Associations of Psychotherapy Dose and SSRI or SNRI Refills With Mental Health Outcomes Among Veterans With PTSD

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Objective: **This study assessed associations between psychotherapy and pharmacotherapy for posttraumatic stress disorder (PTSD) and longitudinal changes in PTSD, depression, and mental health functioning among U.S. veterans diagnosed as having PTSD.** ***Methods:*** **Information about self-reported symptoms experienced from .5 to over three years was collected from 482 veterans diagnosed as having PTSD. Administrative data from the U.S. Department of Veterans Affairs (VA) were used to calculate initiation of a course of selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs), days of medication coverage, and number of PTSD-related psychotherapy visits during the year after a baseline survey. Hierarchical linear modeling was used to analyze the effects of psychotherapy dose, initiation of an SSRI or SNRI, and medication coverage on symptoms over one year.** ***Results:*** **In the year after baseline, over half of the sample (55%) received no psychotherapy for PTSD, and only 8% met the VA's proposed standard of eight PTSD-related sessions within 14 weeks. Nearly half of the participants (47%) were prescribed an SSRI or SNRI and 37% completed a 90-day trial in the year after baseline. Participants' symptoms improved slightly over time. Participants who received eight or more psychotherapy sessions in 14 weeks, completed a 90-day course of SSRIs or SNRIs, or had more days of medication coverage did not improve more than participants who received less treatment.** ***Conclusions:*** **These dose-of-care benchmarks were not related to symptom improvement, highlighting the importance of directly assessing the impact of particular treatments on patient outcomes rather than solely relying on process measures. (*Psychiatric Services* 65:1244–1248, 2014; doi: 10.1176/appi.ps.201300234)**

Access to mental health care in the U.S. Department of Veterans Affairs (VA) is often construed as whether veterans initiate treatment (1,2), but researchers and policy makers have begun to consider whether access also refers to whether veterans receive an adequate amount of care (3,4). This study assessed whether the doses of psychotherapy and pharmacotherapy related to posttraumatic stress disorder (PTSD) contributed to better clinical outcomes among veterans diagnosed as having PTSD.

Clinical practice guidelines provide little guidance on what constitutes an adequate dose of psychotherapy for PTSD (5,6). VA procedure codes indicate session length and modality (for example, individual versus group), but they do not identify a specific treatment approach, such as prolonged exposure therapy or cognitive-processing therapy. Among all VA patients who are diagnosed as having PTSD and who initiate psychotherapy, roughly 25% to 33% complete at least eight or nine sessions (3,4), which some researchers have proposed as an adequate amount of contact for delivery of an evidence-based treatment. The VA has set a performance target for treatment of PTSD among veterans who served in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), or Operation New Dawn (OND). At least 20% of these patients who had two or more visits with a PTSD diagnosis must receive at least eight PTSD-related psychotherapy sessions within a 14-week period, unless they received a similar dose of treatment within the past two years. However, no prior studies have assessed whether this amount actually is associated with better clinical outcomes. This study explored the utility of this process measure of dose of psychotherapy.

PTSD practice guidelines endorse an adequate initial trial (at least eight to 12 weeks) of selective serotonin reuptake inhibitors (SSRIs) or serotonin

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Table 1

Effects of psychotherapy visits for PTSD and of other variables on PTSD, depression, and functioning among 472 veterans[a]

Variable	PTSD		Depression		Functioning	
	B	95% CI	B	95% CI	B	95% CI
Intercept	44.51*	41.13 to 47.90	31.13*	28.98 to 33.27	35.54*	33.41 to 37.68
Male (reference: female)	5.12*	1.62 to 8.63	–.32	–2.54 to 1.90	1.46	–.76 to 3.67
OEF/OIF era (reference: prior eras)[b]	–1.28	–4.79 to 2.22	–1.54	–3.77 to .68	–1.71	–3.94 to .51
Psychotherapy visits (reference: 0)						
1 or 2	6.40*	1.63 to 11.18	1.83	–1.19 to 4.85	–1.77	–4.84 to 1.29
3–7	8.58*	3.30 to 13.85	4.48*	1.13 to 7.82	–4.19*	–7.46 to –.93
≥8	4.72	–3.00 to 12.45	2.66	–2.24 to 7.57	–5.47*	–10.30 to –.63
≥8 in 14 weeks	11.33*	4.51 to 18.15	6.11*	1.78 to 10.45	–8.45*	–12.47 to –4.43
Change per month (slope)						
Overall mean change	–.23*	–.45 to –.01	–.11	–.24 to .03	.11	–.03 to .24
Male (reference: female)	–.03	–.26 to .19	–.03	–.17 to .11	–.005	–.15 to .14
OEF/OIF era (reference: prior eras)[b]	.02	–.21 to .24	–.10	–.24 to .04	.09	–.05 to .23
Psychotherapy visits (reference: 0)						
1 or 2	.07	–.24 to .40	.07	–.13 to .26	–.08	–.28 to .12
3–7	.09	–.23 to .43	.16	–.05 to .36	–.11	–.32 to .10
≥8	.17	–.32 to .68	.005	–.30 to .31	.02	–.29 to .34
≥8 in 14 weeks	.004	–.41 to .42	.03	–.23 to .30	.09	–.17 to .35

[a] Ten veterans who completed ≥8 psychotherapy visits within 14 weeks between the diagnosis of PTSD and the completion of a baseline survey were excluded. For PTSD and depression, negative values indicate better health. For functioning, higher values indicate better health.

[b] OEF/OIF, Operation Enduring Freedom/Operation Iraqi Freedom

*$p<.05$

norepinephrine reuptake inhibitors (SNRIs) in treating PTSD (5,6). Prior analyses found that fewer than two-thirds of VA patients with PTSD who were prescribed SSRIs or SNRIs refilled the prescriptions for at least three or four months (3,7). These guidelines do not specify standards for assessing longer-term medication adherence. One suggested measure of adherence often used in research is the medication possession ratio (MPR), which is the total days' supply of medication (initial prescription and refills) divided by the total days in the follow-up period. Some studies, including studies that involved general medical disorders, have suggested using an MPR of 80% to define good adherence (8,9), although two studies that used that cut-point showed variable outcomes among veterans (10,11)

We tested whether rates of improvement in PTSD, depression, and mental health functioning were associated with having at least eight PTSD-related visits for psychotherapy within 14 weeks, initiation or completion of a 90-day trial of an SSRI or SNRI, and extent of medication coverage, as measured by MPR.

Methods

Study procedures were overseen by the Stanford University School of Medicine Institutional Review Board, and participants provided written informed consent.

Participants

Veterans (N=482) were recruited as part of the Longitudinal Veterans Health Survey, a study of treatment utilization and outcomes among veterans newly diagnosed as having PTSD (7,12). VA administrative data were used to draw a national random sample from all VA outpatients who were between the ages of 18 and 69 and who had an outpatient VA visit with a PTSD diagnosis after not having had a PTSD diagnosis in the prior two years. The index outpatient visit in which the diagnosis was made could be for any service in any VA clinic, and thereafter the participants could have any number of outpatient or inpatient visits. Half of the participants (N=250, 52%) were diagnosed in a general mental health clinic; 11% (N=54) in a PTSD specialty clinic; and 37% (N=178) in other settings, such as primary care. The final sample included 134 male OEF/OIF veterans, 109 female OEF/OIF veterans, 121 male veterans of prior eras, and 118 female veterans of prior eras, with a mean±SD age of 41.2± 13.3. The sample included 327 (68%) whites, 90 (19%) African Americans, 66 (14%) Hispanics or Latinos, and 41 (9%) participants of other race or ethnicity. Additional details about the sample were published previously (7,8).

Procedure

Participants completed a baseline survey by mail between August 2006 and April 2008, a second survey five to 12 months (median=7.6 months) later, and a third survey eight to 28 months (median=17.9 months) after the second survey. A majority completed surveys at time 2 (N=376, 78%) and of those, 307 (82%) returned the time 3 survey, with 64% (N=307) completing both follow-up surveys. Participants who completed both follow-up surveys were more likely than those who completed only the baseline survey to be female (49% versus 39%; $\chi^2=3.86$, df=1, $p<.05$) and to be slightly older (41 versus 38 years; Mann-Whitney U test, $z=-2.64$, $p<.01$).

Measures

PTSD was assessed by the Impact of Event Scale–Revised (13), and depression was measured by the Center for Epidemiologic Studies–Depression (CES-D) scale (14). Functioning was assessed with the mental health aggregate score

Table 2

Effects of trials of SSRIs or SNRIs and of other variables on PTSD, depression, and functioning among 447 veterans[a]

Variable	PTSD		Depression		Functioning	
	B	95% CI	B	95% CI	B	95% CI
Intercept	41.67*	37.90 to 45.32	28.57*	26.24 to 30.90	37.71*	35.28 to 40.14
Male (reference: female)	5.66*	2.07 to 9.26	.06	–2.16 to 2.29	.94	–1.34 to 3.21
OEF/OIF era (reference: prior eras)[b]	–.52	–4.11 to 3.06	–.93	–3.15 to 1.29	–2.30*	–4.56 to –.03
SSRI or SNRI trial (reference: none)						
<90-day trial between diagnosis and baseline survey	4.06	–.53 to 8.66	4.26*	1.42 to 7.11	–4.01	–6.90 to –1.18
<90-day trial within a year after baseline survey	7.71*	2.21 to 13.22	3.97*	.56 to 7.38	–3.37	–6.77 to .05
≥90-day trial within a year after baseline survey	5.61*	.55 to 10.66	2.42	–.71 to 5.55	–2.28	–5.44 to .88
Change per month (slope)						
Overall mean change	–.29*	–.53 to –.05	–.09	–.24 to .06	.11	–.04 to .26
Male (reference: female)	.03	–.19 to .26	.02	–.12 to .17	–.06	–.20 to .08
OEF/OIF era (reference: prior eras)[b]	.05	–.17 to .28	–.07	–.21 to .07	.03	–.11 to .17
SSRI or SNRI trial (reference: none)						
<90-day trial between diagnosis and baseline survey	–.19	–.48 to .09	–.28*	–.46 to –.10	.24*	.07 to .42
<90-day trial within a year after baseline survey	.14	–.20 to .48	.10	–.12 to .31	–.006	–.22 to .21
≥90-day trial within a year after baseline survey	.36*	.04 to .68	.28*	.08 to .48	–.25*	–.44 to –.05

[a] Thirty-five veterans who received a 90-day trial of selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs) between the diagnosis of PTSD and the completion of a baseline survey were excluded. For PTSD and depression, negative values indicate better health. For functioning, higher values indicate better health.

[b] OEF/OIF, Operation Enduring Freedom/Operation Iraqi Freedom

*$p<.05$

of version 2 of the 12-Item Short-Form Health Survey (SF-12) (15), which measures general medical and mental health symptoms and functioning in the past 30 days.

Outpatient psychotherapy visits for a primary or secondary PTSD diagnosis were determined from VA administrative data between the baseline survey and the following year. Visits were coded in the following categories: 0, 1 or 2, 3–7, ≥8, and ≥8 within 14 weeks.

Data from the VA Pharmacy National Data Extracts database were used to identify participants who received a prescription for an SSRI or SNRI as an outpatient. To assess initiation of an SSRI or SNRI between the index visit and the baseline survey, we coded participants by whether they started but did not complete a 90-day trial of an SSRI or SNRI during that time frame. For all veterans prescribed an SSRI or SNRI, we calculated the MPR for the year following the baseline survey by dividing the total days' supply by 365 days, excluding any inpatient stays.

Data analysis

Hierarchical linear modeling (HLM) was fit by restricted maximum likelihood by using the lme4 library from R, version 2.13 (16,17). Preliminary analyses indicated relatively linear slopes of the dependent variables over time (no significant quadratic or cubic functions). Separate models were run to assess the effects of psychotherapy, initiation of an SSRI or SNRI, and continuation of SSRIs and SNRIs on the course of PTSD, depression, and functioning. Each model included the grand intercept across time and subjects, the grand intercept and the grand slope for each person at level 1 of the HLM model, and within-person residuals across time at level 2 of the HLM model. Our primary focus was whether dose of care predicted rate of change in outcomes over time.

Results

Dose of psychotherapy

In the year after the baseline survey, 267 (55%) received no PTSD-related psychotherapy, 83 (17%) received one or two visits, 65 (13%) received three to seven visits, 28 (6%) received eight or more visits, and 39 (8%) received eight or more visits within 14 weeks. Ten participants (2%) were excluded from the HLM analysis because they completed eight psychotherapy visits within 14 weeks during the period between the index visit and the baseline survey. Patients with more PTSD-related psychotherapy visits had more severe symptoms, but dose of psychotherapy did not predict slope of improvement for any clinical outcome variable across time (Table 1). Post hoc analyses comparing individual versus group psychotherapy or restricting the sample only to OEF/OIF veterans did not yield any significant findings for the effect of number of PTSD-related visits on symptom course.

Initiation of SSRIs or SNRIs

Thirty-five participants (7%) were excluded from this analysis because they had completed a 90-day course of an SSRI or SNRI prior to the baseline survey. Of the remaining 447

Table 3

Effects of continuous supply of SSRIs or SNRIs and of other variables on PTSD, depression, and functioning among 247 veterans[a]

Variable	PTSD		Depression		Functioning	
	B	95% CI	B	95% CI	B	95% CI
Intercept	51.20*	43.56 to 58.85	37.13*	32.46 to 41.81	30.10*	25.72 to 34.50
Male (reference: female)	4.90	–.37 to 10.16	–.51	–3.72 to 2.69	1.36	–1.75 to 4.46
OEF/OIF era (reference: prior eras)[b]	4.02	–1.24 to 9.30	–.37	–3.59 to 2.85	–3.70*	–6.81 to –.59
≥90-day trial of SSRIs or SNRIs between diagnosis and baseline survey (reference: <90-day trial)	–.11	–7.75 to 7.53	–1.10	–5.70 to 3.49	–3.75	–8.52 to 1.02
MPR in the year after baseline survey	–1.14	–10.15 to 7.87	–2.14	–7.65 to 3.37	2.23	–3.10 to 7.57
Change per month (slope)						
Overall mean change	–.14	–.65 to .36	–.27	–.58 to .03	.31	–.00 to .63
Male (reference: female)	–.10	–.45 to .25	–.04	–.26 to .17	–.02	–.25 to .20
OEF/OIF era (reference: prior eras)[b]	–.27	–.63 to .08	–.27*	–.49 to –.05	.27*	.04 to .49
≥90-day trial of SSRIs or SNRIs between diagnosis and baseline survey (reference: <90-day trial)	–.33	–.88 to .22	–.18	–.51 to .14	.30	–.04 to .64
MPR within a year after baseline survey	.24	–.35 to .85	.40*	–.03 to .77	–.42*	–.80 to –.03

[a] Veterans (N=235) who were not prescribed a selective serotonin reuptake inhibitor (SSRI) or a serotonin norepinephrine reuptake inhibitor (SNRI) between diagnosis of PTSD and completion of the baseline survey were excluded. Continuous supply was measured by medication possession ratio (MPR). For PTSD and depression, negative values indicate better health. For functioning, higher values indicate better health.

[b] OEF/OIF, Operation Enduring Freedom/Operation Iraqi Freedom

*p<.05

participants, 53% (N=235) had no prescription for an SSRI or SNRI, and 47% (N=212) started but did not complete a 90-day trial between the index visit and the baseline survey. Data about receipt of prescriptions for SSRIs and SNRIs for all patients in the year after the baseline survey indicated that 45% (N=218) had no prescription, 18% (N=85) had a prescription but less than a 90-day supply, and 37% (N=179) had at least 90 contiguous days' supply. Excluding the 35 participants who had completed a 90-day course of an SSRI or SNRI prior to the baseline survey, participants who completed a 90-day trial of medication in the year after the baseline survey showed less improvement than participants who did not have medication (Table 2). Post hoc analyses among OEF/OIF/OND veterans found that those who had a partial 90-day trial between the index visit and the baseline survey experienced significant improvement over time in depression (b=–.38, t=–3.07, df=320, p=.002) and mental health functioning (b=.34, t=2.60, df=291, p=.01).

Continuation of SSRIs and SNRIs

MPRs among patients prescribed an SSRI or SNRI ranged from .01 to 1.00 (mean±SD=.59±.29). Higher MPRs were associated with less improvement in depression and mental health functioning (Table 3). Post hoc analyses among only OEF/OIF veterans, however, found no significant effect for continuous supply of medication on symptom course.

Discussion

Over half of the study participants (55%) received no PTSD-related psychotherapy, and 45% received no SSRIs or SNRIs in the year after the baseline survey, suggesting that many patients did not receive any first-line treatments for PTSD from the VA, despite clinical practice guidelines by the VA and the Department of Defense endorsing these treatments. Contrary to our hypotheses, none of the quality indicators significantly contributed to longitudinal improvement in veterans' functioning. These findings highlight the importance of directly assessing patient outcomes rather than only process measures.

One confounding factor was that more symptomatic patients tend to seek and receive more psychotherapy and take more medications. Our surprising finding that a 90-day trial of SSRIs or SNRIs or more regular medication refills were associated with less improvement in depression and mental health functioning may be influenced by patient behavior: individuals who improve quickly may stop their medications, whereas those who experience continuing symptoms may refill their medications. Similarly, more symptomatic patients may seek more psychotherapy, or providers may insist on greater frequency of sessions.

Another issue was that administrative procedure codes cannot differentiate evidence-based psychotherapies from nonspecific psychotherapies (18). For example, prior studies have shown that veterans who received prolonged exposure (19) or cognitive-processing therapy (20) reported greater improvement in PTSD symptoms (pre-post d=.87–1.52) compared with veterans in this study who received eight or more sessions of psychotherapy in 14 weeks (d=.07). This difference confirms the importance of monitoring specific therapy approaches and not only frequency and quantity of visits.

Our medication measures identified only whether patients refilled their medications, not whether they actually took them, and did not account for patients switching from SSRIs and SNRIs to other classes of medication.

Thus because of our limited measures of adherence, this study was not intended to test the effectiveness of pharmacotherapy, nor could it test the effectiveness of psychotherapy because data on specific types of psychotherapy were not available. We also were unable to examine the joint effects of both psychotherapy and pharmacotherapy in the same model. Our secondary outcome measures, the CES-D and the SF-12, also may not be optimally sensitive to change over time. Although the follow-up response rate was nearly 80%, nonrandomization and a differential response among female and older veterans may have slightly biased our results.

Conclusions

This study confirmed the importance of directly assessing patient outcomes rather than using only process measures. Our results underscore the importance of measuring the type, not only the quantity, of psychotherapy that participants receive and the need for more adequate measures of medication adherence. Given that polypharmacy and concurrent pharmacotherapy and psychotherapy are common in PTSD care (21), future studies should examine the effects of sequenced or augmented treatments rather than those of only one class of medication.

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References

1. Kehle SM, Polusny MA, Murdoch M, et al: Early mental health treatment-seeking among US National Guard soldiers deployed to Iraq. Journal of Traumatic Stress 23:33–40, 2010
2. Lu MW, Carlson KF, Duckart JP, et al: The effects of age on initiation of mental health treatment after positive PTSD screens among Veterans Affairs primary care patients. General Hospital Psychiatry 34:654–659, 2012
3. Spoont MR, Murdoch M, Hodges J, et al: Treatment receipt by veterans after a PTSD diagnosis in PTSD, mental health, or general medical clinics. Psychiatric Services 61: 58–63, 2010
4. Seal KH, Maguen S, Cohen B, et al: VA mental health services utilization in Iraq and Afghanistan veterans in the first year of receiving new mental health diagnoses. Journal of Traumatic Stress 23:5–16, 2010
5. VA/DoD Clinical Practice Guideline for the Management of Post-Traumatic Stress, 2010 Update. Available at www.healthquality.va.gov/ptsd/ptsd-sum_2010a.pdf. Accessed May 6, 2011
6. Forbes D, Creamer M, Bisson JI, et al: A guide to guidelines for the treatment of PTSD and related conditions. Journal of Traumatic Stress 23:537–552, 2010
7. Jain S, Greenbaum MA, Rosen CS: Do veterans with PTSD receive first line pharmacotherapy for PTSD? Results from the Longitudinal Veterans Health Survey. Primary Care Companion to CNS Disorders 14:2, 2012
8. Karve S, Cleves MA, Helm M, et al: Good and poor adherence: optimal cut-point for adherence measures using administrative claims data. Current Medical Research and Opinion 25:2303–2310, 2009
9. Pawloski P, Bruzek R, Hedblom B, et al: Drug characteristics associated with medication adherence across eight disease states. Clinical Medicine and Research 10:156–157, 2012
10. Fortney JC, Pyne JM, Edlund MJ, et al: Relationship between antidepressant medication possession and treatment response. General Hospital Psychiatry 32:377–379, 2010
11. Lockwood A, Steinke DT, Botts SR: Medication adherence and its effect on relapse among patients discharged from a Veterans Affairs posttraumatic stress disorder treatment program. Annals of Pharmacotherapy 43:1227–1232, 2009
12. Rosen CS, Greenbaum MA, Fitt JE, et al: Stigma, attitudes about treatment, and use of psychotherapy in veterans with diagnoses of posttraumatic stress disorder. Journal of Nervous and Mental Disease 11:879–885, 2011
13. Weiss DS, Marmar CR: The Impact of Event Scale–Revised; in Assessing Psychological Trauma and PTSD. Edited by Wilson J, Keane TM. New York, Guilford, 1996
14. Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. Applied Psychological Measurement 1:385–401, 1997
15. Ware JE, Jr, Kosinski M, Keller SD: A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Medical Care 34:220–233, 1996
16. Raudenbush SW, Bryk AS: Hierarchical Linear Models: Applications and Data Analysis Methods. Newbury Park, Calif, Sage, 2002
17. R: A Language and Environment for Statistical Computing. Vienna, Austria, R Foundation for Statistical Computing, 2011
18. Shiner B, D'Avolio LW, Nguyen TM, et al: Measuring use of evidence based psychotherapy for posttraumatic stress disorder. Administration and Policy in Mental Health and Mental Health Services Research 40: 311–318, 2013
19. Eftekhari A, Ruzek JI, Crowley JJ, et al: Effectiveness of national implementation of prolonged exposure therapy in Veterans Affairs care. JAMA Psychiatry 70:949–955, 2013
20. Chard KM, Ricksecker EG, Healy ET, et al: Dissemination and experience with cognitive processing therapy. Journal of Rehabilitation Research and Development 49:667–678, 2012
21. Mohamed S, Rosenheck RA: Pharmacotherapy of PTSD in the US Department of Veterans Affairs: diagnostic- and symptom-guided drug selection. Journal of Clinical Psychiatry 69:959–965, 2008