI factors <sup>12</sup>. The "passive suicidal desire" factor consists of items reflecting precautions to save life, self confidence in ability to commit suicide, and hesitance to reveal suicidal thoughts. The "active suicidal desire" factor consists of the following items: Wish to live, wish to die, reasons for living/ dying, wish to make suicida attempt, duration of suicide ideation/wish, frequency of suicide wish, attitude toward suicidal ideation/wish, deterrents to active attempt, reason for contemplating attempt, and expectancy/anticipation of actual attempt. The "preparation"

factor consists of items reflecting consideration of method, availability of method, and actualization of attempt. Each subject was assigned to a single SSI factor according to severity based on the following rule. Subjects endorsing a Preparation item were assigned to the Preparation factor regardless of endorsement of items of other factors. Subjects endorsing an Active Suicidal Desire item, but not a Preparation item, were assigned to the Active Suicide Desire factor. Finally, subjects endorsing a Passive Suicidal Desire item, but not a Preparation or Active Suicidal Desire item, were assigned to the Passive Suicide Desire Factor.

Randomization by practice prevented blinded assessment. Nonetheless, raters did not participate in the patients' treatment and were held to high standards of inter-rater reliability (reported elsewhere <sup>6</sup>). Moreover, assessment data were not made available to care managers or clinicians except as required for safety. Patients had in-person interviews at 12 and 24 months and telephone assessments at 4, 8, and 18 months after entry.

#### **Data Analysis**

Tests and estimates of intent-to-treat (ITT) differences for outcomes were based on longitudinal models with random effects for clustering by patient, practice, and practice pairs. The ITT sample included all patients with a baseline assessment regardless of treatment and drop-out status during follow-up. Clustering by practice and pairs of practices was negligible and did not impact the analysis. The longitudinal random effects models included main effect and interaction terms that represented ITT contrasts at each of the 4, 8, 12, 18, and 24-month points. The "omnibus" statistic tests for significant ITT contrasts at any one follow-up assessments and is a time by group interaction <sup>14</sup>. For continuous outcomes, analyses were based on SAS PROC MIXED. Both Proc NLMIXED and the GLIMMIX macro in SAS were used to employ two- and three-level random effects models, respectively, for binary outcomes. Given group difference in baseline suicidal ideation (20 vs. 31%; P=.02), this variable was controlled for in all ITT analyses. Such adjustment is appropriate under the random effects models. Moreover, all ITT analyses, except that of the longitudinal suicide ideation outcome, were robust to such an adjustment. Results were also robust with respect to random effects assumptions <sup>15</sup>. Additional robustness existed in intervention differences in missed assessments and drop-out, without making imputation assumptions such as last-observation-carried forward <sup>16</sup>.

## RESULTS

#### Participants' Characteristics, Dropout and Missed Assessments

The participants' demographic and clinical characteristics were reported elsewhere  $^{6}$ . Briefly, 71.6% of participants were women, 30.1% were aged 75 years or older, 32.4% belonged to minorities, 3.8% met poverty status, 36.9% were married, and 56.5% lived alone. Their average HDRS score was 18.1 and their MMSE was 27.4. There were no significant differences in demographic or clinical characteristics between the intervention and usual care groups except in suicidal ideation.

At 24 months, 43% (137/320) of intervention patients and 37% (102/279) of usual care patients failed to have a research assessment (Figure 1). The influence of differences in dropout was assessed by comparing results from our analysis to results under the shared parameter model, which adjusts for such differences. Group assignment did not differ by more than 5%, and P values were not significant. The proportion of missed assessments in the usual care group exceeded that in the intervention group for all assessments with the difference not exceeding 6% points for any assessment. There were no statistically

significant differences among intervention and usual care patients who had the 24-month assessment.

#### Treatment

More intervention (84.9–89%) than usual care patients (49–59%) received antidepressant treatment at 4, 8, 12, 18 and 24 months (Figure 2), including antidepressants (p<0.001) and psychotherapy (p<0.001). There were no significant group differences in combination therapy received at 4, 8, 18 and 24 months, but fewer intervention patients received combined treatment at 12 months (Odds Ratio: 0.25, CI: 0.07–0.89,  $\chi^2$ =4.62, p<0.03).

#### Suicidal Ideation, Attempts, Suicide, and Mortality

In the whole group, intervention patients were more likely to report suicidal ideation (endorse any SSI item) at baseline than usual care patients [29.7% (95/320) vs. 20.4% (57/279), P<.01]. By 4 months, the rates of overall suicidal ideation declined more in intervention than in usual care patients [12.8%: from 29.7% (95/320) to 16.9% (42/248) vs. 3.0%: from 20.4% (57/279) to 17.4% (40/229), P=0.02]. By 24 months, there was a 2.2 times greater decline in raw rates of suicidal ideation in intervention compared to usual care patients [Intervention: 18.3% change: from 29.7% (95/320) to 11.4% (20/176) vs. Usual Care: 8.3% change: from 20.4% (57/279) to 12.1% (21/173); P=0.12].

Ninety percent of patients with positive SSI scores at any point over 24 months endorsed only items of the SSI "active suicide desire" factor. For this reason, further analysis focused on the "active suicide desire" factor (Table 1). Adjusting for baseline difference, the omnibus trend testing ITT differences in change of "active suicidal desire" over time showed a trend favoring the intervention in the whole depressed group (P=0.09) and a significant difference among patients with major depression (P=0.04). Intervention patients with major depression had lower "active suicidal desire" than usual care patients at 4, 8, and 24 months. The differences among patients with minor depression were not significant (P=0.86). Due to low frequency, combined rates are presented for the other two SSI factors, "Preparation" and "Passive suicidal desire" (Table 1). Insufficient number of subjects with either of these two SSI factors prevented meaningful statistical analysis.

Of all patients with positive responses on the SSI, the most frequently endorsed items were item 2 (31%; wish to die), item 3 (29%; reasons for living/dying), and item 1 (15%; wish to live). While they fall within the "active suicide desire" factor, clinicians may classify these items as "passive suicidal ideation". The next most frequently endorsed items were item 11 (3.2%; reason for contemplating attempt), 7 (3%; frequency of suicide wish), 4 (2.7%; wish to make suicide attempt), and 12 (2.4%; consideration of method). In each remaining SSI item, endorsement did not exceed 2%.

During the study, two patients attempted suicide in the intervention arm, and three patients in the usual care arm. One of the attempted suicides in the intervention arm resulted in death. Further information on mortality was obtained through death certificates over a period of 5 years after entry to the study. During this time, 60 (44.7/1000 person years) patients of the intervention arm and 55 (49.7/1000 person years) patients of the usual care arm died <sup>17</sup>. It is possible that some of the deaths after 24 months were due to suicide that was not recorded in death certificates.

#### **Course of Depression**

**Severity of Depression**—The decrease in HDRS from baseline was greater in the intervention than in the usual care group at all assessment points, and the overall omnibus test indicated significance (Table 2). Greater decline in HDRS was also noted in patients

with major depression at each assessment point and overall. There were no significant differences in HDRS decline between intervention and usual care patients with minor depression.

**Treatment Response**—Response was defined as a reduction of baseline HDRS score by 50% or more. In the whole group, intervention patients had higher overall response rates than usual care patients (omnibus trend  $\chi^2(5)=17.3$ , P<.004) and at 4, 8, 12, and 24 months. From 18 to 24 months, 7.3 times more intervention patients (9.4%, from 52.9% to 62.3%) responded to treatment than usual care patients (1.3%, from 45% to 46.3%). At 24 months, 35% more intervention patients had met criteria for response of depression than usual care patients. The number needed to treat (NNT) for response rates at 24 months is 6, i.e. the intervention yielded one additional response for every 6<sup>th</sup> patient. In the subgroup with major depression, intervention patients had higher overall response rates than usual care patients (omnibus trend  $\gamma^2(5) = 17.3$ , P<.004) and at 4 (OR: 3.8, 95% CI: 1.8–8.2, p<0.001), 8 (OR: 2.9, 95% CI: 1.4–6.2, p<0.005), and 24 months (OR: 4.9, 95% CI=2.2.–11.2, P<0.001). There was a 9.4% increase in response rate from 18 to 24 months in patients with major depression of intervention practices (from 54.4% to 63.8%) but a 3.2% (from 42.4% to 39.6%) decline in patients of usual care practices. The NNT for response rates at 24 months was 4 patients. There were no significant differences in response rates between intervention and usual care patients with minor depression.

**Remission**—Remission was defined as an HDRS score lower than 7. In the whole depressed group, intervention had higher remission rates than usual care at 4 and 8 months (Table 3). Usual care remission rates approximated those of intervention at 12, 18 and 24 months. In the major depression group, intervention led to higher remission rates at 4, 8, and again at 24 months but there were no significant differences at 12 and 18 months. At 24 months, 1.44 times more intervention patients had achieved remission than usual care patients (45.4% vs. 31.5%). The NNT showed that the intervention yielded one additional remission for every 7<sup>th</sup> patient. There were no differences in remission rates between intervention and usual care patients with minor depression.

## DISCUSSION

The principal finding of this study is that depressed patients of practices randomized to the PROSPECT intervention had a higher likelihood to receive antidepressant treatment, a greater decline in suicidal ideation, lower depressive symptomatology, and a higher rate of response over 24 months than usual care patients. At any assessment point, 84.9–89% of intervention patients received antidepressants and/or psychotherapy while only 49–59% of usual care patients were treated for depression. The intervention was most effective in reducing suicidal ideation among patients with major depression. The decline was sharpest in the first 4 months and remained low up to 24 months. Similarly, severity of depression remained lower in intervention than usual care patients throughout the 24 months. Among patients with major depression, a greater number achieved remission in the intervention than the usual care group at 4, 8, and 24 months. The intervention had no advantages among patients with minor depression.

To our knowledge, this is the first study of 24-month depression care management focusing on suicidal ideation and depressive psychopathology in older primary care patients. Its findings are consistent with observations in mixed aged <sup>18</sup> primary care patients, including an intervention of 24-months duration <sup>19</sup>. In geriatric patients, the Improving Mood-Promoting Access to Collaborative Treatment (IMPACT) Study provided access up to 12 months to a depression care manager <sup>20</sup>. Primary care patients receiving the IMPACT intervention were more likely to receive antidepressant treatment than usual care patients

and had better depression outcomes. The advantage over usual care was retained 12 months after the end of the intervention, although there was a decline of response and remission rates from 12 to 24 months <sup>21</sup>. In contrast, with continuing depression care management the response and remission rates in the intervention arm of the PROSPECT Study remained high or increased.

In most subjects, suicidal ideation was passive as often is the case in depressed primary care patients <sup>22</sup>. Even passive suicidal ideation requires attention. Depressed elders with passive suicidal ideation are more likely to have history of suicide attempts, higher scores of hopelessness <sup>23</sup>, slower treatment response, and lower rates of response than non-suicidal elders with major depression <sup>24</sup>. Passive suicidal ideation has a stronger association with medical comorbidity and service utilization than active suicidal ideation or no suicidal ideation <sup>5</sup>. Finally, 35% of patients with suicidal ideation change ideator status during the index episode; passive ideators become active or the reverse <sup>23</sup>. Change over time in passive suicidal ideation requires further research to identify treatment responsive and treatment resistant components that may further focus suicide prevention interventions for depressed older primary care patients.

There was one suicide and one suicide attempt in the intervention group, and three suicide attempts in the usual care group. These numbers do not allow statistical study of the relationship of suicidal ideation to suicide or attempts, but underscore the challenge of reducing the risk of suicide in primary care settings. The relationship of reduction in the rate of suicidal ideation, and especially passive or death ideation, to suicide remains to be determined.

Over 24 months, 49.7% of depressed intervention patients achieved remission (HDRS<7). Remission, defined as an almost asymptomatic state, is the optimal outcome because it is associated with low relapse rate and high function <sup>25</sup>. Randomized acute antidepressant trials show that 30–40% of patients achieve remission <sup>26</sup>. A controlled maintenance treatment trial showed that 65% of elderly patients with major depression remained in remission over 24 months while treated with paroxetine and monthly psychotherapy <sup>27</sup>. The remission rate of the PROSPECT intervention was somewhat lower than this figure. Nonetheless, demonstrating that a care management intervention can maintain almost half of depressed primary care patients in remission is evidence of a meaningful level of effectiveness.

While antidepressant prescriptions have been rising, many depressed primary care patients receive no antidepressant treatment <sup>19</sup>. Poor treatment adherence further compromises their care <sup>28</sup>. In this study, more than 84% of intervention patients received antidepressants or psychotherapy throughout the study, while only 49–59% of usual care patients received any antidepressant treatment.

Depression almost doubles the risk for death in community samples <sup>29</sup>. Patients of PROSPECT intervention practices with major depression had lower mortality than those in usual care practices (adjusted hazard ratio: 0.55, 95% CI: 0.36–0.84) over a 52.8 month median follow-up <sup>17</sup>, but there were no differences in mortality among patients with minor depression. This observation is consistent with reduced all-cause mortality reported in patients receiving antidepressants over 40 months in the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) study <sup>30</sup>.

The benefits of the PROSPECT intervention on suicidal ideation and on depression were limited to patients with major depression. Patients with minor depression had overall favorable outcomes regardless of treatment assignment. At 24 months, only 6.2% of usual care patients had any suicidal ideation and 60.6% had achieved remission of minor

depression. Given limited resources, patients with major depression should be the target of a care management intervention.

Limitations of the study include the use of SSI as the sole method for ascertaining suicidal ideation, the lack of information on discrete medical problems of participants, and on specific antidepressant treatments received by each group. Randomization at the practice level compromised the ability to blind raters. Covering the cost of citalopram and IPT limits study of cost as a barrier to treatment. Finally, attrition was relatively high, perhaps because the study enrolled a probability sample consisting of subjects less interested in study participation than help-seeking patients. Nonetheless, probability sampling permits safer generalization of findings. Moreover, the baseline clinical characteristics of those assessed at 24 months were similar to those of the sample initially entered. Finally, taking drop-out into consideration did not influence differences between treatment groups significantly. Another limitation is that suicidal ideation was assessed at single points in time although suicide thoughts wax and wane.

Strengths of this study include its random sampling and a sensitive screening approach designed to identify most patients with depression. These procedures allow generalization of findings to whole practices. Furthermore, the practices were heterogeneous and consisted of small, large, inner city, rural, academic, and privately owned practices. Finally, patients with suicidal ideation, cognitive impairment, and medical burden were included in the sample. Therefore, these findings may be relevant to real-world practices.

Primary care is a strategic point from which to fight suicidality and depression since most elderly patients suffering from these syndromes are treated by primary care physicians. Sustained collaborative care maintains high utilization of antidepressant treatment, reduces suicidal ideation, and increases response and remission rates of major depression over a period of two years. Rising response and remission rates between the 18<sup>th</sup> and the 24<sup>th</sup> month underscore the value of long term care. These observations suggest that sustained collaborative care increases both depression-free days and perhaps longevity.

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### References

- 1. Goldsmith, SK. Reducing Suicide: A National Imperative. Washington, DC: National Academy Press; 2002.
- Conwell Y, Thompson C. Suicidal behavior in elders. Psychiatr Clin North Am 2008;31:333–356. [PubMed: 18439452]

- Conwell Y, Duberstein PR, Cox C, Herrmann JH, Forbes NT, Caine ED. Relationships of age and axis I diagnoses in victims of completed suicide: a psychological autopsy study. Am J Psychiatry 1996;153:1001–1008. [PubMed: 8678167]
- Lyness JM, Caine ED, King DA, Cox C, Yoediono Z. Psychiatric disorders in older primary care patients. J Gen Intern Med 1999;14:249–254. [PubMed: 10203638]
- Bartels SJ, Coakley E, Oxman TE, et al. Suicidal and death ideation in older primary care patients with depression, anxiety, and at-risk alcohol use. Am J Geriatr Psychiatry 2002;10:417–427. [PubMed: 12095901]
- Bruce ML, Ten Have TR, Reynolds CF 3rd, et al. Reducing suicidal ideation and depressive symptoms in depressed older primary care patients: a randomized controlled trial. JAMA 2004;291:1081–1091. [PubMed: 14996777]
- Unutzer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. JAMA 2002;288:2836–2845. [PubMed: 12472325]
- Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62. [PubMed: 14399272]
- Mulsant BH, Alexopoulos GS, Reynolds CF 3rd, et al. Pharmacological treatment of depression in older primary care patients: the PROSPECT algorithm. Int J Geriatr Psychiatry 2001;16:585–592. [PubMed: 11424167]
- Spitzer, R.; Gibbon, M.; Williams, JB. Structured Clinical Interview for Axis I DSM-IV Disorders (SCID). Washington, D.C.: American Psychiatric Association Press, Inc.; 1995.
- 11. 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;12:189–198. [PubMed: 1202204]
- Beck AT, Kovacs M, Weissman A. Assessment of suicidal intention: the Scale for Suicide Ideation. J Consult Clin Psychol 1979;47:343–352. [PubMed: 469082]
- Witte TK, Joiner TE Jr, Brown GK, et al. Factors of suicide ideation and their relation to clinical and other indicators in older adults. J Affect Disord 2006;94:165–172. [PubMed: 16740318]
- Ten Have TR, Kunselman AR, Pulkstenis EP, Landis JR. Mixed effects logistic regression models for longitudinal binary response data with informative drop-out. Biometrics 1998;54:367–383. [PubMed: 9544529]
- Litiere S, Alonso A, Molenberghs G. Type I and Type II Error Under Random-Effects Misspecification in Generalized Linear Mixed Models. Biometrics 2007;63:1038–1044. [PubMed: 17425642]
- Little R, Yau L. Intent-to-treat analysis for longitudinal studies with drop-outs. Biometrics 1996;52:1324–1333. [PubMed: 8962456]
- Gallo JJ, Bogner HR, Morales KH, Post EP, Lin JY, Bruce ML. The effect on mortality of a practice-based depression intervention program for older adults in primary care. A cluster randomized trial. Annals of Internal Medicine 2007;146:689–698. [PubMed: 17502629]
- Katon WJ, Schoenbaum M, Fan MY, et al. Cost-effectiveness of improving primary care treatment of late-life depression. Arch Gen Psychiatry 2005;62:1313–1320. [PubMed: 16330719]
- Rost K, Nutting P, Smith JL, Elliott CE, Dickinson M. Managing depression as a chronic disease: a randomised trial of ongoing treatment in primary care. BMJ 2002;325:934. [PubMed: 12399343]
- Unutzer J, Katon W, Callahan CM, et al. Depression treatment in a sample of 1,801 depressed older adults in primary care. J Am Geriatr Soc 2003;51:505–514. [PubMed: 12657070]
- 21. Hunkeler EM, Katon W, Tang L, et al. Long term outcomes from the IMPACT randomised trial for depressed elderly patients in primary care. BMJ 2006;332:259–263. [PubMed: 16428253]
- 22. Schulberg HC, Lee PW, Bruce ML, et al. Suicidal ideation and risk levels among primary care patients with uncomplicated depression. Ann Fam Med 2005;3(6):523–528. [PubMed: 16338916]
- Szanto K, Reynolds CF 3rd, Conwell Y, Begley AE, Houck P. High levels of hopelessness persist in geriatric patients with remitted depression and a history of attempted suicide. J Am Geriatr Soc 1998;46(11):1401–6. [PubMed: 9809762]
- Szanto K, Mulsant BH, Houck P, Dew MA, Reynolds CF 3rd. Occurrence and course of suicidality during short-term treatment of late-life depression. Arch Gen Psychiatry 2003;60:610–617. [PubMed: 12796224]

- 25. Lecrubier Y. How do you define remission? Acta Psychiatr Scand 2002;106:7–11. [PubMed: 12366462]
- Thase ME, Entsuah AR, Rudolph RL. Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. Br J Psychiatry 2001;178:234–241. [PubMed: 11230034]
- Reynolds CF 3rd, Dew MA, Pollock BG, et al. Maintenance treatment of major depression in old age. N Engl J Med 2006;354:1130–1138. [PubMed: 16540613]
- Gilbody S, Whitty P, Grimshaw J, Thomas R. Educational and organizational interventions to improve the management of depression in primary care: a systematic review. JAMA 2003;289:3145–3151. [PubMed: 12813120]
- Bruce ML, Leaf PJ, Rozal GP, Florio L, Hoff RA. Psychiatric status and 9-year mortality data in the New Haven Epidemiologic Catchment Area Study. Am J Psychiatry 1994;151:716–721. [PubMed: 8166313]
- Berkman LF, Blumenthal J, Burg M, et al. Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. JAMA 2003;289:3106–3116. [PubMed: 12813116]

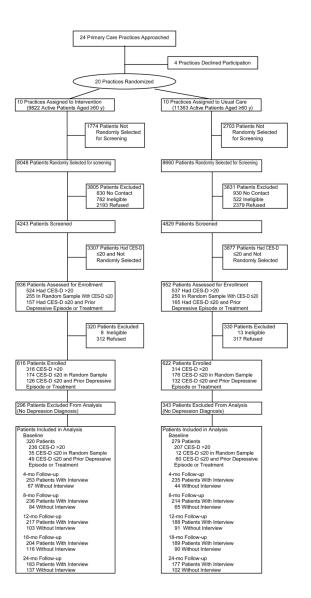
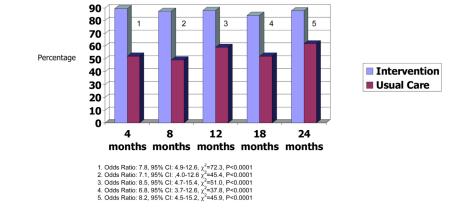


Figure 1. Flowchart of Progress Through the Phases of the PROSPECT Trial Abbreviation: CES-D: Center for Epidemiologic Studies Depression Scale





Percentage of Depressed Older Primary Care Patients Who Received Treatment for Depression, by Assessment Point

Table 1

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Rates of Suicidal Ideation Over Time

				*						
	No. with Su	cidal Ideat	No. with Suicidal Ideation/No. Analyzed (%)	.zed (%)						
	Intervention	ntion	Usual Care	Care	Οd	Odds Ratio	P Value	Omn	Omnibus Test <sup>**</sup>	t**
All depressed patients	N	%	Ν	%	OR	95%CI		$\chi^{2}=9.6$	df=5	P=.09
Baseline Active <sup>+</sup>	89/320	27.5	52/279	18.6	1	:				
Preparation <sup>++</sup>	6/320	1.9	5/279	1.8	1	:				
4 mo Active	40/248	16.1	36/229	15.7	2.2	1.0-4.9	.04			
Preparation	2/248	0.8	4/229	1.7	:	-	1			
8 mo Active	40/233	17.2	39/210	18.6	3.1	1.4–6.8	.005			
Preparation	1/233	0.4	1/210	0.5	;	-				
12 mo Active	30/213	14.1	23/186	12.4	1.8	0.8-4.3	.18			
Preparation	1/213	0.5	2/186	1.1	;	-				
18 mo Active	24/200	12.0	18/181	9.9	1.5	0.6–3.6	.43			
Preparation	1/200	0.5	0/181	0	;	-				
24 mo Active	20/176	11.4	20/173	11.6	2.1	0.8–5.5	.11			
Preparation	0/176	0	1/173	0.6	:		-			
Major Depression								$\chi^{2=} \ 11.4$	df=5	P= .04
Baseline Active	74/214	34.6	43/182	23.6	;	1	I			
Preparation	5/214	2.3	5/182	2.7	:	-				
4 mo Active	34/170	20.0	28/145	19.3	2.5	1.1-6.2	.05			
Preparation	1/170	0.6	4/145	2.8	1					
8 mo Active	33/160	20.6	34/135	25.2	4.2	1.7 - 10.5	.002			
Preparation	1/160	0.6	1/135	0.7	1	-	-			
12 mo Active	23/146	15.8	17/117	14.5	2.2	0.8–5.9	.14			
Preparation	0/146	0	1/117	0.9	:	-				
18 mo Active	19/134	14.2	16/113	14.2	2.1	0.7–5.9	.17			
Preparation	0/134	0	0/113	0	1					
24 mo Active	14/124	11.3	16/109	14.7	3.2	1.1–9.5	.04			

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	Intervention	ation	Usual Care	Care	Odo	Odds Ratio	P Value	Omn	Omnibus Test**	t**
All depressed patients	z	%	N	%	OR	95%CI		χ <sup>2</sup> =9.6	df=5	P=.09
Preparation	0/124	0	1/109	0.9	:	;	-			
Clinically significant minor depression only								$\chi^{2}{=}1.9$	df=5	P=.86
Baseline Active	15/106	14.2	76/6	9.3	;	1	I			
Preparation	1/106	0.9	<i>L6/0</i>	0	-	1	-			
4 mo Active	6/78	7.7	8/84	9.5	1.8	0.4–8.9	.47			
Preparation	1/78	1.3	0/84	0	-	1	-			
8 mo Active	7/73	9.6	5/75	6.7	1.2	0.2–6.6	.81			
Preparation	0/73	0	0/75	0	-	1	-			
12 mo Active	7/67	10.4	69/9	8.7	1.1	0.2–5.7	06.			
Preparation	1/67	1.5	1/69	1.4	-	1	-			
18 mo Active	5/66	7.6	2/68	2.9	0.5	0.1–3.7	.46			
Preparation	1/66	1.5	0/68	0	-	-	-			
24 mo Active	6/52	11.5	4/64	6.2	0.8	0.1 - 4.4	.74			
Preparation	0/52	0	0/64	0	:	:				

Abbreviation: CI: Confidence Interval

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\* The discrepancies between 4, 8, 12, 18, and 24-month denominators and Figure 1 are due to incomplete or missing data on the Scale for Suicidal Ideation among some participants who were interviewed at these times.

\*\* Omnibus Tests were conducted in order to detect group differences in longitudinal change of Active Suicidal Desire from baseline. Omnibus Tests and Odds Ratios were not computed for Preparation because of its infrequent occurrence.

<sup>+</sup>Active: "Active Suicidal Desire" factor of the SSI

++ Preparation: "Preparation" factor plus "Passive Suicidal Desire" factor of the SSI

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Depression Severity Over Time

	Mea	n (SD) I	Mean (SD) HDRS Score	ore						
	Intervention	ention	Usual Care	Care	Group Difference in Change from Baseline	ange from Baseline	P Value	шO	Omnibus Test <sup>*</sup>	st*
All depressed patients	Mean	SD	Mean	SD	Group difference	95%CI		$\chi^{2}=33.6$	df=5	P< .001
Baseline	18.61	6.12	17.51	5.82			.73			
4 mo	11.24	7.51	13.57	8.42	-3.5	-4.7 to -2.3	<.001			
8 mo	10.45	7.39	11.38	7.49	-2.1	-3.4 to -0.9	<.001			
12 mo	9.77	7.28	10.35	6.78	-1.8	-3.1 to -0.5	.006			
18 mo	9.73	7.94	9.76	6.82	-1.3	-2.6 to 0.04	.06			
24 mo	8.81	7.51	9.28	6.54	-1.9	-3.2 to -0.5	.007			
Major Depression								$\chi^{2}=33.2$	df=5	P<.001
Baseline	21.05	5.74	19.72	5.54			.82			
4 mo	12.59	7.74	15.87	8.40	-4.6	-6.1 to -3.0	<.001			
8 mo	11.69	7.93	12.85	7.27	-2.4	-4.0 to -0.8	.004			
12 mo	10.42	7.62	11.21	7.11	-1.9	-3.6 to $-0.3$	.02			
18 mo	10.46	8.21	11.15	7.21	-1.9	-3.6 to -0.2	.03			
24 mo	9.53	7.84	10.43	6.70	-2.2	-3.9 to -0.5	.01			
Clinically significant minor depression only								$\chi^{2}=5.2$	df=5	P=.39
Baseline	13.69	3.23	13.36	3.70	-		.76			
4 mo	8.34	6.07	9.44	6.76	-1.4	-3.1 to 0.4	.14			
8 mo	7.81	5.23	8.72	7.20	-1.5	-3.3 to 0.4	.11			
12 mo	8.39	6.33	8.86	5.91	-1.1	-3.0 to .8	.24			
18 mo	8.25	7.19	7.45	5.41	0.2	-1.7 to 2.1	.86			
24 mo	7.03	6.36	7.34	5.80	7	-2.7 to 1.3	.51			

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Abbreviations: CI: Confidence interval; HDRS: Hamilton Depression Rating Scale

 $^{\ast}_{\rm P}$  values calculated with the Wald statistic adjusting for baseline ideation and HDRS scores

Table 3

Depression Remission (HDRS<7) Over Time

	No. with HI	<b>DRS Score</b>	No. with HDRS Score <7/No. Analyzed (%)*	zed (%)*						
	Intervention	ntion	Usual Care	Care	odd	Odds Ratio	P Value	Om	Omnibus Test <sup>*</sup>	st *
All depressed patients	Z	%	N	%	OR	95%CI		$\chi^{2}=7.6$	df=5	P<.18
4 mo	82/253	32.4	59/235	25.1	1.9	1.0–3.6	.05			
8 mo	97/236	41.1	68/215	31.8	2.1	1.1-4.0	.02			
12 mo	87/217	40.1	62/188	33.1	1.8	0.9–3.6	.07			
18 mo	89/204	43.6	72/189	38.1	1.6	0.8 - 3.1	.19			
24 mo	91/183	49.7	75/177	42.4	1.8	0.9–3.5	.10			
Major Depression								$\chi^{2} = 12.0$	df=5	P<.03
4 mo	46/173	26.6	23/151	15.2	3.1	1.3-7.5	.01			
8 mo	58/161	36.0	31/138	22.5	2.9	1.2–6.9	.01			
12 mo	53/148	35.8	38/119	31.9	1.3	0.6–3.1	.55			
18 mo	55/136	40.4	36/118	30.5	2.0	0.8-4.8	.12			
24 mo	59/130	45.4	35/111	31.5	2.9	1.2-7.0	.02			
Clinically significant minor depression only								$\chi^{2}$ = 4.5	df=5	P= .49
4 mo	36/80	45.0	36/84	42.9	1.2	0.4–3.0	.76			
8 mo	39/75	52.0	37/76	48.7	1.4	0.5-3.7	.54			
12 mo	34/69	49.3	24/69	34.8	2.7	1.0-7.8	.06			
18 mo	34/68	50.0	36/71	50.7	1.0	0.4–2.8	86.			
24 mo	32/53	60.4	40/66	60.6	0.9	0.3–2.8	.86			
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Abbreviations: CI: Confidence interval; HDRS: Hamilton Depression Rating Scale

\* The discrepancies between 4, 8, 12, 18, and 24-month denominators and Figure 1 are due to incomplete or missing data on the Scale for Suicidal Ideation among some participants who were interviewed at these times.

<sup>+</sup>Differences with respect to longitudinal change since baseline.