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Comorbid mental disorders, depression symptom severity, and role impairment among Veterans initiating depression treatment through the Veterans Health Administration

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Abstract

Background: Psychiatric comorbidities may complicate depression treatment by being associated with increased role impairments. However, depression symptom severity might account for these associations. Understanding the independent associations of depression severity and comorbidity with impairments could help in treatment planning. This is especially true for depressed Veterans, who have high psychiatric comorbidity rates.

Methods: 2,610 Veterans beginning major depression treatment at the Veterans Health Administration (VHA) were administered a baseline self-report survey that screened for diverse psychiatric comorbidities and assessed depression severity and role impairments. Logistic and generalized linear regression models estimated univariable and multivariable associations of depression severity and comorbidities with impairments. Population attributable risk proportions (PARPs) estimated the relative importance of depression severity and comorbidities in accounting for role impairments.

Results: Nearly all patients (97.8%) screened positive for at least one comorbidity and half (49.8%) for 4+ comorbidities. The most common positive screens were for generalized anxiety disorder (80.2%), posttraumatic stress disorder (77.9%), and panic/phobia (77.4%). Depression severity and comorbidities were significantly and additively associated with impairments in multivariable models. Associations were attenuated much less for depression severity than for comorbidities in multivariable versus univariable models. PARPs indicated that 15-60% of role impairments were attributable to depression severity and 5-32% to comorbidities.

Limitations: The screening scales could have over-estimated comorbidity prevalence. The cross-sectional observational design cannot determine either temporal or causal priorities.

Conclusions: Although positive screens for psychiatric comorbidity are pervasive among depressed VHA patients, depression severity accounts for most of the associations of these comorbidities with role impairments.

Keywords

comorbidity; depression symptom severity; depression; functioning; role impairment; Veterans; Veterans Health Administration

Introduction

Depression is a leading cause of disability worldwide (GBD 2019 Diseases and Injuries Collaborators, 2020). Effective long-lasting treatments remain elusive for many patients (Steinert, Hofmann, Kruse, & Leichsenring, 2014; Zisook et al., 2016). Psychiatric comorbidity is an important predictor of poor treatment outcomes, and thus a potential treatment target (Campbell et al., 2007; Davis et al., 2010; Warden et al., 2009). The increased role impairment associated with comorbidity (Steiner et al., 2017; Nichter,

Norman, Haller, & Pietrzak, 2019; Kessler et al., 2015) might account for the association of comorbidity with treatment outcome, as role impairment predicts poor treatment outcome (Sheehan, Nakagome, Asami, Pappadopulos, & Boucher, 2017; Solomon et al., 2008). To the extent that this is true, special strategies might be needed to treat comorbid psychiatric disorders in addition to the depression (Coplan, Aaronson, Panthangi, & Kim, 2015). However, the associations of psychiatric comorbidities with role impairment might be explained by depression symptom severity, which is known to be associated with greater role impairment (Hammer-Helmich et al., 2018; Guico-Pabia, Fayyad, & Soares, 2012) and is also correlated with psychiatric comorbidities (IsHak et al., 2014; Steiner et al., 2017). The extent to which the associations of psychiatric comorbidities with role impairment are due to depression symptom severity is unknown. Moreover, the extent to which depression symptom severity and comorbidity interact in their joint effects on impairment is unclear. Understanding these independent and joint effects of depression symptom severity and psychiatric comorbidity on role impairment might help in individual treatment planning (Malhi et al., 2013). This might be especially important for Veterans, given the high prevalence of depression among Veterans (Hoerster et al., 2012; Lehavot, Hoerster, Nelson, Jakupcak, & Simpson, 2012) and the high rates of psychiatric comorbidity among depressed Veterans (Richardson et al., 2017), and especially those who receive treatment through the Veterans Health Administration (VHA; Davis et al., 2016; Trivedi et al., 2015).

Research on comorbidity and impairment among depressed Veterans has focused mainly on comorbid posttraumatic stress disorder (PTSD; Forchuk et al., 2020; Ikin, Creamer, Sim, & McKenzie, 2010; Nichter et al., 2019). An exclusive focus on PTSD is a limitation because depression is also comorbid with a wide range of other mental disorders (Lai, Cleary, Sitharthan, & Hunt, 2015; Trivedi et al., 2015) and the prevalence of these disorders as well as multimorbidity (i.e., a single patient having 3 or more disorders) is especially high among VHA patients (Davis et al., 2016; Trivedi et al., 2015). Moreover, depression severity is typically not considered in these studies (Ikin et al., 2010; Nichter et al., 2019) but is important to account for given that more severely depressed patients generally also have more comorbidities (Hammer-Helmich et al., 2018; Guico-Pabia et al., 2012).

Using data from a large national sample of VHA patients initiating depression treatment, the current report presents data on: (1) the distribution of depression symptom severity; (2) the prevalence of self-reported screens for common comorbid mental disorders among these depressed patients; (3) the associations of these comorbidity screens with depression severity; (4) the gross associations of depression severity and comorbidities with key indicators of role impairment (severe role impairment and days out of role); and (5) the extent to which depression severity and comorbidities have joint additive or interactive associations with role impairment. We also calculate population attributable risk proportions (PARPs) to estimate the relative importance of depression severity and psychiatric comorbidities in accounting for role impairments.

Methods

Sample

Patients were recruited between December 2018 and June 2020 in weekly national samples of VHA patients making incident outpatient visits in the prior week for depression treatment as identified through electronic medical records. Patients had to receive either an antidepressant prescription, psychotherapy, or an appointment for psychotherapy. Outpatient settings included both primary care and specialty mental health clinics. We excluded patients who had any past-year VHA visit with a diagnosis of major depression, antidepressant medication prescription, or suicide attempt based on our desire to focus on incident treatment encounters for current depressive episodes. We also excluded patients who had any lifetime VHA visit with a diagnosis of bipolar disorder, nonaffective psychosis, dementia, intellectual disabilities, autism, Tourette's disorder, stereotyped movement disorders, or borderline intellectual functioning, or ever received a prescription of either antimanic or antipsychotic medication (see Supplementary Table 1 for ICD-9-CM and ICD-10-CM codes).

Targeted patients received letters inviting them to participate in a study of depression treatment that would require completing a self-report web or phone-based baseline questionnaire averaging 45 minutes with a $50 incentive and a 3-month self-report web or phone-based follow-up questionnaire averaging 20 minutes with a $25 incentive. The letter included an 800 number to ask questions or opt-out of the study. We called patients over the next week and closed out individuals who could not be reached within the three calls. We under-sampled patients who received an antidepressant prescription but not psychotherapy to enrich the sample with patients receiving psychotherapy. A weight was subsequently used to adjust for this under-sampling prior to analysis.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The Institutional Review Board of Syracuse VA Medical Center, Syracuse, New York, approved these procedures.

Measurements

Administrative variables.—We abstracted information on socio-demographics (age, sex, race/ethnicity, highest education level, employment status, marital status), medical history, and characteristics of the target incident visit for depression treatment from VHA electronic medical records for all patients to whom we mailed invitation letters (n=55,106). This information was used to examine baseline predictors of study participation.

Comorbid mental disorders.—Patients reported whether the following comorbidities, in addition to their depression, were a presenting problem: panic/anxiety disorders; phobias; PTSD; obsessive-compulsive disorder (OCD); generalized anxiety disorder (GAD); mania, manic depression, or bipolar disorder; problems with anger control; problems with alcohol or drug use. Patients who reported a comorbidity as a presenting problem were categorized

as having that comorbidity (panic and phobias were combined). Patients who reported mania, manic depression, or bipolar disorder were excluded from the study.

We also screened for lifetime psychiatric comorbidities with an expanded self-report version of the questions in the Family History Research Diagnostic Criteria (FH-RDC) interview (Andreasen, Endicott, Spitzer, & Winokur, 1977; Andreasen, Rice, Endicott, Reich, & Coryell, 1986) focused on the patient rather than family members. Patients reported the number of months out of the prior 12 in which they experienced symptoms of each disorder for which they had a positive lifetime FH-RDC screen. Using information from the FH-RDC and other self-reported symptoms, we additionally assessed the presence of comorbid mental disorders as described below.

A positive screen for panic/phobia required the patient both to endorse the FH-RDC stem question and to report either panic attacks or phobic fears severe enough to require change in daily behaviors 7+ months over the past year. A positive screen for GAD required the patient to endorse the FH-RDC stem question for GAD, report the presence of GAD symptoms for 7+ of the past 12 months, and endorse the presence of symptoms consistent with Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; American Psychiatric Association, 2013) Criteria A (anxiety and worry occurring more days than not about a number of events or activities) and C (anxiety and worry associated with 3 or more of 6 psychophysiological symptoms) in responses to questions that encapsulated these criteria in the comorbidity subscale of the Remission from Depression Questionnaire (Zimmerman et al., 2013) and the Quick Inventory of Depression Symptomatology Self-Report (QIDS-SR; Rush et al., 2003). A positive screen for OCD required the patient to endorse the FH-RDC stem question about having obsessions or compulsions during all 12 of the past 12 months. Clinically significant problems with anger attacks were defined as present if the patient reported anger attacks 7+ of the past 12 months and reported in the section on temperament in the questionnaire that one or more of three statements described them either *a lot* or *exactly* (sometimes I get so furious that I could hurt someone; I snap at people when I get angry; sometimes I get so mad that I trash everything) (Akiskal et al., 2005). A positive screen for substance use disorder was based on responses to the questions and threshold scoring rules in the Patient-Reported Outcomes Measurement Information System (PROMIS) 30-day Alcohol/Substance Use Short Form-7a (Patient-Reported Outcomes Measurement Information System (PROMIS) Health Organization, 2014). Drugs assessed included nicotine, opioids, stimulants, tranquilizers, marijuana or hashish, heroin or fentanyl, and other non-prescription illegal drugs. The PROMIS short form has been found to have a low sensitivity and may thus miss cases of problematic substance use (Gibbons et al., 2016). A positive screen for PTSD required a projected score of 38+ on the PTSD Checklist for DSM-5 (PCL-5; Blevins, Weathers, Davis, Witte, & Domino, 2015) based on responses to the 6-item short-form version of the PCL-5 (Zuromski et al., 2019) calibrated to the full PCL-5.

Depression symptom severity.—The 16-item QIDS-SR (Rush et al., 2003) assessed depression symptom severity in the prior two weeks. QIDS-SR scores (Chronbach's α=0.675) were transformed into depressive severity categories of *very severe*, *severe*,

moderate, and *mild* based on established transformation rules (IDS-QIDS, 2020) between the QIDS-SR and Hamilton Rating Scale for Depression (Hamilton, 1960).

Role impairments.—Role impairments due to depression were assessed with a modified version of the Sheehan Disability Scale (Leon, Olfson, Portera, Farber, & Sheehan, 1997). Patients rated how much their depression interfered with their ability to work, participate in family and home life, and participate in social activities in the past 2 weeks (Chronbach's α=0.847). Responses were recorded on a labelled 0-10 visual analogue scale with labels and numerical entry options of *not at all* (0), *mildly* (1-3), *moderately* (4-6), *markedly* (7-9), and *extremely* (10). Responses of 7-10 were collapsed to define *severe* role impairment. Patients also reported the number of days in the past 2 weeks that their depression and related symptoms caused them either to (i) miss a full day of school or work or be unable to carry out normal daily responsibilities (full days out of role) or (ii) feel so impaired that even though they were at school or work, their productivity was reduced or they were able to work only for part of the day (partial days out of role). Separate measures were computed and analyzed for any full days out of role, number of such days among patients with any, any full or partial days out of role, and number of such days among patients with any.

Analysis procedures

We compared administrative variables between respondents and non-respondents using logistic regression. We then used the R program *sbw* (Zubizarreta, Li, Allouah, & Greifer, 2020) to create a stable balancing weight to adjust for significant differences between respondents and the full target sample on significant predictors of nonresponse (Zubizarreta, 2015). The remaining analyses were conducted with these weighted data using SAS version 9.4. Cross-tabulations estimated associations of depression severity with socio-demographics, comorbidity screens, and impairment indicators. We then examined associations of depression severity, comorbidity screens, and both in predicting impairment using logistic regression models to predict the dichotomous indicators of role impairment and generalized linear models (GLMs) to predict number of days out of role. Logistic regression coefficients and these coefficients +/− 2 standard errors were exponentiated to create odds ratios (ORs) and 95% confidence intervals (CIs). Coefficients from the GLMs were reported in their natural metrics. Various combinations of link functions and error distributions were considered in the GLMs to select a preferred specification using standard diagnostic procedures (Buntin & Zaslavsky, 2004) (see Supplementary Table 2 for model diagnostics). Each regression model adjusted for socio-demographics (age, sex, race/ethnicity, education, employment status, marital status). Both additive and interactive associations between depression severity and comorbidity screens were considered. Finally, we calculated the PARPs of depression severity and comorbidity screens predicting each role impairment indicator (Mansournia & Altman, 2018). The balanced repeated replications method (BRR; Krewski & Rao, 1981) calculated design-based estimates of PARP standard errors using Census Regions to define BRR strata and random half-samples of clinics within strata to define BRR sampling-error calculation units.

Results

Comparison of the analytic sample with the full original sample

We sent letters to 55,106 patients and reached exactly 17,000 by telephone. The other patients either were not reached after 3 calls (n=27,603), their phone numbers no longer worked (n=6,828), or they moved with no forwarding information (n=3,675) (Supplementary Figure 1). Among the 17,000 patients contacted, 6,298 agreed to participate and 4,164 completed the baseline questionnaire (24.4% cooperation rate). We subsequently excluded 1,554 respondents because they did not report that depression was either a primary or secondary presenting problem (n=471) or reported no depression severity in the 2 weeks before baseline assessment (n=271), had a history of bipolar disorder or nonaffective psychosis not found in VHA records (n=728), or reported current suicidality (n=84). The final analytic sample included the 2,610 respondents who passed all study inclusion and exclusion criteria and participated in the baseline survey. As described in detail elsewhere (Puac-Polanco et al., in press), patients who responded to the questionnaire were, on average, more likely to be older, female, Non-Hispanic White, and currently married (reduced odds ratios among the under-represented categories ranged from 0.58 to 0.83). However, the multivariate association of administrative predictors with participation was weak (area under curve=.59). We nonetheless weighted the analytic sample to adjust for these small differences prior to carrying out analyses.

Sample characteristics

Three-quarters (76.8%) of patients in the weighted sample were male. Most patients were Non-Hispanic White (62.1%), currently married (52.5%), and had at least a college degree (57.2%) (Supplementary Table 3). Compared to patients with moderate or mild depression, those with severe and very severe depression were significantly more likely to be young, female, non-White, disabled, unemployed, never married, and have less than a college education.

Prevalence of positive screens for comorbid mental disorders overall and by depression symptom severity

The weighted distribution of depression symptom severity (standard error) was 29.5% (0.9) mild, 33.8% (0.9) moderate, 20.8% (0.8) severe, and 15.8% (0.7) very severe. Nearly all patients (97.8%), regardless of depression severity, screened positive for at least one comorbid mental disorder and nearly half (49.8%) screened positive for 4+ comorbid disorders (Table 1). The most common positive screens were for GAD (80.2%), PTSD (77.9%), and panic/phobia (77.4%). Patients with severe or very severe depression were significantly more likely than those with mild or moderate depression to screen positive for each comorbid mental disorder and for 4+ comorbid disorders.

Distribution of role impairment overall and by depression symptom severity

Approximately half (49.3%) of all patients reported any severe impairment due to depression over the past 2 weeks (Table 2). Severe role impairment within domains ranged from 38.7% for work impairment to 42.9% for social impairment. More than half of patients (55.6%)

reported any full days and 79.8% reported any full or partial days out of role due to depression in the past 2 weeks. Among patients who reported any such days, mean numbers were 3.7 and 6.2 days, respectively. Each role impairment indicator was significantly associated with depression symptom severity (severe role impairment χ^2_3=314.6-484.9, p<.001; any days out of role χ^2_3=186.5-254.4, p<.001; number of days out of role F_3=88.9-135.7, p<.001).

Impact of comorbidities on the associations of depression severity with impairments

In models adjusted for socio-demographics, depression severity was associated significantly with severe role impairment in each individual role domain and any domain overall (χ^2_3=245.8-381.0, p<.001), with ORs in the range of 8.6-17.9 for very severe, 4.8-7.5 for severe, and 2.3-3.6 for moderate, compared to mild depression (Table 3, Part IA). These associations decreased only modestly in models that further controlled for comorbidities (χ^2_3=201.2-333.3, p<.001) (Table 3, Part IB). Broadly similar patterns were found for the associations of depression severity with days out of role, where associations were attenuated only modestly when controls were introduced for comorbidities (any days χ^2_3=134.7-200.2, p<.001 in Table 3, Part IIA and χ^2_3=106.8-155.0, p<.001 in Table 3, Part IIB; number of days F_3=149.5-344.1, p<.001 in Table 3, Part IIA and F_3=140.9-307.2, p<.001 in Table 3, Part IIB). Regression coefficients were consistently monotonic and statistically significant across the range of depression severity.

Interactions between depression severity and comorbidities were globally nonsignificant in predicting 2 of the 4 dichotomous measures of severe impairment in role domains (ability to work and social life; χ^2_3=13.1-15.0, p=0.665-0.784), both dichotomous measures of days out of role (χ^2_3=14.3-28.7, p=0.052-0.711), and number of full or partial days out of role (F_3=22.7, p=0.202; Supplementary Table 4). A total of 7 individually significant interactions were found for the other indicators of role impairment. Three of these involved PTSD: ORs in the range of 0.1-0.5 for interactions with each of the 3 depression severity dummies predicting any severe role impairment. Three other significant interactions involved GAD: ORs in the range of 2.2-2.4 for interactions with severe depression predicting any severe role impairment and severe role impairment in family and home life; and a negative interaction (b=−0.5) with severe depression predicting number of full days out of role. The final significant interaction was an OR of 0.4 between anger problems and very severe depression in predicting severe impairment in family and home life.

Impact of depression severity on the associations of comorbidities with impairments

In additive models that included each comorbid disorder and adjusted for socio-demographics only, the 6 dichotomies for comorbidities were associated significantly with all impairment measures (χ^2_6=58.0-93.7, p<.001; F_6=15.0-47.0, p=<.001-0.020; Table 4, Parts IA and IIA). The ORs predicting the dichotomous impairment measures were consistently significant and elevated for comorbid panic/phobia (OR=1.2-1.6), PTSD (OR=1.4-1.8), and GAD (OR=1.4-1.6) and less consistently so for comorbid OCD (OR=1.2 for social life and family and home life), anger (OR=1.3-1.4 for any full days out of role and family and home life), and substance use (OR=1.7 for any full days out of role). Only PTSD significantly predicted the number of full days out of role (b=0.2), and 4 of the 6 comorbid

conditions significantly predicted number of full or partial days out of role (b=0.1-0.2 for panic/phobia, PTSD, GAD, and substance use).

All 29 of the significant coefficients described in the prior paragraph became smaller and 21 became non-significant in models that further controlled for depression severity, even though comorbidities remained significant overall in predicting all but two of the outcomes (the exceptions being any severe role impairment and number of full days out of role; χ^2_6=17.3-43.6, p<.001-0.008; F_6=16.1, p<.001; Table 4, Parts IB and IIB). We also examined the possibility of interactions among the screens for comorbid conditions both with and without controls for depression severity. This was done by examining the joint predictive associations of number and types of comorbidities with analysis methods used in our previous studies of comorbidity (Alonso et al., 2018; Merikangas et al., 2007). No significant interactions were found in these models (χ^2_5=2.9-9.6, p=0.089-0.713; F_5=3.7-5.7, p=0.334-0.601; Supplementary Table 5).

Population attributable risk proportions for role impairment

PARPs were calculated to quantify the relative importance of depression severity and psychiatric comorbidities in accounting for the indicators of role impairment. This was done separately in additive models and in models allowing for interactions between depression severity and the comorbidity screens (Table 5 and Supplementary Table 6). The decision whether to include or exclude the interactions turned out to have little impact on the estimates. In models that did not include interactions, the proportions of severe role impairment in specific roles or any of these roles due to depression severity (i.e., estimated proportional reductions in observed role impairment if depression severity could be reduced to mild while the comorbidity screens remained as observed in the sample) were in the range of 43.6-60.1%. These were substantially higher than the proportions of severe role impairment due to the comorbidity screens (i.e., estimated proportional reductions in observed role impairments if comorbidities were removed while pure depression severity remained as observed in the sample), which were in the range 11.8-31.7%. It is noteworthy in the latter regard that the estimated PARPs due to the comorbidity screens likely over-estimate the PARPs due to true comorbid disorders because positive comorbidity screens are likely to include subthreshold comorbidities. Despite this, the PARPs due to depression severity averaged about 2.5 times as high as those due to the comorbidity screens.

The situation was different for any full or partial days out of role, in which PARPs were similar for depression severity (14.6-30.0%) and the comorbidity screens (12.8-25.2%) but the PARPs for the number of such days were much higher for depression severity (24.4-30.3%) than the comorbidity screens (4.7-11.5%). We also calculated PARPs associated with simultaneously making all depression mild and removing all comorbidities. It is noteworthy that these PARP estimates were generally somewhat smaller than the sum of the estimates for depression severity alone and comorbidities alone, as this finding is consistent with the fact that the interactions found between depression severity and the comorbidity screens were generally weak but negative.

Discussion

In this large national sample, nearly all patients screened positive for at least one psychiatric comorbidity, more than three out of four patients screened positive for comorbid panic/phobia, PTSD, or GAD, and nearly half screened positive for 4+ comorbid mental disorders. These estimates are substantially higher than those typically observed among depressed non-Veteran patients (Gao et al., 2013; Rosellini et al., 2018). Although striking, these findings are not completely surprising in light of prior evidence that Veterans have higher rates of mental and physical morbidities overall than civilians (Hoerster et al., 2012; Lehavot et al., 2012) and that patients treated through the VHA have greater health needs than Veterans who receive health care in other settings (Petersen et al., 2010; Rogers et al., 2004). The prevalence estimates of comorbidity screens were also substantially higher than those in a previous large study of VHA primary care patients that relied on diagnostic codes rather than self-reports to assess mental disorders (Trivedi et al., 2015). This finding might be because our screens overdiagnosed but is also consistent with the observation that comorbid psychiatric disorders are often undiagnosed and untreated among patients in treatment for depression (Zimmerman, 2016). Our findings suggest that VHA Veterans initiating depression treatment should be universally screened for comorbid mental disorders, since it appears that it is not a matter of if they will screen positive for a comorbid disorder, but rather, which comorbidity.

We also found substantial role impairments in the sample. Nearly half of patients reported severe role impairment in at least one role domain and nearly four out of five patients reported any full or partial days out of role due to depression during the 2 weeks prior to baseline. The high degree of role impairment supports the continued provision of comprehensive, patient-centered approaches to help Veterans with depression function in their home, social, and work lives (US Department of Veterans Affairs, 2020a; US Department of Veterans Affairs, 2020b).

Most previous research on psychiatric comorbidity among depressed Veterans focused on PTSD (Forchuk et al., 2020; Ikin et al., 2010; Nichter et al., 2019). However, we found that comorbid panic/phobia and GAD screens are as prevalent as PTSD screens. Furthermore, the associations of these other comorbid disorders with role impairment are broadly comparable to those associated with PTSD. This finding underscores the point that research on and treatment for comorbidities among depressed patients should include other disorders, particularly anxiety disorders, rather than just PTSD.

Consistent with previous research (Hammer-Helmich et al., 2018; Guico-Pabia et al., 2012), we found that depression severity was significantly associated with role impairments. We also found, again consistent with prior research (Steiner et al., 2017; Nichter et al., 2019; Kessler et al., 2015), that most of the psychiatric comorbidities screened for here were associated significantly with role impairments. Extending previous work, though, we found that depression symptom severity was much more strongly associated with role impairments than were the comorbidity screens. Patients with very severe depression had approximately 15 times the odds of any severe role impairment and 7 times the odds of any full or partial days out of role compared to patients with mild depression even after accounting

for a wide range of psychiatric comorbidities. Importantly, these comorbidity controls were conservative in that they captured not only threshold comorbidities but also the subthreshold cases because we used screening measures rather than clinical diagnoses. The high estimates for the depression severity and role impairment associations are especially salient considering that more than one in three patients had severe or very severe depression. These very high estimates also indicate that depression symptom severity may be a useful indicator for potential role impairments. Based on our results, it is very likely that VHA patients who screen positive for severe or very severe depression also experience substantial role impairments, and clinicians should screen for potential work, family, or social impairment that patients may not disclose when initiating treatment. Identifying and improving role impairment is important not only for helping patients' immediate functioning but potentially for long-term treatment outcomes.

We found in multivariate models that associations of comorbidities with impairment became considerably weaker, and in most cases statistically nonsignificant, after adjusting for depression severity. This finding suggests that previously observed associations of psychiatric comorbidities with impairment may have been due, at least in part, to patients with comorbid mental disorders having more severe depression than patients without psychiatric comorbidities. These findings suggest that other mechanisms than solely role impairment likely explain why depressed patients with psychiatric comorbidities have worse treatment outcomes. However, there were still some noteworthy associations after controlling for depression severity. PTSD and GAD were both associated with elevated relative odds of work impairment. Previous research has found that PTSD symptoms, including avoidance, hyperarousal, and sleep disturbances, poorly affect work performance and absenteeism (Rodriguez et al., 2012). GAD has also previously been associated with role impairments and especially work impairment (Henning et al., 2007), as persistent worrying may impede one's ability to concentrate or be productive. Panic/phobia may have been associated with social life impairment since this group included patients with social phobia. Anger problems are associated with violence and aggression (Crane & Testa, 2014; Shorey et al., 2011), which may lead to family dysfunction and potential impairment in family and home life, as observed in this analysis. It was surprising that OCD and substance use were not associated with role impairments. These findings may be because our measure of role impairment pertained specifically to impairment due to depression, and patients with OCD or substance use may have attributed role impairments to those disorders, rather than depression. Although it was common for patients to screen positive for more than one comorbidity, we did not find evidence of interactions between comorbid disorders in predicting impairment. Furthermore, there was little evidence of synergistic effects between depression symptom severity and psychiatric comorbidities.

Strengths and limitations

There are some limitations to note. First, because the data were cross-sectional, the temporal order of associations cannot be established. Second, we had a low survey response rate. Although few baseline differences were found between patients who participated in the study and those who did not and we weighted our data to account for these small differences, the possibility of selection bias cannot be excluded. Third, psychiatric disorders

and symptoms were self-reported in screening scales, which can result in overestimation of comorbid disorder prevalence (Zimmerman & Chelminski, 2006; Zuromski et al., 2019) and may bias estimates toward the null by including subthreshold disorders. Fourth, many comorbidities share overlapping symptoms with depression (Gros, Simms, & Acierno, 2010; Zbozinek et al., 2012) and it is possible that some of the positive screens for comorbidity tapped into facets of depression rather than true comorbidities. In a related way, the QIDS-SR may have captured psychiatric symptom severity and distress generally, rather than specifically depression symptom severity. Fifth, because we excluded patients on antipsychotic medications, we may have excluded some patients who were treated in the past for treatment resistant depression. Lastly, our sample included only treatment-seeking patients. Because individuals with greater depression symptom severity, role impairment, and psychiatric comorbidities are more likely to receive treatment than those without these characteristics (Kessler et al., 2003), this may have induced selection bias (and more specifically, collider-stratification bias [Cole et al., 2010]) since inclusion in our sample was conditional on receiving treatment. As such, population-level associations of depression symptom severity and psychiatric comorbidities with role impairment may be weaker than those observed here. However, it is unlikely that these associations are entirely explained by potential selection bias since they have also been documented in nontreatment seeking samples (Nichter et al., 2019; Kessler et al., 2003).

The study also has several strengths. First, it is based on a large national sample of VHA Veterans seeking treatment for depression. Second, the self-reported measures for psychiatric disorders helped capture comorbidities that would have been missed using diagnoses. Third, we examined the impact of several comorbid mental disorders, rather than solely PTSD.

Conclusion

Providing effective and long-lasting depression treatment for Veterans is imperative given substantial role impairment caused by depression and the key role of depression in Veteran suicides (Hoerster et al., 2012; Lehavot et al., 2012; Office of Mental Health and Suicide Prevention, 2020). Our results suggest that focusing treatment plans on depression symptom reduction may play a greater role in improving Veterans' role impairments than targeting psychiatric comorbidities. However, psychiatric comorbidities were also related to role impairment and as evidenced by the PARPs, addressing both depression symptom reduction and psychiatric comorbidity management would likely be the most beneficial for achieving optimal functioning. This information is useful for clinicians and important to communicate to patients with severe role impairment who may believe that their comorbidities are mainly responsible for their impairment. Future research should examine prospective relationships of psychiatric comorbidities, depression symptom severity, and role impairment changes over time and in relation to symptomatic treatment response.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

CI	confidence interval
BIC	Bayesian information criterion
BRR	balanced repeated replications
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
FH- RDC	Family History Research Diagnostic Criteria
GAD	general anxiety disorder
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
OCD	obsessive- compulsive disorder
OR	odds ratio
PARP	Population attributable risk proportion
PCL-5	PTSD Checklist for DSM-5
PROMIS	Patient- Reported Outcomes Measurement Information System (PROMIS)
PTSD	posttraumatic stress disorder
QIDS- SR	Quick Inventory of Depression Symptomatology Self- Report
SE	standard error
VHA	Veterans Health Administration

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Highlights

- Positive psychiatric comorbidity screens are pervasive among depressed VHA patients
- Depressed VHA patients experience substantial role impairments
- Depression severity is strongly associated with role impairments
- Role impairments are attributable much more to depression severity than comorbidity
- Depression severity accounts for most of the comorbidity-impairment associations

Table 1.

Positive screens for comorbid mental disorders among VHA Veterans initiating depression treatment overall and by depression symptom severity

			Depression symptom severity								
	Total (n=2,610)		Very severe (n=417)		Severe (n=533)		Moderate (n=869)		Mild (n=791)		
	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	χ^2_3
Comorbid disorder											
Panic/phobia	77.4	(0.8)	89.5	(0.6)	84.2	(0.7)	75.3	(0.8)	68.4	(0.9)	86.7*
PTSD	77.9	(0.8)	89.2	(0.6)	84.7	(0.7)	78.6	(0.8)	66.2	(0.9)	106.6*
GAD	80.2	(0.8)	93.3	(0.5)	86.4	(0.7)	79.9	(0.8)	69.3	(0.9)	115.2*
OCD	23.5	(0.8)	30.1	(0.9)	28.5	(0.9)	21.6	(0.8)	18.6	(0.8)	29.5*
Anger	48.9	(1.0)	59.9	(1.0)	52.6	(1.0)	47.1	(1.0)	42.6	(1.0)	36.4*
Substance	16.1	(0.7)	21.3	(0.8)	15.6	(0.7)	16.5	(0.7)	13.3	(0.7)	12.9*
Any	97.8	(0.3)	99.1	(0.2)	98.6	(0.2)	98.3	(0.3)	96.1	(0.4)	16.4*
Number of comorbidities											
Exactly 1	7.0	(0.5)	0.9	(0.2)	3.3	(0.4)	7.8	(0.5)	12.1	(0.6)	66.2*
Exactly 2	15.1	(0.7)	6.5	(0.5)	11.8	(0.6)	15.2	(0.7)	21.9	(0.8)	56.6*
Exactly 3	25.9	(0.9)	23.2	(0.8)	22.9	(0.8)	27.9	(0.9)	27.3	(0.9)	6.7
4+	49.8	(1.0)	68.5	(0.9)	60.6	(1.0)	47.4	(1.0)	34.9	(0.9)	154.3*

GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; PTSD, posttraumatic stress disorder; SE, standard error; VHA, Veterans Health Administration.

Notes. Estimates are weighted. Chi-square tests examined differences in the distributions of variables between depression symptom severity groups.

*Significant at the .05 level, two-sided test.

Table 2.

Baseline role impairment among VHA Veterans initiating depression treatment overall and by depression symptom severity

	Total (n=2,610)		Depression symptom severity: Very severe (n=417)		Severe (n=533)		Moderate (n=869)		Mild (n=791)		
	Est	(SE)	Est	(SE)	Est	(SE)	Est	(SE)	Est	(SE)	χ^2_3 / F_3
I. Severe role impairment											
Ability to work (%)	38.7	(1.0)	67.3	(0.9)	51.4	(1.0)	34.8	(0.9)	18.7	(0.8)	314.6*
Family and home life (%)	41.7	(1.0)	77.9	(0.8)	56.2	(1.0)	37.1	(0.9)	17.5	(0.7)	463.5*
Social life (%)	42.9	(1.0)	77.4	(0.8)	58.3	(1.0)	40.8	(1.0)	15.9	(0.7)	484.9*
Any (%)	49.3	(1.0)	89.1	(0.6)	77.5	(0.8)	58.9	(1.0)	31.1	(0.9)	481.5*
II. Days out of role due to depression											
Any full days (%)	55.6	(1.0)	81.2	(0.8)	66.2	(0.9)	54.9	(1.0)	35.2	(0.9)	254.4*
Any full or partial days (%)	79.8	(0.8)	94.8	(0.4)	88.0	(0.6)	80.8	(0.8)	64.9	(0.9)	186.5*
Number of full days[a] (mean)	3.7	(0.1)	6.0	(0.2)	4.4	(0.2)	3.0	(0.1)	2.1	(0.1)	88.9*
Number of full or partial days[b] (mean)	6.2	(0.1)	9.0	(0.2)	5.9	(0.2)	2.1	(0.1)	4.2	(0.2)	135.7*

SE, standard error; VHA, Veterans Health Administration.

Notes. Estimates are weighted. Chi-square tests examined differences in the distributions of dichotomous variables between depression symptom severity groups. F tests examined differences in the distributions of continuous variables (number of days) between depression symptom severity groups.

*Significant at the .05 level, two-sided test.

[a]Among patients who reported any full days out of role.

[b]Among patients who reported any full or partial days out of role.

Table 3.

Associations of depression symptom severity with role impairment among VHA Veterans initiating depression treatment[a]

	Very severe		Severe		Moderate		
	Est	(95% CI)	Est	(95% CI)	Est	(95% CI)	χ^2_3/F_3
I. Severe role impairment							
A. Without controls for comorbidity							
Ability to work	8.57*	(6.40-11.47)	4.75*	(3.66-6.17)	2.33*	(1.84-2.95)	245.83*
Family and home life	15.13*	(11.13-20.56)	5.83*	(4.51-7.54)	2.73*	(2.16-3.45)	349.98*
Social life	17.89*	(13.09-24.45)	7.54*	(5.79-9.81)	3.61*	(2.84-4.59)	380.95*
Any	16.06*	(11.28-22.87)	7.44*	(5.74-9.64)	3.08*	(2.51-3.80)	364.42*
B. With controls for comorbidity							
Ability to work	7.35*	(5.45-9.92)	4.25*	(3.26-5.54)	2.16*	(1.70-2.75)	201.18*
Family and home life	13.33*	(9.75-18.22)	5.32*	(4.09-6.91)	2.60*	(2.05-3.29)	302.23*
Social life	15.96*	(11.60-21.96)	6.89*	(5.27-9.01)	3.46*	(2.72-4.40)	333.34*
Any	14.65*	(10.22-20.98)	6.96*	(5.35-9.05)	2.97*	(2.41-3.66)	324.30*
II. Days out of role due to depression							
A. Without controls for comorbidity							
Any full days	7.08*	(5.24-9.56)	3.49*	(2.75-4.44)	2.20*	(1.79-2.71)	200.19*
Any full or partial days	8.51*	(5.33-13.57)	3.67*	(2.70-4.98)	2.20*	(1.75-2.77)	134.67*
Number of full days[b]	0.65*	(0.51-0.78)	0.45*	(0.32-0.58)	0.09	(−0.04-0.22)	149.53*
Number of full or partial days[c]	0.88*	(0.77-0.98)	0.62*	(0.52-0.72)	0.28*	(0.18-0.38)	344.05*
B. With controls for comorbidity							
Any full days	5.94*	(4.36-8.09)	3.09*	(2.41-3.95)	2.07*	(1.68-2.55)	154.98*
Any full or partial days	7.21*	(4.49-11.58)	3.26*	(2.39-4.45)	2.05*	(1.62-2.59)	106.77*
Number of full days[b]	0.64*	(0.51-0.78)	0.44*	(0.31-0.58)	0.09	(−0.04-0.22)	140.90*
Number of full or partial days[c]	0.85*	(0.74-0.96)	0.60*	(0.49-0.70)	0.27*	(0.17-0.37)	307.17*

CI, confidence interval; VHA, Veterans Health Administration.

Note. Estimates are weighted.

*Significant at the .05 level, two-sided test.

[a]Each row represents the results of a separate multivariable regression model predicting indicators of role impairment due to depression in the past 2 weeks. Mild depression severity was the reference group in every model. Each model controlled for socio-demographic characteristics listed in Supplementary Table 3, and models in Subparts B additionally included controls for psychiatric comorbidities. Logistic regression was used for 6 of the 8 outcomes, the exceptions being the 2 outcomes in Part II involving numbers of days out of role. Generalized linear models (GLMs) were used to predict those outcomes. The estimates reported are odds ratios for the logistic models and metric regression coefficients for the GLMs, which specified an original scale, square root link function, and normal error distribution. See Supplementary Table 2 for the diagnostics used to select this link function and error structure.

[b]Models were conducted among patients who reported any full days out of role.

[c]Models were conducted among patients who reported any full or partial days out of role.

Table 4.

Associations of psychiatric comorbidities with role impairment among VHA Veterans initiating depression treatment[a]

	Panic/phobia		PTSD		GAD		OCD		Anger		Substance		
	Est	(95% CI)	Est	(95% CI)	Est	(95% CI)	Est	(95% CI)	Est	(95% CI)	Est	(95% CI)	χ^2_6/F_6
I. Severe role impairment													
A. Without controls for depression severity													
Ability to work	1.30*	(1.04-1.62)	1.81*	(1.45-2.26)	1.60*	(1.26-2.02)	1.05	(0.86-1.28)	1.08	(0.91-1.28)	1.23	(0.97-1.54)	74.70*
Family and home life	1.27*	(1.02-1.57)	1.53*	(1.24-1.89)	1.47*	(1.17-1.83)	1.25*	(1.03-1.51)	1.36*	(1.15-1.61)	1.10	(0.88-1.37)	78.15*
Social life	1.61*	(1.30-2.00)	1.59*	(1.29-1.96)	1.40*	(1.12-1.74)	1.21*	(1.00-1.47)	1.11	(0.94-1.31)	1.11	(0.89-1.39)	83.90*
Any	1.29*	(1.05-1.58)	1.50*	(1.23-1.83)	1.44*	(1.17-1.78)	1.17	(0.96-1.43)	1.15	(0.97-1.37)	1.07	(0.85-1.35)	63.22*
B. With controls for depression severity													
Ability to work	1.17	(0.93-1.48)	1.51*	(1.19-1.91)	1.30*	(1.01-1.66)	0.96	(0.77-1.18)	0.97	(0.80-1.16)	1.19	(0.93-1.51)	25.54*
Family and home life	1.13	(0.90-1.41)	1.21	(0.97-1.53)	1.12	(0.88-1.42)	1.14	(0.92-1.40)	1.24*	(1.03-1.48)	1.04	(0.82-1.32)	17.26*
Social life	1.47*	(1.17-1.85)	1.26	(1.00-1.58)	1.06	(0.83-1.34)	1.10	(0.89-1.35)	0.97	(0.81-1.17)	1.05	(0.82-1.33)	21.15*
Any	1.16	(0.93-1.44)	1.18	(0.95-1.46)	1.12	(0.90-1.41)	1.04	(0.84-1.30)	1.03	(0.86-1.24)	1.01	(0.79-1.29)	8.01
II. Days out of role due to depression													
A. Without controls for depression severity													
Any full days	1.24*	(1.01-1.53)	1.41*	(1.15-1.73)	1.57*	(1.27-1.95)	1.22	(1.00-1.49)	1.25*	(1.06-1.49)	1.68*	(1.33-2.12)	93.70*
Any full or partial days	1.47*	(1.17-1.86)	1.43*	(1.14-1.80)	1.43*	(1.12-1.82)	1.09	(0.85-1.40)	1.22	(0.99-1.50)	1.22	(0.91-1.64)	57.96*
Number of full days[b]	0.09	(−0.03-0.21)	0.17*	(0.04-0.29)	0.06	(−0.07-0.19)	0.00	(−0.09-0.10)	−0.03	(−0.12-0.05)	0.04	(−0.06-0.15)	15.05*
Number of full or partial days[c]	0.13*	(0.03-0.23)	0.16*	(0.06-0.25)	0.15*	(0.05-0.25)	0.01	(−0.07-0.09)	−0.01	(−0.08-0.06)	0.12*	(0.03-0.21)	46.95*
B. With controls for depression severity													
Any full days	1.15	(0.93-1.42)	1.20	(0.97-1.48)	1.32*	(1.06-1.65)	1.14	(0.93-1.40)	1.17	(0.98-1.39)	1.66*	(1.30-2.11)	43.63*
Any full or partial days	1.37*	(1.08-1.74)	1.24	(0.97-1.56)	1.21	(0.94-1.55)	1.00	(0.78-1.30)	1.13	(0.92-1.40)	1.19	(0.88-1.61)	22.54*
Number of full days[b]	0.04	(−0.07-0.16)	0.11	(−0.01-0.23)	−0.05	(−0.17-0.07)	−0.01	(−0.10-0.08)	−0.07	(−0.16-0.01)	0.05	(−0.06-0.15)	7.89*
Number of full or partial days[c]	0.09	(0.00-0.18)	0.08	(−0.01-0.17)	0.04	(−0.05-0.13)	−0.03	(−0.10-0.05)	−0.05	(−0.12-0.01)	0.10*	(0.01-0.18)	16.11*

CI, confidence interval; GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; PTSD, posttraumatic stress disorder; VHA, Veterans Health Administration.

Note. Estimates are weighted.

*Significant at the .05 level, two-sided test.

[a]Each row represents the results of a separate multivariable regression model predicting indicators of role impairment due to depression in the past 2 weeks. All models included each comorbid disorder and controlled for socio-demographic characteristics listed in Supplementary Table 3, and models in Subparts B additionally included controls for depression severity. Logistic regression was used for 6 of the 8 outcomes, the exceptions being the 2 outcomes in Part II involving numbers of days out of role. Generalized linear models (GLMs) were used to predict those outcomes. The estimates reported are ORs for the logistic models and metric regression coefficients for the GLMs, which specified an original scale, square root link function, and normal error distribution. See Supplementary Table 2 for the diagnostics used to select this link function and error structure.

[b]Models were conducted among patients who reported any full days out of role.

[c]Models were conducted among patients who reported any full or partial days out of role.

Table 5.

Population attributable risk proportions of role impairment due to depression severity, psychiatric comorbidity, and both among VHA Veterans initiating depression treatment[a]

	Depression severity		Psychiatric comorbidity		Both	
	%	(95% CI)	%	(95% CI)	%	(95% CI)
I. Severe role impairment						
Ability to work	45.5	(43.9-47.1)	31.7	(28.9-34.5)	67.9	(65.9-70.0)
Family and home life	54.1	(53.0-55.1)	22.0	(19.3-24.8)	69.3	(67.6-71.1)
Social life	60.1	(59.0-61.2)	24.3	(21.5-27.0)	75.0	(73.6-76.5)
Any	43.6	(42.6-44.6)	11.8	(10.3-13.2)	56.1	(54.8-57.3)
II. Days out of role due to depression						
Any full days	30.0	(28.8-31.3)	25.2	(23.6-26.8)	54.6	(52.9-56.4)
Any full or partial days	14.6	(13.8-15.5)	12.8	(11.2-14.4)	32.8	(30.7-35.0)
Number of full days[b]	24.4	(22.8-26.1)	4.7	(2.3-7.1)	24.9	(22.0-27.9)
Number of full or partial days[c]	30.3	(29.2-31.4)	11.5	(10.0-13.0)	39.8	(38.1-41.5)

CI, confidence interval; VHA, Veterans Health Administration.

[a]Implications of reducing depression severity to mild and eliminating all comorbidities (individually or if both conditions were true).

[b]Models were conducted among patients who reported any full days out of role.

[c]Models were conducted among patients who reported any full or partial days out of role.