Published in final edited form as:
Compr Psychiatry. 2008 ; 49(3): 238–246. doi:10.1016/j.comppsych.2007.06.012.

Gender Differences in Depression Symptoms in Treatment-Seeking Adults: STAR*D Confirmatory Analyses

Sheila M Marcus, MD[*],
Department of Psychiatry, University of Michigan Medical School

Kevin B. Kerber, MD,
Department of Psychiatry, University of Michigan Medical School

A. John Rush, MD,
Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas

Stephen R. Wisniewski, Ph.D.,
Epidemiology Data Center, GSPH, University of Pittsburgh

Andrew Nierenberg, MD,
Department of Psychiatry, Harvard University

G. K. Balasubramani, Ph.D.,
Epidemiology Data Center, GSPH, University of Pittsburgh

Louise Ritz, MBA,
National Institute of Mental Health

Susan Kornstein, MD,
Virginia Commonwealth University

Elizabeth A. Young, MD, and
Department of Psychiatry and Mental Health Research Institute, University of Michigan

Madhukar H. Trivedi
Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas

Abstract

Background—While epidemiologic research consistently reports greater prevalence of major depressive disorder in women, small sample sizes in many studies do not allow for full elaboration of illness characteristics. This paper examines gender differences in terms of illness attributes in a cohort of 2541 outpatients from across the United States who enrolled in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study.

Method—Confirmatory analyses were performed in 2541 outpatients comparing men and women with regard to socio-demographic features, comorbid Axis I and Axis III conditions, and illness

*Corresponding Author: University of Michigan Department of Psychiatry, 4250 Plymouth Rd., Ann Arbor, MI 48105. Phone: (734) 764-0245, Fax: (734) 936-8907; email: smmarcus@umich.edu.

DECLARATION OF INTEREST
Research Support Eli Lilly

characteristics. Results were compared to those of our previous report on the initial population of the first 1500 individuals enrolled in STAR*D.

Results—In both samples, nearly two-thirds of the sample (62.5%) were women. Women had greater symptom severity, but men had more episodes of major depression, despite no difference in the length of illness. No differences in age of onset emerged. As in the first cohort, women showed greater rates of an anxiety disorder, bulimia and somatoform disorder, as well as more past suicide attempts, while men showed more alcohol and substance abuse. Women reported more appetite, weight, hypersomnia, interpersonal sensitivity, gastrointestinal and pain complaints, and less suicidal ideation. Irritability was equally common in men and women.

Conclusion—This large analysis confirmed most of the clinical features and co-morbidities found to be more prevalent in the first cohort of women. Additionally, this analysis corroborated previous research suggesting higher rates of atypical and anxious depression in women, but refuted the notion of an "irritable depression" found in men. The report confirmed the 1.7:1 ratio for depression seen across genders in the National Comorbidity Survey.

Keywords

Women; Depression; Prevalence; Gender

INTRODUCTION

Gender differences in rates of depression are well established, and seen in both epidemiological and treatment-seeking samples.[1,2] Gender differences in severity, symptom prevalence and comorbidity have received less attention, particularly since it may be difficult to have a large enough sample of cases to evaluate these parameters.[3] Previous analyses of these parameters in clinic populations have often studied a sample from a single site; thus, differences reported may be influenced by the specific demographics of the particular site. The Sequenced Treatment Alternatives to Relieve Depression Project is a series of multi-site treatment trials involving 14 geographically dispersed regional centers and 41 clinical sites across the United States. This provides a unique opportunity to examine these factors in a very large, nationally representative population of depressed outpatients in primary care and psychiatric settings.

In our previous report of the first 1500 STAR*D participants, we found a number of significant gender differences in both symptom profiles and comorbidities.[4] Women, as compared to men, demonstrated greater overall severity, earlier age of onset, more years since onset of depression, and a longer index episode. Symptoms that women reported to a greater extent than men included increased appetite and weight gain, low energy, somatic complaints and greater interpersonal sensitivity. Women reported more comorbid symptoms consistent with anxiety and eating disorders, while men reported comorbid symptoms that indicated more alcohol and substance abuse, in line with the gender ratios observed for these parent disorders.[5] The current report presents confirmatory analyses on a total of 2541 outpatients with nonpsychotic major depressive disorder (MDD) who entered into the STAR*D trial. In this report, we compare the findings from the current sample to the findings from the first 1500 participants reported on in the initial analysis.[4] The new analysis is intended to determine whether the findings in the initial sample are replicated in this larger sample. Given the robustness of many findings in the original sample of women, we anticipate that comorbid anxiety and eating disorders will retain greater prevalence in women within this sample. Likewise, we anticipate that appetite dysregulation and weight gain, as well as other atypical symptoms will be replicated as symptoms more common within women in this group. The importance of these findings for clinicians caring for women will be highlighted.

METHOD

This report evaluates a broadly representative clinical sample of outpatients with nonpsychotic MDD enrolled in the STAR*D (www.star-d.org) trial. The rationale and design of STAR*D have been detailed elsewhere.[6,7] This paper provides data on 2541 participants enrolled in STAR*D after the initial 1500 were enrolled and reports on analyses designed to replicate findings on the initial 1500 participants enrolled in STAR*D.

Briefly, STAR*D will define prospectively which of several treatments are most effective for outpatients with non-psychotic MDD who have an unsatisfactory clinical outcome to an initial and, if necessary, subsequent treatment(s). Eligible and consenting STAR*D enrollees are treated initially (Level 1) with a selective serotonin reuptake inhibitor. Those with an adequate clinical response to Level 1 treatment may enter a 12-month naturalistic follow-up phase. Those without such a response may enter one or more subsequent randomized controlled trials through a total of 4 additional possible levels of treatment.

The STAR*D infrastructure includes the National Coordinating Center in Dallas, the Data Coordinating Center in Pittsburgh, 18 primary care settings, and 23 specialty (psychiatric) care settings. The institutional review boards at the National Coordinating Center, the Data Coordinating Center, and the Regional Centers and Clinical Sites approved the study protocol.

Clinical Research Coordinators (CRCs) located at the clinical sites are trained and certified in implementing the treatment protocol and in data collection methods (screening, application of inclusion and exclusion criteria, and collecting clinical data). Additionally, the CRCs administer some of the clinician-rated instruments, ensure completion of the self-rated instruments, and act as liaison between the Clinical Sites and the Regional, National and Data Coordinating Centers.

Research outcome data are collected via telephone interviews with trained Research Outcomes Assessors (ROAs) who are not located at the clinical sites and are masked to treatment type. An automated telephone-based Interactive Voice Response (IVR) system obtains additional outcome data.[8]

Study Population

This sample was identified from 2541 consecutive participants enrolled in STAR*D.[6,7] Outpatients in both primary care and specialty settings, identified by their clinician as having non-psychotic major depression requiring treatment, were approached to consider participating in STAR*D. All risks, benefits, and adverse events associated with the trial were explained to potential participants who provided written informed consent prior to study participation.

At baseline, participants 18–75 years of age who met the Diagnostic and Statistical Manual of Mental Disorders' (DSM-IV)[9] criteria for single or recurrent nonpsychotic MDD were considered for the study. At study entry, participants had to score ≥ 14 (moderate intensity) on the CRC-rated 17-item Hamilton Rating Scale for Depression ($HRSD_{17}$).[10] Those with bipolar disorder or psychotic symptoms (lifetime) were excluded, as were those with a current primary diagnosis of obsessive compulsive or eating disorder, substance abuse/dependence or suicide risk requiring inpatient care, or a seizure disorder or other general medical condition (GMC) contraindicating medications used in the first two treatment levels. All other psychiatric and general medical comorbidities were allowed. Participants were excluded if they had previously not responded in the current episode to an adequate treatment trial of any medication used in the first two treatment steps of the protocol. Participants could not be breastfeeding or pregnant at study entry, or planning to be so in the subsequent nine months.

Assessments

At baseline, the CRCs collected standard demographic information, self-reported psychiatric history (including an assessment of suicidality) and severity of depressive symptoms as assessed by the $HRSD_{17}$. The CRCs completed the Cumulative Illness Rating Scale (CIRS), a 14-item interviewer-administered scale that gauges the severity/morbidity of GMCs relevant to different organ systems.[11,12] Three scores were generated by the CIRS. One score indicated the number of the 14 possible comorbid GMCs (Categories Endorsed), another score captured the average severity score of the domains endorsed (Severity Index), and the third was based on the sum of the severity scores across the domains endorsed (Total Severity).

A brief 16-item depression severity scale, the Quick Inventory of Depressive Symptomatology ($QIDS\text{-}SR_{16}$) was also completed by the patient at each visit. 13,14 The $QIDSSR_{16}$ rated the nine criterion symptom domains (range 0–27) needed to diagnose a major depressive episode (MDE) by DSM-IV. Additionally, the Psychiatric Diagnostic Screening Questionnaire (PDSQ) was completed by each participant.[15] This self-report instrument was used to determine the presence of comorbid psychiatric symptoms relevant to each disorder. The total number of symptom items relevant to each disorder was calculated and based on a threshold of the number of symptoms endorsed, the relevant Axis I disorder was declared to be present or absent.[16]

Research outcome data were collected via telephone interviews with trained Research Outcomes Assessors (ROAs) who were not located at the clinical sites and were masked to treatment type. The ROA used a telephone interview at baseline to collect the $HRSD_{17}$ and the 30-item Inventory of Depressive Symptomatology ($IDS\text{-}C_{30}$) which used unconfounded items to measure both core criterion diagnostic symptoms and associated symptoms of depression. 17,18 Based on the results of the $IDS\text{-}C_{30}$, participants were classified as having the atypical subtype of depression or the melancholic subtype of depression.[19] For atypical depression, we required a score of 0–2 on the item that rates reactivity of mood, and required that two or more of the following be present: hypersomnia rated as 2 or 3, increased appetite rated as 2 or 3 or increased weight rated as 2 or 3, interpersonal rejection sensitivity rated as 3, and leaden paralysisrated as 2 or 3.[20] To declare the presence of endogenous or melancholic features, we required that reactivity of mood be scored as 2 or 3 or pleasure/enjoyment be rated as 2 or 3, and 3 or more of the following be present: early morning insomnia rated as 3, mood worsening in the morning rated as >1, distinct quality of mood rated as 3, decreased appetite rated as >1 or weight decrease rated as 3, negative view of self rated as >1, and psychomotor slowing or psychomotor agitation rated as >1.[19] The definition of anxious depression was derived using the Hamilton Rating Scale for Depression and Anxiety Somatization Factor Score, in which individuals scoring 7 or greater on symptom questions including: psychic anxiety, appetite, somatic energy, somatic anxiety, loss of insight, and hypochondriasis were considered to have an anxious depression. The scores for the nine criterion domains of depression were obtained from the $IDS\text{-}C_{30}$ as follows: (1) Insomnia was defined based on the highest score on any one of the four relevant items (sleep onset insomnia, mid-nocturnal insomnia, early morning insomnia, hypersomnia) (2) Appetite/Weight change was defined based on the highest score on any one of the four relevant items (appetite increased, appetite decreased, weight decrease, weight increase) (3) psychomotor changes was based on the highest score on the psychomotor slowing or psychomotor agitation items. The other domains (4) sad mood (5) concentration/ decision making (6) self-outlook (7) suicidal ideation (8) involvement and (9) energy/ fatigability scores were based on the individual items from the $IDS\text{-}C_{30}$ scores. The presence or absence of the symptom for each domain was assessed if the score for the domain was greater than zero.

An automated telephone-based Interactive Voice Response (IVR) system obtained additional outcome data.[8] The IVR collected participant health perceptions via the 12-Item Short Form Health Survey (SF-12);[21,22] quality of life via the Quality of Life Enjoyment & Satisfaction

Questionnaire (Q-LES-Q), a 16-item self-report tool assessed the degree of enjoyment and satisfaction experienced by participants in various areas of daily functioning;[23] and the participant's report of daily function via the 5-item Work and Social Adjustment Scale (WSAS).[24]

Statistical Methods

Data are presented as percentages for categorical variables, and as means, standard deviation, median, and observed ranges for continuous variables. Chi-square goodness of fit tests were used to compare the distribution of the categorical variables among men and women, and a t-test or a nonparametric Wilcoxan Signed Rank test was used to compare continuous variables among men and women. To adjust for differences in age, epthnicity, and severity of depression between men and women, logistic regression and cumulative logistic regression models were used for discrete variables such as marital status. For continuous variables other than psychiatric history features (e.g., age at onset of the first major depressive episode (MDE), number of MDEs, length of the current MDE, and length of illness — time from onset of first MDE to study entry), analysis of covariance methods were used to control for age. For the psychiatric history variables, data were ranked and then analysis of covariance methods were used. The association of gender with the presence of specific presenting symptoms as measured by the IDS-C_{30}, where a symptom was considered to be present with an item score of at least one, was analyzed using a chi-square test and logistic regression analyses, adjusted for age. Note that the sample size varies between parameters due to missing data. The statistical significance for all tests was set at $p < .05$.

RESULTS

Demographics

The demographic features of this second STAR*D sample (Table 1) were similar to those of the first sample with the exception of the percentage of participants recruited from primary care settings. In the first sample (n=1500), 35.5% of the participants were recruited from primary care, while in the second sample (n=2541), 41.8% of the participants were recruited from primary care. Race, ethnicity, employment status, and marital status were similar in the two samples. As in the first sample, approximately 63% of the second sample participants were female.

Table 2 presents the baseline characteristics of the second sample by gender. Many of the gender differences found in the demographics of the previous sample were replicated in this sample. The mean age of women was lower in both samples, and in the current sample the mean age of women (39.4+13.3 years) was 3 years on average lower than that of men (42.4 +13.1 years). We found a greater proportion of Hispanic women (17.2%) than Hispanic men (10.1%) ($p<.0001$), as was true in the first sample. Other findings that held true across both samples included a significant difference in the distribution of subject across employment categories ($p<.0001$) with a greater likelihood of retirement among men (7.4%) than women (4.4%). Additionally, there was a significant difference in the distribution of subjects across the marital status categories ($p=.0035$) where there were more widowed women (4.4%) than men (1.8%).

Clinical features and comorbidities

Several clinical features seen within the first group of 1500 women were replicated in this sample of 2541 women. As seen in the previous report, women were more likely to have past suicide attempts (18.4%) than men (11.9%) ($p=0.0002$ adjusted). While in the last sample of 1500 there was no reported difference in the frequency of current suicidal ideation, in this sample men reported more current suicidal ideation (49.2%) than women (46.7%) ($p=0.0093$).

Men reported more previous episodes of major depression in both the original 1500 participants (men=7.2±12 episodes; women=4.7±7 episodes) and in the current replication (men=8.2±16.1 episodes; women=4.6±9.4 episodes), although this difference only reached statistical significance in the current analysis (adjusted p<.0001). Women had slightly higher levels of depressive symptoms as measured by the clinician-rated IDS (men=33.7±11.3; women=36.3 ±11.4; adjusted p<.0001) and the $HRSD_{17}$ (men=19.0± 6.4; women=20.0±6.5;adjusted p=. 0006), as well as the self-reported QIDS (men=14.7±4.3; women=15.9±4.3; adjusted p<.0001). In the current study, age of onset of major depression, length of current episode of depression and total length of illness did not differ between men and women, though we found a significant difference for all three factors in our original report.

Depressive symptom differences

Table 3 compares men and women with regard to symptoms as measured by the IDS-C_{30} obtained by the ROA. In our first analysis, women reported more appetite increase, weight increase, somatic complaints, sympathetic arousal symptoms, gastrointestinal symptoms and interpersonal sensitivity.[4] In this analysis, all of these symptoms again demonstrated significantly greater frequencies in women, with the exception of sympathetic arousal. Additionally, mid nocturnal insomnia emerged as a more common symptom in this sample of women but not in the first cohort. Our previous findings of symptoms more common in men (i.e., decreased appetite and increased psychomotor agitation) did not replicate in this sample, though men did report more suicidal ideation in this sample.

Table 4 presents the nine criterion domains used to diagnose a major depressive episode by DSM-IV. Women reported more changes in sleep, (OR 1.5 p=.0465) in weight and appetite, (OR = 1.5, p= 0.0001) as well as greater fatiguability and energy change, (OR = 1.7; p =0.0004), and lower rates of suicidal ideation (OR =.8, p=.0093).

Table 5 compares gender with regard to the likelihood of nine concurrent Axis I disorders as assessed by the PDSQ. Note that the method requires a high threshold to declare a condition present, thereby likely underestimating the prevalence of a number of conditions. Women were more likely than men to have generalized anxiety disorder (OR = 1.7, p<.0001), somatoform disorder (OR = 2.8, p=.01) and bulimia (OR = 3.1, p<.0001), while men were more likely to suffer both alcohol (OR =.4, p<.0001) and drug abuse (OR =.4, p<.0001). In the first cohort, women were more likely than men to have obsessive compulsive disorder, but this finding was not confirmed in this sample.

Table 6 examines three depressive subtypes (anxious, atypical and melancholic) and their relative frequency in women and men. Women demonstrated greater frequency of atypical depression than men (18.1% vs. 13.1%, adjusted p=.004). Note that both leaden paralysis (another diagnostic symptom of atypical depression) and mood reactivity did not differ between men and women. The melancholic subtype of depression was equally common in men (19.6%) and women (18.6%). However, more women (47.3%) than men (39.8%, adjusted p=.0006) met criteria for anxious depression.

DISCUSSION

We found several gender differences between depressed men and depressed women in both our original sample[4] and our present sample. Our finding of greater symptom severity in women replicates most[4,25] but not all [6] previous studies. We found that men had more MDEs in this sample than in our previous report.[4] It is worth noting, however, that the number of episodes by self-report may be a major limitation of this finding. This contrasts with the higher rates of relapse and recurrence for women that have been reported in other clinical population studies.

[27,28] However, in the National Comorbidity Survey, rates of relapse and chronicity were not associated with gender.[29]

Rates of concurrent comorbid Axis I disorders were similar to those from our previous report (i.e. more generalized anxiety, bulimia and somatization disorder in women, and more alcohol and substance abuse and dependence in men). Similar findings have been reported in previous studies. In one longitudinal epidemiological study, the prevalence of MDD and of one or two anxiety disorders was about two-fold higher in women than in men.[30] In epidemiologic samples, greater rates of substance abuse/dependence comorbid with depression have been reported previously in men[31] as has the greater frequency of eating disorders in clinical populations of women.[32]

Epidemiological data have found that completed suicide is more common in men, while suicide attempts are more common in women.[33,34] In line with this, more women attempted suicide in both STAR*D samples, though men reported more suicidal ideation in the current sample.

The striking consistency of these findings across two large cohorts of depressed outpatients suggests that these differences are robust, although not all of them were expected on a theoretical basis. More depressive episodes in men coupled with their greater substance abuse may reflect low treatment-seeking in men, which may lead to more episodes before entering treatment. However, the finding of more episodes in men was not explained by a longer total illness in this sample. In the previous sample, men did have a longer length of illness and a younger age at onset of the first MDE than women. Consequently, the finding of more MDEs in men may be explained by a greater propensity by men to view the MDE as having ended when it had not, or by factors in women that prolong episodes.

Some investigators have questioned whether there may be unique gender-based patterns of depressive illness. Hypotheses have been put forward that suggest there may be “male depression” that differs from classic depression.[35] In neither analysis did irritable mood emerge as more common in men, despite clinical lore that men show more mood irritability. In fact, both genders showed high rates of self-reported irritable mood (79% of men and 83% of women). It is possible that men may show more externalizing behaviors with their irritable mood, and this leads clinicians to conclude that men demonstrate more irritability. But these data do suggest that depressed men are more likely to engage in alcohol and substance abuse during their depressive illness.

In contrast to the findings in men, our current and previous reports show that a number of symptoms emerged as more common in women. Many of these findings, including increased appetite and weight, somatization and interpersonal sensitivity, have been previously reported in women.[26,3,36] While we found that atypical depression was more common in women, it was only increased by 1.3 fold in women over men and was present in less than 20% of depression cases. Likewise, anxious depression was more common in women and present in 47.3% of women. Melancholic depression was equally common in men and women.

There are several aspects of these STAR*D gender findings that are of clinical and therapeutic importance. For males, the greater number of depressive episodes which appear to precede treatment, suggest that increased attention to treatment engagement strategies and psychoeducation targeting males may be helpful to increase their connection to care. Moreover, the findings of increased substance abuse in men, corroborated in numerous other studies, highlights the importance of substance abuse screening for all men treated for depression. The findings of the STAR*D study suggest that irritability is not a prominent feature which reliably predicts depression in men any more often than in women.

Women more frequently complain of appetite increase and weight gain during episodes of depression. In some studies this increase in weight, and particularly abdominal weight, has been linked to increases in cortisol, which may increase insulin resistance.[37] This symptom is disturbing for many women and contributes to the demoralization that accompanies depression. It is imperative that the clinicians caring for women take this symptom into consideration when prescribing antidepressants. Coupling cognitive and behavioral treatment with medication, specifically targeting food intake, and suggesting that women maintain food and dietary logs when beginning antidepressants, may help to maintain normal weight. Moreover, exercise may reduce weight gain associated with depression, and has been demonstrated to improve mood symptoms and augument depression treatment in some studies.[38] Screening for eating disorders in women, is also necessary, given the increased frequency of bulimia in depressed women. Careful monitoring for suicidality is essential when treating both genders, given the increased frequency of attempts in women, and completions in men. The anxiety more often reported by women, may be one of the symptoms that contributes to suicidality. Appropriately targeting anxiety symptoms with appropriate pharmacologic and psychotherapeutic treatments should be paramount in all women reporting anxiety. Finally, increased symptom severity reported by women, suggests the needs for aggressive management, using evidence-based psychotherapies such as cognitive behavioral treatment, interpersonal therapy, and pharmacotherapy. Many studies suggest that there is many women receive treatment that is suboptimal; as such it is essential that clinicians carefully monitor mood symptoms throughout treatment to promote full remission.

CONCLUSION

In this confirmatory analysis, the ratio of 1.7:1 between women and men who seek treatment and are willing to be recruited is similar to that found in community samples such as the National Comorbidity Survey and argues against increased treatment-seeking in women. While increased symptom severity in women was not unexpected based on the work of previous investigators, the greater number of episodes in men was somewhat surprising. The comorbidities more frequently reported by women (anxiety disorders, somatization, and bulimia) as well as men (alcohol and substance abuse) have been suggested in prior studies.

Analysis of future data regarding response to treatment types within the STAR*D study will add much needed information to our understanding of pharmacotherapy and cognitive treatments of depression in women, and will add significantly to the baseline information presented here.

Acknowledgments

This project has been funded with Federal funds from the National Institute of Mental Health, National Institutes of Health, under Contract N01MH90003 to UT Southwestern Medical Center at Dallas (P.I.: A.J. Rush). The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government. The authors appreciate the editorial support of Jon Kilner, MS, MA, and the secretarial support of Fast Word Information Processing Inc. (Dallas, Texas).

References

1. Bebbington PE. The origins of sex differences in depressive disorder: bridging the gap. Int Rev Psychiatry 1996;7:295–332.
2. Nolen-Hoeksema, S. Sex differences in depression. Stanford: Stanford University Press; 1990.
3. Frank E, Carpenter LL, Kupfer DJ. Sex differences in recurrent depression: are there any that are significant? Am J Psychiatry 1988;145:41–45. [PubMed: 3337291]

4. Marcus SM, Young EA, Kerber KB, Kornstein S, Farabaugh AH, Mitchell J, et al. Gender differences in depression: findings from the Star*D study. J Affec Dis 87:141–150.
5. Kessler RC, McGonagle KA, Zhao S, Nelson S, Hughes M, Eschleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994;54:313–21. [PubMed: 9107147]
6. Fava M, Rush AJ, Trivedi MH, Nierenberg AA, Thase ME, Sackeim HA, et al. Background and rationale for the sequenced treatment alternatives to relieve depression (STAR*D) study. Psych Clin N Amer 2003;26:457–94.
7. Rush AJ, Fava M, Wisniewski SR, Lavori PW, Trivedi M, Sackeim HA, et al. Sequenced Treatment alternatives to relieve depression (Star*D) rationale and design. Cont Clin Trials 2004;25:119–142.
8. Kobak KA, Greist JH, Jefferson JW, Mundt JC, Katzelnick DJ. Computerized assessment of depression and anxiety over the telephone using interactive voice response. MD Computing 1999;16:64–68. [PubMed: 10439605]
9. American Psychiatric Association. (DSM-IV). Vol. 4. Washington DC: American Psychiatric Association Press, Inc; 1994. Diagnostic and statistical manual of mental disorders.
10. Hamilton M. A rating scale for depression. J Neurology Neurosurgery Psychiatry 1960;23:56–62.
11. Linn BS, Linn MW, Gurel L. Cumulative illness rating scale. J Amer Ger Soc 1968;16:622–626.
12. Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the cumulative illness rating scale. Psychiatry Res 1992;41:237–248. [PubMed: 1594710]
13. Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Arnow B, Klein DN, et al. The 16-item inventory of depressive symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS): a psychometric evaluation in patients with chronic major depression. Biolog Psychiatry 2003;54:573–83.
14. Trivedi MH, Rush AJ, Ibrahim HM, Carmody TJ, Biggs MM, Suppes T, et al. The inventory of depressive symptomatology, clinician rating (IDS-C) and self-report (IDS-SR), and the quick inventory or depressive symptomatology, clinician rating (QIDS-C) and self-report (QIDS-SR) in public sector patients with mood disorders: a psychometric evaluation. Psychol Med 2004;34:73–82. [PubMed: 14971628]
15. Zimmerman M, Mattia JI. The reliability and validity of a screening questionnaire for 13 DSM-IV Axis I disorders (the psychiatric diagnostic screening questionnaire) in psychiatric outpatients. J Clin Psychiatry 1999;60:677–683. [PubMed: 10549684]
16. Rush AJ, Zimmerman M, Wisniewski SR, Fava M, Hollon SD, Warden D, et al. Comorbid psychiatric disorders in depressed outpatients: demographic and clinical features. J Affect Dis 2005;87:43–55. [PubMed: 15894381]
17. Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The inventory of depressive symptomatology (IDS): psychometric properties. Psychol Med 1996;26:477–486. [PubMed: 8733206]
18. Rush AJ, Carmody T, Reimitz PE. The inventory of depressive symptomatology (IDS): clinician (IDS-C) and self-report (IDS-SR) ratings of depressive symptoms. Int J Methods Psych Res 2000;9:45–59.
19. Khan AY, Carrithers J, Preskorn SH, Wisniewski, Lear R, Rush AJ, et al. Clinical and demographic factors associated with DSM-IV melancholic depression. Ann Clin Psychiatry 2006;18:91–8. [PubMed: 16754414]
20. Novick JS, Stewart JW, Wisniewski SR, Cook IA, Many R, Nierenberg AA, et al. Clinical and demographic features of atypical depression in outpatients with major depressive disorder: preliminary findings from STAR*D. J Clin Psychiatry 2005;66:1002–1012. [PubMed: 16086615]
21. Sugar CA, Sturm R, Lee TT, Sherbourne CD, Olshen RA, Wells KB, et al. Empirically defined health states for depression from the SF-12. Health Serv Res 1998;33:911–928. [PubMed: 9776942]
22. Ware JE, Kosinksi M, Keller S. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220–33. [PubMed: 8628042]
23. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of life enjoyment and satisfaction questionnaire: a new measure. Psychopharm Bull 1993;29:321–26.

24. Mundt JC, Mareks IM, Shear K, Greist JH. The work and social adjustment scale (WSAS): a simple accurate measure of impairment in functioning. Br J Psychiatry 2002;180:461–64. [PubMed: 11983645]
25. Angst J, Dobler-Mikola A. Do the diagnostic criteria determine the sex ratio in depression? J Affect Dis 1984;7:189–98. [PubMed: 6241203]
26. Young MA, Scheftner WA, Fawcett J, Klerman GL. Gender differences in the clinical features of unipolar major depressive disorder. J Nerv Ment Dis 1990;178:200–03. [PubMed: 2307973]
27. Bracke P. Sex differences in the course of depression: evidence from a longitudinal study of a representative sample of the Belgian population. Soc Psychiatry Psychiatr Epidemiol 1998;33:420–29. [PubMed: 9766168]
28. Mueller TI, Leon AC, Keller MB, Solomon DA, Endicott J, Coryell W, et al. Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. Amer J Psychiatry 1999;156:1000–0006. [PubMed: 10401442]
29. Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB. Sex and depression in the national comorbidity survey I: lifetime prevalence, chronicity and recurrence. J Affec Dis 1993;29:85–96.
30. Breslau N, Schultz L, Peterson E. Sex differences in depression: a role for pre-existing anxiety. Psych Res 1995;58:1–12.
31. Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry 1997;54:313–21. [PubMed: 9107147]
32. Woodside DB, Garfinkel PE, Lin E, Goering P, Kaplan AS, Goldbloom D, et al. Comparisons of men with full or partial eating disorders, men without eating disorders, and women with eating disorders in the community. Amer J Psychiatry 2001;158:570–74. [PubMed: 11282690]
33. Black DW, Winokur G, Nasrallah A. Suicide in subtypes of major affective disorder. A comparison with general population suicide mortality. Arch Gen Psychiatry 1987;44:878–80. [PubMed: 3662743]
34. Schneider B, Philipp M, Muller MJ. Psychopathological predictors of suicide in patients with major depression during a 5-year follow-up. Eur Psych 2001;16:283–88.
35. Walinder J, Rutz W. Male depression and suicide. Inter Clin Psychopharm 2001;16:S21–S24.
36. Katz MM, Klerman GL, Hirschfield RMA, et al. Substudies on the phenomenology of the depressive disorders. 1987Unpublished manuscript
37. Duclos M, Marquez Pereira P, Barat P, Gatta B, Roger P. Increased cortisol bioavailability, abdominal obesity, and the metabolic syndrome in obese women. Obes Res 2005;13:1157–66. [PubMed: 16076984]
38. Trivedi MH, Greer TL, Grannenmann BD, Church TS, Galper DI, Sunderajan P, et al. TREAD: Treatment with Exercise Augmentation for Depression: study rationale and design. Clin Trials 2006;3:291–305. [PubMed: 16895046]

Table 1

Baseline Characteristics (N=2541)

Baseline Characteristics	%
Setting	
Primary Care	41.8
Specialty Care	58.2
Race	
White	75.4
Black or African American	17.2
Other	7.4
Ethnicity-Hispanic	14.5
Sex-Female	62.5
Marital Status	
Never Married	30.7
Married	40.8
Divorced	25.1
Widowed	3.4
Employment Status	
Unemployed, not looking	21.7
Unemployed, looking	16.5
Employed	56.3
Retired	5.5
Family History of Depression	53.8

Baseline Characteristics	Mean (SD)	Median (observed Range)
Age	40.5 (13.3)	40 (18–75)
Education (Yrs.)	13.3 (3.2)	13 (0–26)
Income (Dollars)	2403 (3311)	1500 (0–5000)
General Medical Comorbidities		
Categories Endorsed	3.1 (2.4)	3 (0–12)
Total Score	4.4 (3.9)	3 (0–30)
Severity Index	1.2 (0.6)	1.2 (0–4)
Age at onset of 1st MDE Episode	25.7 (14.6)	21 (2–74)
Number of MDE Episodes	6 (12.5)	3 (1–99)
Length of Current MDE Episode (Mos.)	24 (50.2)	8 (0–586)
Length of Illness (Yrs.)	14.9 (13.1)	11 (0.5–63)
$HRSD_{17}$ (ROA)	19.6 (6.5)	20 (1–38)
IDS-C_{30} (ROA)	35.3 (11.4)	35 (3–70)
QIDS-SR_{16}	15.5 (4.4)	16 (2–27)

Compr Psychiatry. Author manuscript; available in PMC 2009 October 8.

Table 2

Baseline Characteristics and Their Association with Gender

	Men N=952 (37.5%)		Women N= 1589 (62.5%)			
Characteristics	**n**	**%**	**n**	**%**	**Unadj. p-value**	**Adj. p-value[1]**
Setting					<.0001	**<.0001**
Primary Care	342	35.9	721	45.4		
Specialty Care	610	64.1	868	54.6		
Race					0.0087	**0.0009**
White	750	78.8	1167	73.4		
Black or African American	138	14.5	298	18.8		
Other	64	6.7	124	7.8		
Ethnicity-Hispanic					<.0001	
No	856	89.9	1315	82.8		
Yes	96	10.1	273	17.2		
Marital Status					0.0035	**<.0001**
Never Married	300	31.6	478	30.1		
Married	402	42.4	633	40.0		
Divorced	230	24.2	405	25.5		
Widowed	17	1.8	70	4.4		
Employment Status					<.0001	**0.0050**
Unemployed, not looking	168	17.7	383	24.1		
Unemployed, looking	168	17.7	250	15.8		
Employed	543	57.2	884	55.7		
Retired	70	7.4	69	4.4		
Suicidality						
Attempted Suicide					<.0001	**0.0002**
No	839	88.1	1293	81.6		
Yes	113	11.9	292	18.4		
Present Suicide Risk					0.6334	0.5268
No	928	97.5	1540	97.2		
Yes	24	2.5	45	2.8		

Characteristics	N	Men N=952 (37.5%) Mean(SD)	Men N=952 (37.5%) Median	Women N=1589 (62.5%) Mean(SD)	Women N=1589 (62.5%) Median	Unadj.p-value	Adj.p-value[1]
Age	2539	42.4 (13.1)	43	39.4 (13.3)	39	<.0001	---
Education (Yrs.)	2530	13.8 (2.9)	14	13.1 (3.4)	13	<.0001	**<.0001**
GMC							
Categories Endorsed	2541	3.1 (2.4)	3	3.0 (2.4)	3	0.4102	0.1251
Total Score	2541	4.6 (4.2)	3	4.3 (3.7)	3	0.0288	0.9464
Severity Index	2541	1.2 (0.7)	1.2	1.2 (0.6)	1.2	0.3921	0.5781
Age at Onset of 1st MDE	2509	26.6 (14.8)	23	25.1 (14.5)	20	0.0027	0.4618
Number of Episodes	2146	8.2 (16.1)	3	4.6 (9.4)	2	<.0001	**<.0001**
Length of Episode (Mos.)	2513	26.8 (56.3)	8	22.3 (46)	7	0.2907	0.4889
Length of Illness (Yrs.)	2507	15.9 (13.5)	12	14.3 (12.8)	10	0.0093	0.7008
$HRSD_{17}$ (ROA)	2322	19 (6.4)	19	20 (6.5)	20	0.0004	**0.0006**
$IDSC_{30}$ (ROA)	2308	33.7 (11.3)	34	36.3 (11.4)	36	<.0001	**<.0001**
$QIDS\text{-}SR_{16}$	2523	14.7 (4.3)	15	15.9 (4.3)	16	<.0001	**<.0001**

[1] Adjusted for Age and Ethnicity

Compr Psychiatry. Author manuscript; available in PMC 2009 October 8.

Compr Psychiatry. Author manuscript; available in PMC 2009 October 8.

Table 3

Association of Individual IDS-C_{30} symptoms with Gender

	Men N=952 (37.5%)	Women N=1589 (62.5%)	Unadjusted		Adjusted	
IDS-C30 (ROA) items	**% Present**	**% Present**	**O.R.**	**p-value**	**O.R.**	**p-value[1]**
Sleep Onset Insomnia	64.5	68.4	1.2	0.0474	1.0	0.8745
Mid-Nocturnal Insomnia	76.6	80.9	1.3	0.0145	1.3	**0.0496**
Early Morning Insomnia	51.6	51.3	0.9	0.8978	0.9	0.1556
Hypersomnia	23.6	24.8	1.1	0.5295	1.1	0.3608
Mood-Sad	96.6	97.8	1.6	0.0691	1.4	0.2294
Mood-Irritable	79.4	82.8	1.3	0.0370	1.1	0.4281
Mood-Anxious	82.1	84.3	1.2	0.1638	1.0	0.9982
Reactivity of Mood	71.9	74.5	1.1	0.1709	1.0	0.9699
Mood Variation	20.1	20.8	1.0	0.6770	1.0	0.9024
Quality of Mood	76.0	74.5	0.9	0.4093	0.9	0.2706
Appetite-Decreased	40.5	45.6	1.2	0.0161	1.1	0..4505
Appetite-Increased	16.3	24.1	1.6	<.0001	1.6	**<.0001**
Weight-Decrease	28.8	29.6	1.0	0.6668	0.9	0.1670
Weight-Increase	19.4	25.7	1.4	0.0005	1.4	**0.0007**
Concentration/Decision Making	89.0	91.1	1.3	0.0897	1.1	0.6646
Outlook-Self	77.8	81.2	1.2	0.0461	1.1	0.6196
Outlook-Future	74.3	75.5	1.1	0.5105	1.0	0.7701
Suicidal Ideation	49.2	46.6	0.9	0.2336	0.8	**0.0093**
Involvement	82.0	84.7	1.2	0.0918	1.1	0.8520
Energy/Fatigability	84.9	91.4	1.9	<.0001	1.7	**0.0004**
Pleasure/Enjoyment	72.3	72.6	1.0	0.8547	0.9	0.1434
Sexual Interest	60.7	65.7	1.2	0.0155	1.1	0.1786
Psychomotor Slowing	61.0	62.4	1.1	0.5110	1.0	0.6362
Psychomotor Agitation	63.1	62.7	1.0	0.8520	0.8	0.0782
Somatic (pain) Complaints	73.2	79.8	1.5	0.0002	1.3	**0.0091**
Sympathetic Arousal	66.9	70.1	1.2	0.1066	1.1	0.4719
Panic/Phobic Symptoms	36.9	39.2	1.1	0.2558	0.9	0.5319
Gastrointestinal	32.2	45.3	1.7	<.0001	1.7	**<.0001**

	Men N=952 (37.5%)	Women N=1589 (62.5%)	Unadjusted		Adjusted	
IDS-C30 (ROA) items	**% Present**	**% Present**	**O.R.**	**p-value**	**O.R.**	**p-value[1]**
Interpersonal Sensitivity	55.9	64.7	1.5	<.0001	1.3	**0.0037**
Leaden Paralysis/Physical Energy	43.4	44.5	1.1	0.5838	0.9	0.6878

[1] Adjusted for Age, Ethnicity and Baseline Severity $HRSD_{17}$

Table 4

Association of Gender with Criterion Domains of Depression

	Men N=952 (37.5%)	Women N=1589 (62.5%)	Unadjusted		Adjusted[1]	
QIDS (ROA)	**%**	**%**	**O.R.**	**p-value**	**O.R.**	**p-value**
Insomnia			1.7	0.0056	1.5	**0.0465**
Not Endorsed	6.2	3.7				
Endorsed	93.8	96.3				
Sad mood			1.6	0.0691	1.4	0.2294
Not Endorsed	3.4	2.2				
Endorsed	96.6	97.8				
Appetite/weight			1.7	<.0001	1.5	**0.0001**
Not Endorsed	34.3	23.9				
Endorsed	65.7	76.1				
Concentration			1.3	0.0897	1.1	0.6646
Not Endorsed	11.0	8.9				
Endorsed	89.0	91.1				
Self-outlook			1.2	0.0461	1.1	0.6196
Not Endorsed	22.2	18.8				
Endorsed	77.8	81.2				
Suicidal ideation			0.9	0.2336	0.8	**0.0093**
Not Endorsed	50.8	53.3				
Endorsed	49.2	46.7				
Involvement			1.2	0.0918	1.0	0.8520
Not Endorsed	18.0	15.3				
Endorsed	82.0	84.7				
Energy/fatigue			1.9	<.0001	1.7	**0.0004**
Not Endorsed	15.1	8.6				
Endorsed	84.9	91.4				
Psychomotor			1.0	0.7645	0.9	0.3195
Not Endorsed	17.0	16.5				
Endorsed	83.0	83.5				

[1] Adjusted for Age, Ethnicity and Baseline Severity HRSD17

Table 5

Association of Gender With Other Axis I Disorder Defined by the PDSQ (using 90% Specificity)

	Men N=952 (37.5%)	Women N=1589 (62.5%)	Unadjusted		Adjusted[1]	
PDSQ	**%**	**%**	**O.R.**	**p-value**	**O.R.**	**p-value**
Anxiety Disorder			2.0	<.0001	1.7	**<.0001**
Absent	85.6	75.2				
Present	14.4	24.8				
OCD			1.0	0.8236	0.8	0.2172
Absent	85.6	85.9				
Present	14.4	14.1				
Panic			1.3	0.0418	1.1	0.5793
Absent	89.2	86.5				
Present	10.8	13.5				
Social Phobia			1.3	0.0115	1.1	0.2715
Absent	73.7	68.9				
Present	26.3	31.1				
PTSD			1.2	0.0835	1.1	0.4028
Absent	84.4	81.7				
Present	15.6	18.3				
Agoraphobia			1.2	0.0927	1.2	0.5296
Absent	89.6	87.3				
Present	10.4	12.7				
Alcohol Abuse			0.5	<.0001	0.4	**<.0001**
Absent	82.6	91.4				
Present	17.4	8.6				
Drug Abuse			0.5	<.0001	0.4	**<.0001**
Absent	88.7	94.2				
Present	11.3	5.8				
Somatoform			3.1	0.0013	2.8	**0.0102**
Absent	98.9	96.8				
Present	1.1	3.2				
Hypochondriasis			1.5	0.0708	1.3	0.2213

Compr Psychiatry. Author manuscript; available in PMC 2009 October 8.

	Men N=952 (37.5%)	Women N=1589 (62.5%)	Unadjusted		Adjusted[1]	
PDSQ	**%**	**%**	**O.R.**	**p-value**	**O.R.**	**p-value**
Absent	96.5	94.9				
Present	3.5	5.1				
Bulimia			3.1	<.0001	3.1	**<.0001**
Absent	94.1	83.8				
Present	5.9	16.2				

[1] Adjusted for Age, Ethnicity and Baseline Severity $HRSD_{17}$

OCD = Obsessive Compulsive Disorder

PTSD = Post-Traumatic Stress Disorder

Table 6

Baseline Characteristics and Their Association with Gender

Characteristics	Men N=952 (37.5%)		Women N= 1589 (62.5%)		Unadj. p-value	Adj. p-value[1]
	n	%	n	%		
Anxious Depression					0.0003	**0.0006**
No	551	60.2	796	52.7		
Yes	364	39.8	714	47.3		
Melancholic Depression					0.5564	0.5030
No	736	80.4	1230	81.4		
Yes	179	19.6	281	18.6		
Atypical Depression					0.0015	**0.0040**
No	795	86.9	1238	82.0		
Yes	120	13.1	272	18.0		

[1] Adjusted for Age and Ethnicity