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PRINCIPAL INVESTIGATOR:
Robert M. Bray, Ph.D.

CONTRACTING ORGANIZATION: Research Triangle Institute
Research Triangle Park, NC 27709

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Robert M. Bray, Ph.D.; Kristine L. Rae Olmsted, MSPH; Jessica Nelson

E-Mail: rmb@rti.org;krolmsted@rti.org; jnelson@rti.org

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14. ABSTRACT
During the last year, the study team completed follow-up data collection, garnering high retention rates for the 666 participants (93% overall at 3-month follow-up, 90% overall at 6-month follow-up, and 87% overall at 12-month follow-up). Investigators received complete survey and administrative datasets and are conducting full analyses of the data. A design manuscript was published by the journal *Contemporary Clinical Trials* in November 2014. Investigators continued work on multiple manuscripts and presentations, including the main outcomes, cost-effectiveness, service utilization, trajectories of PTSD outcomes, and two qualitative study manuscripts, among others. Investigators have also presented study-related findings at multiple conferences including the Psychological Health and Resilience Summit in September 2014 in Falls Church, VA, the 56th International Military Testing Association Conference in October 2014 in Hamburg, Germany, the 30th Annual Meeting of the International Society for Traumatic Stress Studies (ISTSS) in November 2014 in Miami, FL, the American Psychiatric Association 168th Annual Meeting in May 2015 in Toronto, Canada, and the Military Health System Research Symposium (MHSRS) in August 2015 in Ft. Lauderdale, FL.

15. SUBJECT TERMS
Collaborative care; PTSD; military; depression; primary care; care management; preference-based stepped care; follow-up data collection; data analysis; manuscript writing; presentations

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INTRODUCTION:

The purpose of the STEPS UP (**ST**epped **E**nhancement of **P**TSD **S**ervices **U**sing **P**rimary Care) trial is to compare centralized telephonic care management with preference-based stepped PTSD and depression care to optimized usual care. We hypothesize that the STEPS UP intervention will lead to improvements in (1) PTSD and depression symptom severity (primary hypothesis); (2) anxiety and somatic symptom severity, alcohol use, mental health functioning, work functioning; (3) costs and cost-effectiveness. We further hypothesize that qualitative data will show (4) patients, their family members, and participating clinicians find that the STEPS UP intervention is an acceptable, effective, and satisfying approach to deliver and receive PTSD and depression care.

STEPS UP is a six-site, two–parallel arm (N = 666) randomized controlled effectiveness trial with 3-month, 6-month, and 12-month follow-up comparing centralized telephonic stepped- care management to optimized usual PTSD and depression care. In addition to the existing PTSD and depression treatment options, STEPS UP includes web-based cognitive behavioral self- management, telephone cognitive-behavioral therapy, continuous RN nurse care management, and computer-automated care management support. Both arms can refer patients for mental health specialty care as needed, preferred and available. The study uses sites currently running RESPECT-Mil, the existing military primary care-mental health services practice network, to access site health care leaders and potential study participants at the 6 study sites.

If eventually implemented, given our findings we expect that STEPS UP will increase the likelihood that military personnel with unmet PTSD- and depression-related health care needs will get timely, effective, and efficient PTSD and depression care. The real world utility and

feasibility of the STEPS-UP intervention can improve on what the Institute of Medicine has described as a 15 year science to service gap. STEPS UP is available to roll out immediately, reinforcing and facilitating pathways to PTSD and depression recovery within the Military Health System.

BODY:

Activities this year included ongoing project management, completion of data collection, acquisition of administrative data, as well as finalizing, cleaning, and producing codebooks, and analysis of manuscripts. The project was on pace in terms of timeline and milestones according to the approved Statement of Work, despite considerable administrative delays and uncertainties in timeline and funding. Below we discuss each task activity in turn.

Table 1. Milestones by Task	**Year 1**				**Year 2**				**Year 3**				**Year 4**				**Year 5**				**Year 6**			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
	Sept 09	Dec 09	Mar 10	June 10	Sept 10	Dec 10	Mar 11	June 11	Sept 11	Dec 11	Mar 12	June 12	Sept 12	Dec 12	Mar 13	June 13	Sept 13	Dec 13	Mar 14	June 14	Sept 14	Dec 14	Mar 15	June 15
Task 1: Develop Intervention																								
Develop protocol, tools, manuals	x	x	x	x	x	x	x	x	x															
Hire staff and conduct training							x	x	x	x	x													
Provider Interviews & Expert Panel		x	x																					
Task 2: Conduct Randomized Effectiveness Trial																								
Develop protocol/instruments	x	x	x	x	x	x	x	x																
Obtain IRB approval	x	x	x	x	x	x	x	x	x	x	x	x												
Conduct pilot test									x	x														
Recruit & consent participants*									x	x	x	x	x	x	x	x								
Conduct data collection										x	x	x	x	x	x	x	x	x	x	x				
Analysis and Writing													x	x	x	x	x	x	x	x	x	x	x	x
Task 3: Create an Effective Research Structure																								
Hold research team meetings	x	x	x	x	x		x		x		x		x		x		x		x		x		x	
Implement QA/QC procedures	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Submit reports	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

In terms of <u>data collection</u>, the study team completed follow-up data collection in October 2014, keeping the data collection window open slightly longer than planned to capture the final assessments on a few patients. Final follow-up rates for the 666

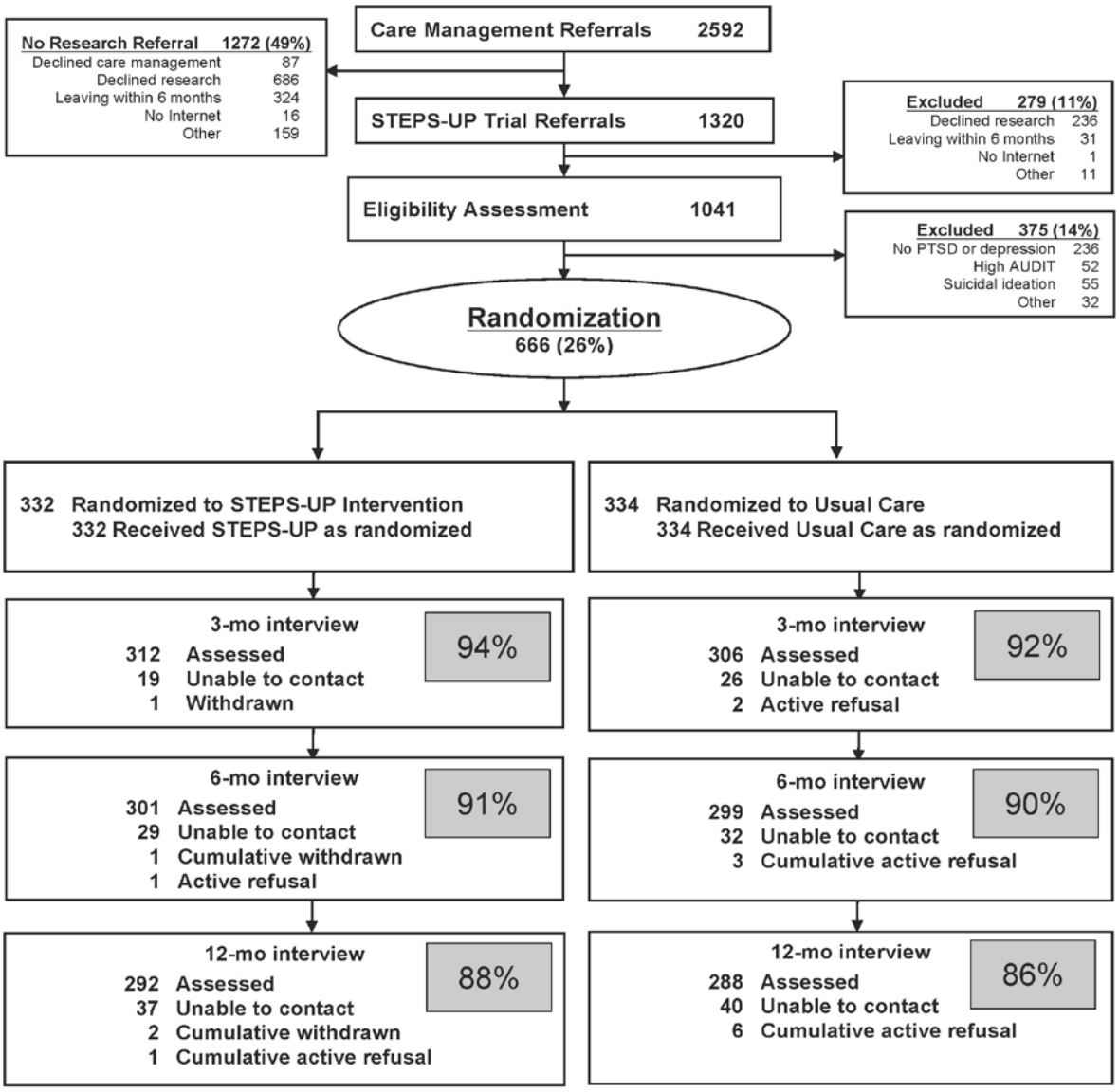
participants in the study are as follows and are considered to be excellent (see Figure 1): 93% overall 3-month follow-up rate (94% in STEPS UP intervention arm; 92% in OUC arm); 90% overall 6-month follow-up rate (91% in STEPS UP intervention arm; 90% in OUC arm); and 87% overall 12-month follow-up rate (88% in STEPS UP intervention arm; 86% in OUC arm). Final administrative datasets were received in May 2015; all institutions now have access to the eligibility, baseline, 3-month, 6-month, and 12-month survey datasets, as well as FIRST STEPS, M2, and MDR administrative service use datasets.

In terms of analysis and writing, the study team continues to plan and prepare publications and presentations. In November 2014, a manuscript describing the overall design and methods of the STEPS UP study was published in *Contemporary Clinical Trials* (see Appendix A). The primary outcomes manuscript is under review for publication (see Appendix B). Also, a qualitative study manuscript describing barriers to engagement is under review for publication (see Appendix C). Several other planned manuscripts are in the analysis and writing phases. The intervention materials are also in preparation.

The study team has also presented multiple study-related presentations and posters at various conferences in the past year, including the Psychological Health and Resilience Summit (September 2014, Falls Church, VA), the 56th International Military Testing Association Conference (October 2014, Hamburg, Germany), the 30th Annual Meeting of the International Society for Traumatic Stress Studies (ISTSS; November 2014, Miami, FL), the American Psychiatric Association 168th Annual Meeting (May 2015, Toronto, Canada), and the Military Health System Research Symposium (MHSRS; August 2015, Ft. Lauderdale, FL). Currently, presentations on the study design and findings are planned for the 2015 Defense Centers of Excellence for Psychological Health and Traumatic Brain

Injury (DCoE) Summit: Continuum of Care and Care Transitions in the Military Health System in September 2015 in Falls Church, VA, two presentations at the 57th International Military Testing Association Conference in September 2015 in Stockholm, Sweden,

Figure 1. Study flow diagram. Percentage in gray box is response rate by follow-up assessment and treatment arm.



and multiple presentations and posters are planned for the 31st Annual Meeting of the International Society for Traumatic Stress Studies (ISTSS) in November 2015 in New Orleans, LA. A full list of study publications and presentations is presented below in the "Reportable Outcomes" section of this report.

In terms of research team meetings, study investigators continued to participate in multiple routine weekly conference calls and other communications as necessary to ensure timely completion of all tasks throughout the year.

In terms of ongoing QA/QC procedures, during the last year, continuing review packages for the lead WRNMMC IRB, Ft. Bliss, Ft. Bragg, Ft. Carson, and JBLM sites were approved by the lead WRNMMC IRB, local site IRBs, and HRPO; these packages have a new expiration date of 07 May 2016. After consultation with the local DDEAMC and lead WRNMMC IRBs, investigators submitted IRB closure report packages for the Ft. Campbell and Ft. Stewart sites because study activities are no longer physically occurring at the study sites. These closure reports were approved by the local DDEAMC and lead WRNMMC IRBs in May 2015 and by HRPO in June 2015. Investigators plan to submit IRB closure report packages for the remaining sites during the next quarter. RTI submitted for continuing review on 20 April 2015 and received approval.

Several amendments were approved by the local and lead WRNMMC IRBs during the last year. In September 2014, the lead WRNMMC IRB approved an amendment updating the core protocol and DHCC Data Safeguarding Plan to remove language regarding the "Safe Harbor method" and describe the administrative service use data being requested for analyses. Also, amendments to update site personnel at the lead WRNMMC site, Ft. Bliss, Ft. Bragg, Ft. Carson, and JBLM (including adding a new Site PI at JBLM) were approved with

continuing review packages in May 2015.

The STEPS UP team held a final meeting with the DSMB in February 2015 to discuss and review study status.

Specific Contributions of RTI

During the past year, RTI continued ongoing routine maintenance and evaluation of the study website and conducted the final follow up assessments with study participants. The RTI team was unable to make expected work progress early in this reporting year due to work stoppage pending USAMRAA confirmation of the 1-year extension without additional funds (EWOF), which did not arrive until 23 January 2015.

After confirmation of the EWOF, RTI resumed work, engaging in data editing, cleaning, and preparation of data files and comprehensive codebooks for the eligibility, baseline, 3-month, 6-month and 12- month follow-up assessments, and the M2 and MDR administrative datasets. These datasets and codebooks were finalized and shared with all organizations on the STEPS UP team.

RTI also played a lead role in statistical analyses of the study findings for the primary outcomes manuscript in consultation with study partners. RTI also contributed to the writing and preparation of the manuscript reporting the main outcomes of the trial.

Finally, RTI continued internal and team discussions, planning, and preparation for analyses and writing of several additional manuscripts. RTI investigators continued to be involved in all aspects of project management and maintaining the SharePoint data system as the study repository for all aspects the study data, instruments, and manuscripts.

Administrative Delays

All three organizations (HJF, RAND, and RTI) experienced administrative delays in

negotiating the budget for the allowable one-year extension without funds (EWOF). It was clear early on that investigators would need an extension to conduct analyses and complete study deliverables, primarily due to extensive administrative delays in the beginning of the study period. However, there was an extended process in negotiating the extension officially from late February/early March 2014, until 23 January 2015. These administrative delays substantially slowed investigator capability to analyze data and initiate dissemination efforts. HJF, RAND, and RTI requested a second EWOF in order to complete approved analyses and reporting activities for the study. USAMRAA issued notification in August 2015 that an additional 6-month EWOF would be granted which extended the award period of performance through 29 February 2016.

KEY RESEARCH ACCOMPLISHMENTS:

The specific aims of this project were as follows:

Aim 1: To assess whether active duty primary care patients with PTSD and/or depression randomly assigned to 12 months of STEPS UP will report significantly reduced PTSD and depression symptoms (primary outcomes) compared to those randomly assigned to optimized usual care.

Aim 2: To evaluate whether active duty primary care patients with PTSD randomly assigned to 12 months of STEPS UP will report significantly reduced symptoms of anxiety and somatic symptom severity, alcohol use, mental health functioning, and work functioning (secondary outcomes) compared to those randomly assigned to 12 months of optimized usual care.

Aim 3: To examine whether active duty primary care patients with PTSD and/or depression randomly assigned to 12 months of STEPS UP have significantly lower direct and indirect costs

of care and a more favorable cost-effectiveness ratio (tertiary outcomes) compared to those randomly assigned to 12 months of optimized usual care.

Aim 4: To use state-of-the-art qualitative methods to examine participant, clinician, care manager, and family member perceptions of STEPS UP as well as associated intervention outcomes.

As of August 2016, we can report on Aims 1 and 2, and partially report on Aim 4, although at the time of this report, all findings were still undergoing peer review and are not yet published. Thus, they must be considered preliminary. For Aim 3, we obtained the necessary data in May 2015 but do not have analyses or results to report at the time of this report. For Aim 4, we have a second paper underway, but results are not yet available.

In regard to Aim 1, we found that compared to usual care, participants in the STEPS UP intervention arm reported significantly greater reductions in PTSD and depression symptoms over 12-months of follow-up as shown in Table 2. Differences in effects were statistically significant at 12-months for PTSD and at 6- and 12-months for depression. The STEPS UP intervention was also associated with clinically significant improvements (for every 12 patients (with PTSD) or 11 patients (with depression), we see a 50% improvement in symptoms).

In regard to Aim 2, we also detected significant changes in several secondary outcomes as shown in Table 3. The STEPS UP intervention arm was significantly associated with decreased physical symptom burden (as measured by the PHQ-15), improved mental health functioning (as measured by the SF-12 mental component), but no changes for alcohol consumption (as measured by the AUDIT-C), physical health function (as measured by the SF-12 physical component) or pain (intensity or interference).

Table 2. PTSD and depression related outcomes among study patients.

Outcome	CACT (n=332)	Usual Care (n=334)	Measure (95% CI)	p-value
PTSD (PDS) Severity				
0 to 3 months	-2.95[1] (0.53)	-2.73 (0.54)	-0.23 (-1.72,1.26)	0.59
0 to 6 months	-4.86 (0.61)	-3.42 (0.60)	-1.43 (-3.11, 0.25)	**0.057**
0 to 12 months	-6.07 (0.68)	-3.54 (0.72)	-2.53 (-4.47,-0.59)	**0.0029**
Depression (SCL-20)				
0 to 3 months	-0.29[1] (0.04)	-0.20 (0.04)	-0.08 (-0.19, 0.03)	0.062
0 to 6 months	-0.44 (0.05)	-0.25 (0.05)	-0.19 (-0.32, -0.06)	**0.0007**
0 to 12 months	-0.56 (0.05)	-0.31 (0.05)	-0.26 (-0.41, -0.11)	**<0.0001**
≥50% Improvement, PTSD				**0.023**
0 to 3 months	11.5[2] (36)	9.5 (29)	1.25[3] (0.74, 2.09)	0.40
0 to 6 months	19.3 (58)	13.4 (40)	1.55 (0.99, 2.40)	0.0510
0 to 12 months	25.0 (73)	17.0 (49)	1.62 (1.08, 2.43)	**0.0194**
≥50% Improvement, Depression				**0.014**
0 to 3 months	12.2[2] (38)	10.8 (33)	1.14[3] (0.70, 1.88)	0.60
0 to 6 months	21.3 (64)	13.8 (41)	1.70 (1.11, 2.61)	**0.0149**
0 to 12 months	29.7 (86)	20.6 (59)	1.65 (1.13, 2.42)	**0.0100**

[1] mean (SE)
[2] percent improved (number improved)
[3] odds ratio (95% confidence limits)
PDS=PTSD Diagnostic Scale
SCL-20=Hopkins Symptom Checklist, 20 item depression screen

Table 3. Changes in secondary outcomes among study patients from baseline to each follow-up assessment.

	CACT (n=332)	**Usual Care (n=334)**	**Measure (95% CI)**	**Overall P Value**
AUDIT-C, mean (SE)				0.24
0 to 3 months	-0.26 (0.12)	-0.29 (0.12)	-0.04 (-0.28, 0.36)	
0 to 6 months	-0.34 (0.13)	-0.33 (0.12)	-0.001 (-0.35, 0.35)	
0 to 12 months	-0.54 (0.14)	-0.20 (0.14)	-0.33 (-0.72, 0.06)	
PHQ-15, mean (SE)				**0.0252**
0 to 3 months	-1.12 (0.25)	-0.58 (0.25)	-0.53 (-1.22, 0.15)	
0 to 6 months	-1.56 (0.26)	-0.69 (0.29)	-0.88 (-1.64, -0.11)	
0 to 12 months	-2.29 (0.33)	-0.92 (0.31)	-1.37 (-2.26, -0.47)	
SF-12, mean (SE)				
Physical (PCS)				0.65
0 to 3 months	-1.02 (0.41)	-1.16 (0.44)	0.14 (-1.04, 1.31)	
0 to 6 months	-0.64 (0.45)	-1.10 (0.46)	0.46 (-0.80, 1.72)	
0 to 12 months	-1.11 (0.47)	-1.25 (0.55)	0.14 (-1.29, 1.57)	
Mental (MCS)				**0.014**
0 to 3 months	4.31 (0.65)	4.13 (0.65)	0.18 (-1.62, 1.98)	
0 to 6 months	5.78 (0.74)	3.51 (0.74)	2.28 (0.23, 4.33)	
0 to 12 months	8.10 (0.80)	4.93 (0.82)	3.17 (0.91, 5.42)	
Pain Intensity, mean (SE)				0.32
0 to 3 months	-0.17 (0.13)	0.02 (0.11)	-0.19 (-0.51, 0.14)	

0 to 6 months	-0.18 (0.13)	0.08 (0.13)	-0.26 (-0.61, 0.10)	
0 to 12 months	-0.25 (0.15)	0.08 (0.12)	-0.33 (-0.74, 0.07)	
Pain Interference, mean (SE)				0.36
0 to 3 months	0.09 (0.19)	0.27 (0.13)	-0.17 (-0.54, 0.20)	
0 to 6 months	-0.05 (0.15)	0.18 (0.14)	-0.23 (-0.63, 0.18)	
0 to 12 months	-0.19 (0.16)	0.20 (0.17)	-0.39 (-0.85, 0.07)	

AUDIT-C=Consumption items of the Alcohol Use Disorders Identification Test
PHQ-15=Patient Health Questionnaire somatic symptom severity score
MCS=SF-12 Mental Component Summary score
PCS=SF-12 Physical Component Summary score

We also examined three symptoms of suicidality (for questions of "hopelessness about the future," "thoughts of death and dying," and "thoughts of ending one's life") that are part of the depression measure, and found that these were significantly reduced in the STEPS UP condition as well. Specifically, repeated measures analysis (treatment group, by time, and their interaction) revealed statistically significant reductions in suicide-related SCL-20 items in the STEPS UP arm (versus no change in usual care) for "hopelessness about the future" (p=0.04), "thoughts of death and dying" (p=0.003), and in "thoughts of ending one's life (p=0.04).

To further understand the findings in Aims 1 and 2, we also examined the process of care. We found that the STEPS UP intervention was also significantly associated with more telephone contacts and more months on an appropriate PTSD and depression medication than the usual care group as noted in Table 4.

Table 4. Patient reported mental health service use by treatment group (mean, SE).

			Treatment Effect	
	CACT (n=332)	**Usual Care (n=334)**	**Measure (95% CI)**	**P****
Individual Therapy Visits				0.49
3 months prior to enrollment	2.66* (0.27)	2.68 (0.45)	-0.02 (-1.06, 1.01)	
0 to 3 months	2.94 (0.26)	2.86 (0.26)	0.08 (-0.62, 0.79)	
3 to 6 months	2.82 (0.29)	2.32 (0.24)	0.50 (-0.24, 1.24)	
6 to 12 months	3.66 (0.47)	3.55 (0.41)	0.11 (-1.11, 1.33)	
Telephone Contacts				**<0.0001**
3 months prior to enrollment	1.53 (0.14)	2.56 (0.63)	-1.03 (-2.30, 0.25)	
0 to 3 months	3.05 (0.22)	1.76 (0.13)	1.·29 (0.80, 1.79)	
3 to 6 months	2.72 (0.31)	1.46 (0.13)	1.26 (0.59, 1.92)	
6 to 12 months	3.30 (0.35)	1.99 (0.22)	1.31 (0.51, 2.12)	
Months of Depression Medication[1]				**0.0129**
3 months prior to enrollment	0.67 (0.06)	0.77 (0.06)	-0.10 (-0.26, 0.07)	
0 to 3 months	1.30 (0.07)	1.13 (0.08)	0.16 (-0.05, 0.37)	
3 to 6 months	1.37 (0.08)	1.22 (0.08)	0.15 (-0.07, 0.37)	
6 to 12 months	2.42 (0.16)	2.02 (0.16)	0.40 (-0.05, 0.84)	
Months of PTSD Medication[2]				**0.0122**
3 months prior to enrollment	0.47 (0.05)	0.51 (0.06)	-0.04 (-0.18, 0.11)	
0 to 3 months	1.05 (0.07)	0.85 (0.07)	0.20 (-0.003, 0.39)	

3 to 6 months	1.20 (0.08)	0.88 (0.08)	0.32 (0.10, 0.53)	
6 to 12 months	2.03 (0.16)	1.60 (0.15)	0.43 (0.003, 0.86)	

[1] Any antidepressant medication
[2] Any selective serotonin reuptake inhibitor or prazosin
* mean (standard error)
** p for treatment difference averaged over 3-, 6-, and 12-month assessments

Finally, we also examined adverse events. There were no participant deaths and no psychiatric emergencies or hospitalizations determined to be study related.

In regard to Aim 4, we have one paper under review that examines patient and provider perspectives on the STEPS UP intervention (see Appendix C). Specifically, the study included patients recruited for the study, health care providers working within site clinics, and the care managers employed within the study to implement the intervention protocol.

Results of the qualitative analysis raised a number of issues, which fell into two main categories: structural factors associated with the system itself and institutional attitudes and cultural issues across the U.S. military. Structural issues included concerns about the existing capacity of the system, for example whether there were enough providers available to address the populations' needs and the constraints on clinic hours and scheduling practices. The institutional attitude and cultural issues fell into two main areas: attitudes and perceptions among the leadership and the concern that those attitudes could result in negative career repercussions for those who access care.

The findings reveal that despite these significant efforts, stakeholders within the Army medical system still perceive significant barriers to care. Efforts to ensure adequate, timely, and quality access to mental health care for service members will need to appropriately respond to capacity constraints and organizational and institutional culture.

REPORTABLE OUTCOMES:

Publications:

Engel, CC; Jaycox, L; Freed, MC; Bray, RM; Brambilla, D; Zatzick, D; Litz, B; Tanielian, T; Novak, LA; Lane, ME; Belsher, BE; Rae Olmsted, K; Evatt, DP; Vandermaas-Peeler, R; Unützer, J; & Katon, WJ. Centrally assisted collaborative telecare for posttraumatic stress disorder and depression among military personnel attending primary care: A randomized controlled trial. Under review.

Tanielian TL, Jaycox LH, Farmer C, Woldetsadik M, Moen S, Epley C. Barriers to engaging service members in mental health care within the military health system. Under review.

Freed MC, Novak LA, Killgore WDS, Rauch SAM, Koehlmoos TP, Ginsberg JP, Krupnick J, Rizzo A, Andrews A, Engel CC. (In press). IRB and Research regulatory delays within the military healthcare setting: Do they really matter? And if so, why and for whom? American Journal of Bioethics.

Ramchand, R., Rudavsky, R., Grant, S., Tanielian, T., & Jaycox, L. (2015). Prevalence of, risk factors for, and consequences of posttraumatic stress disorder and other mental health problems in military populations deployed to Iraq and Afghanistan. Current Psychiatry Reports, published online 16 April 2015. doi: 10.1007/s11920-015-0575-z. Available at: http://rd.springer.com/article/10.1007/s11920-015-0575-z.

Engel, CC; Bray, RM; Jaycox, L; Freed, MC; Zatzick, D; Lane, M E; Brambilla, D; Rae Olmsted, KL; Vandermaas-Peeler, R; Litz, B; Tanielian, T; Belsher, BE; Evatt, DP; Novak, LA; Unützer, J; & Katon, WJ. (2014). Implementing collaborative primary care for depression and posttraumatic stress disorder: Design and sample for a randomized trial in the U.S. military health system. Contemporary Clinical Trials, 39(2), 310-319. doi: 10.1016/j.cct.2014.10.002.

Presentations:

Freed, MC. (November 2015). A Randomized Trial of Centrally Assisted Collaborative Telecare Management for PTSD and depression in military primary care. Part of ISTSS Symposium: Trauma Informed Practice: A Tale of Two Collaborative Primary Care Treatment Trials. Accepted for presentation at the 31st Annual Meeting of the International Society for Traumatic Stress Studies, New Orleans, LA.

Freed, M., Belsher, B., Novak, L., Liu, X., Evatt, D., Jaycox, L., Bray, R., Engel, C. (November 2015). Suicide risk and PTSD in military primary care populations: From epidemiology to practice. Part of ISTSS Symposium: A Translational Approach to Posttraumatic Risk Behaviors across Trauma Exposed Patient Populations. Accepted for presentation at the 31st Annual Meeting of the International Society for Traumatic Stress Studies, New Orleans, LA.

Belsher, B., Jaycox, L., Evatt, D., Freed, M., Engel, C.C., Novak, L., Lucio, W., Bray, R. (November 2015). Bridging the Health System: Evaluating Patterns of Behavioral Health Utilization among Active Duty Soldiers with Trauma Symptoms in a Stepped, Collaborative

Care Intervention. Poster accepted for presentation at the 31st Annual Meeting of the International Society for Traumatic Stress Studies, New Orleans, LA.

Evatt, D., Belsher. B., Jaycox, L., Freed, M., Novak, L., Beech, E., Thonsen, L., Bray, R., & Engel. C. (November 2015). Relationship between Alcohol Misuse, Alcohol Screening, and Treatment Outcomes in STEPS-UP. Poster accepted for presentation at the 31st Annual Meeting of the International Society for Traumatic Stress Studies, New Orleans, LA.

Bray, R. M., Engel, C.C., Williams, J., Jaycox, L., Lane, M. E., & Freed, M.C. (September 2015). PTSD Trajectories in Collaborative Care Treatment Among U.S. Soldiers. Accepted for presentation at the 57th International Military Testing Association Conference, Stockholm, Sweden.

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Jaycox L; Tanielian T, Farmer C, Woldetsadik M, Moen S. (November 2014). Qualitative Study of Soldiers within Primary-Care Interventions to Improve PTSD and Depression. Part of ISTSS Symposium: Implementing Traumatic Stress Services in Military Primary Care: Treatment & Trials. Engel CC (chair). 30th Annual Meeting of the International Society for Traumatic Stress Studies (ISTSS), Miami, FL.

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CONCLUSION:

This is the first randomized trial to assess collaborative care for active component military personnel and one of few trials to assess collaborative primary care for PTSD. Results show that the centrally assisted collaborative care model with stepped psychosocial and pharmacologic management (STEPS UP intervention) is likely to improve outcomes of PTSD and depression in military personnel within primary care. The qualitative study component will help identify patient and provider perceptions of barriers to accessing mental health care in the MHS and help evaluate acceptability of the intervention across stakeholder groups. Furthermore, investigators are currently conducting cost-effectiveness analyses, which will help measure and understand the value of the intervention. Overall, the STEPS UP intervention enhancements are

feasible and implementable within the MHS. Results from the trial have the potential to inform decisions about providing mental health care within the MHS and improving the lives of service members.

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LIST OF APPENDICES:

Appendix A: Design Manuscript

Engel CC, Bray RM, Jaycox L, Freed MC, Zatzick D, Lane ME, Brambilla D, Rae Olmsted KL, Vandermaas-Peeler R, Litz B, Tanielian T, Belsher BE, Evatt DP, Novak LA, Unützer J, Katon WJ. (2014). Implementing collaborative primary care for depression and posttraumatic stress disorder: Design and sample for a randomized trial in the U.S. military health system. Contemporary Clinical Trials, 39(2), 310-319. doi: 10.1016/j.cct.2014.10.002.

Appendix B: Main Outcomes Manuscript (under review)

Engel, CC; Jaycox, L; Freed, MC; Bray, RM; Brambilla, D; Zatzick, D; Litz, B; Tanielian, T; Novak, LA; Lane, ME; Belsher, BE; Rae Olmsted, K; Evatt, DP; Vandermaas-Peeler, R; Unützer, J; & Katon, WJ. Centrally assisted collaborative telecare for posttraumatic stress disorder and depression among military personnel attending primary care: A randomized controlled trial. Under review.

Contemporary Clinical Trials 39 (2014) 310–319

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Implementing collaborative primary care for depression and posttraumatic stress disorder: Design and sample for a randomized trial in the U.S. military health system ☆

Charles C. Engel [a,d,*], Robert M. Bray [b], Lisa H. Jaycox [a], Michael C. Freed [c,d], Doug Zatzick [e], Marian E. Lane [b], Donald Brambilla [b], Kristine Rae Olmsted [b], Russ Vandermaas-Peeler [b], Brett Litz [f], Terri Tanielian [a], Bradley E. Belsher [c,d], Daniel P. Evatt [c], Laura A. Novak [c], Jürgen Unützer [e], Wayne J. Katon [e]

[a] RAND Corporation, Washington, DC, USA
[b] RTI International, Research Triangle Park, NC, USA
[c] Deployment Health Clinical Center, Bethesda, MD, USA
[d] Uniformed Services University of the Health Sciences, Bethesda, MD, USA
[e] Department of Psychiatry and Behavioral Sciences, University of Washington Medical School, Seattle, WA, USA
[f] VA Boston Healthcare System and Department of Psychiatry, Boston University School of Medicine, Boston, MA, USA

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ABSTRACT

Background: War-related trauma, posttraumatic stress disorder (PTSD), depression and suicide are common in US military members. Often, those affected do not seek treatment due to stigma and barriers to care. When care is sought, it often fails to meet quality standards. A randomized trial is assessing whether collaborative primary care improves quality and outcomes of PTSD and depression care in the US military health system.
Objective: The aim of this study is to describe the design and sample for a randomized effectiveness trial of collaborative care for PTSD and depression in military members attending primary care.
Methods: The STEPS-UP Trial (STepped Enhancement of PTSD Services Using Primary Care) is a 6 installation (18 clinic) randomized effectiveness trial in the US military health system. Study rationale, design, enrollment and sample characteristics are summarized.
Findings: Military members attending primary care with suspected PTSD, depression or both were referred to care management and recruited for the trial (2592), and 1041 gave permission to contact for research participation. Of those, 666 (64%) met eligibility criteria, completed baseline assessments, and were randomized to 12 months of usual collaborative primary care versus STEPS-UP collaborative care. Implementation was locally managed for usual collaborative care and centrally managed for STEPS-UP. Research reassessments occurred at 3-, 6-, and 12-months. Baseline characteristics were similar across the two intervention groups.
Conclusions: STEPS-UP will be the first large scale randomized effectiveness trial completed in the US military health system, assessing how an implementation model affects collaborative care impact on mental health outcomes. It promises lessons for health system change.

1. Introduction

The 2014 Institute of Medicine report, "Treatment for Posttraumatic Stress Disorder in Military and Veteran

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* Corresponding author at: RAND Corporation, 1200 South Hayes Street, Arlington, VA 22202, USA. Tel.: +1 703 413 1100x5466.

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Populations: Final Assessment" [1] emphasized an urgent need to expand Department of Defense (DoD) and Department of Veterans Affairs (VA) capacity for integrated, coordinated, and evidence-based PTSD care. The prevalence of PTSD and depression in the U.S. military is estimated at 13%–18% after deployment to Iraq and Afghanistan, with 28% reporting serious symptoms of PTSD, anxiety, or depression [2,3]. These problems are significant contributors to military attrition, absenteeism, misconduct, and sick call visits [4–6]. However, less than half of U.S. military members with PTSD receive mental health treatment [2,3,5,7], and only half of those getting treatment receive minimally adequate care [3].

Mental health care in the military is unusual in some ways. Typically, both providers and patients work for the military—sometimes even for the same commanding officer. Providers consistently experience clear and competing obligations to military and patient interests. Perhaps not surprisingly, underuse of military mental health care is associated with military member concerns about the potential for treatment to harm to their career, mistrust of military mental health providers, and fears of negative reactions from leaders and peers [2,3]. While the U.S. military health system offers challenges, delays and barriers to PTSD care are a national problem, with one study estimating a 12-year median time from PTSD onset to first treatment [8]. The average term of U.S. military enlistment hovers near five years, and therefore a comparable delay in military mental health treatment is simply too long.

Systems-level "collaborative care" is an established method of increasing the reach, quality and outcomes of mental health care in a variety of settings [9]. Large, well-conducted randomized trials indicate that collaborative care improves outcomes for patients with depression and anxiety [10–12], depression and related suicidal ideation [13,14], depression and chronic health conditions (e.g., diabetes, asthma) [15], panic disorder [16], persistent physical symptoms such as chronic pain [17–19] and analgesic management [20]. Cost-effectiveness analyses suggest that costs associated with collaborative care-related improvements are within a range considered acceptable for public health improvements [21]. For PTSD, however, there has only been one randomized trial of collaborative primary care, a negative trial completed in VA [22].

Since 2007, the Army has implemented collaborative care worldwide using the same model tested in the VA trial [23,24], but insufficient access to and quality of military mental health care remain a recurrent concern [3,7,25–27]. Despite implications for current and future wartime health system response, there have been no controlled trials of collaborative care completed in the military health system, a service system with the mission of providing health care for over 9 million beneficiaries including active duty military personnel and their families at a rising annual cost of $52 billion in 2012 [28].

A large multisite randomized effectiveness trial is underway comparing a scalable, centrally managed primary care treatment package using collaborative care for PTSD and depression (STEPS-UP, STepped Enhancement of PTSD Services Using Primary Care) versus a widely practiced and locally implemented primary care collaborative care model used in the U.S. Army health system (UCPC, Usual Collaborative Primary Care). This paper describes the design and methods employed in this trial, a six military installation (18 primary care clinic) randomized effectiveness trial comparing the impact of 12-months of clinical intervention (STEPS-UP versus UCPC). The randomized design will offer a valid assessment of benefit for new versus current health system practice. The effectiveness design, aimed to equip leaders and policy makers with evidence to guide decision-making, is expected to yield maximally generalizable findings, relevant cost-effectiveness information, and qualitative assessments of related clinician and beneficiary views of their care. In short, if STEPS-UP demonstrates superior clinical and cost effectiveness and is acceptable to patients and providers, it will be immediately ready for rapid scaling and implementation.

2. Study design

2.1. Interventions

Both intervention arms involve elements of collaborative care. Collaborative care is a service delivery package that accommodates empirically validated psychotherapies and evidence-based pharmacologic approaches. Collaborative care is not a type of psychotherapy per se. Three or four basic strategies are used to increase consistent delivery of effective, guideline-concordant care [29,30]. Oxman et al. [31] summarize these in a "Three Component Model": (1) prepared primary care practice using clinical tools for screening, diagnosing, and measurement-based symptom assessment; (2) care management to help clinical teams track treatment response, insure follow-up and continuity of care, and to help patients adhere to treatment and know their treatment options; and (3) enhanced mental health specialty care interface to insure optimal and efficient expert consultation wherein care managers meet weekly with a specialist to review their caseload and convey recommendations to the primary care team. Four additional aspects of collaborative care include (4) telephonic treatment and communications for efficiency and to reduce patient and provider burden; (5) real time registries for tracking indicators of patient treatment response; (6) stepped treatment sequencing strategies that maximize patient choice and match treatment intensity to illness severity and trajectory; and (7) centralized implementation to monitor performance across sites, reduce variation and enhance scalability [30,32–38].

Table 1 uses these 7 collaborative care elements for a comparative view of study treatment (STEPS-UP) and comparison (Usual Collaborative Primary Care, UCPC) interventions.

2.2. Comparison intervention: Usual Collaborative Primary Care (UCPC)

In 2007 Army primary care clinics began to implement a collaborative care approach called "RESPECT-Mil" (Re-Engineering Primary Care Treatment of PTSD and Depression in the Military) based on a sustainable version of the previously described Three Component Model [31,34]. Dietrich et al. found that the model significantly improved depression care quality, treatment response and depression remission [34]. In other studies the model showed sustainability, and high fidelity was associated with better treatment response [39]. RESPECT-Mil adapted the model to the military and successfully tested for military primary care feasibility [23]. Added to the original Three

Table 1
Intervention components—STEPS-UP versus Usual Collaborative Primary Care (UCPC).

Component	Steps-up	UCPC
1. Prepared practice		
Patient screening:	Depression (PHQ-2), PTSD (PC-PTSD), self-harm (PHQ-9i)	Depression (PHQ-2), PTSD (PC-PTSD), Self-Harm (PHQ-9i)
Diagnostic aids:	Depression (PHQ-9), PTSD (PCL-C)	Depression (PHQ-9), PTSD (PCL-C)
2. Nurse care management		
Nurse visit schedule	Within 2 weeks of referral and minimum every 4 weeks after	Within 2 weeks of referral and minimum every 4 weeks after
Patient screening:	Alcohol Misuse (AUDIT-C), mania (MDQ)	None
Symptom severity tracking:	Depression (PHQ-9), PTSD (PCL-C), suicide risk assessment	Depression (PHQ-9), PTSD (PCL-C), suicide risk assessment
Continuity monitoring:	Primary care, specialty care, military care (including deployments and field exercises), and civilian care (TRICARE, VA, other)	Restricted to military primary care practice
Nurse skills training:	Motivational interviewing, behavioral activation, problem solving, and web-based decision support training	Web-based decision support training
3. Specialty interface	Site-level and central enhancements	Site-level enhancements only
Clinic-based specialist:	Present and fully model integrated	No model integration if present
Case-level reviews:	Central and site specialists (weekly)	Site specialist only (weekly)
4. Stepped care	Psychopharmacologic and Psychotherapeutic Options	Pharmacologic Options only
Self-management:	Web-based PTSD and depression self-management options	None
Phone therapies:	Phone CBT for PTSD and depression	None
Face-to-face therapies:	Phone CBT for PTSD and depression	None
5. Telephone use	Phone CBT, local and central phone care management, phone-based training and team meetings	Local phone care management
6. Registries	Reports covering patient-level treatment response and aggregate caseload analysis	Individual patient tracking only
7. Implementation	Centrally managed	Site managed
Clinical implementation:	Central phone therapists, central case management, centrally run case and caseload reviews, and centrally moderated peer-supported learning	Case-based review
Continuing education:	Centrally moderated and led	Site dependent

Component Model were routine primary care screening for PTSD and depression, primary care diagnostic assessments for those screening positive (PTSD Checklist, or PCL-C, for PTSD; 9 item Patient Health Questionnaire, or PHQ-9, for depression), and care management for PTSD.

When the STEPS-UP trial started, all 18 participating primary care clinics (6 Continental U.S. installations) and 88 total Army primary care clinics (37 worldwide installations) practiced RESPECT-Mil, hereafter referenced as UCPC. Each installation had a "primary care champion" overseeing that installation's program and a "behavioral health champion", usually a psychiatrist, that meet with all installation care managers once weekly to review their caseload and provide feedback to primary care with care manager assistance. Patients in UCPC were assigned an onsite care manager. Care managers were instructed to contact patients within two weeks of program referral and then every four weeks thereafter. They were to assess PTSD and depression severity and monitor adherence to primary care provider (PCP) prescribed psychoactive medications at each care manager contact. Patients followed in mental health specialty care were discharged from the program. The only controlled trial of this model was a negative VA study [22].

2.3. Test Intervention: STEPS-UP Collaborative Care

STEPS-UP was designed as second-generation collaborative primary care for PTSD and depression in the military. The goal is to reduce PTSD and depression through reliable implementation of evidence-based psychotherapy and pharmacotherapy practices. Central implementation ensures that the package is delivered feasibly and with fidelity across sites and settings (military, civilian, primary care, and specialty mental health) and facilitates scalability during changing military and population needs.

STEPS-UP builds on existing UCPC infrastructure by: (1) enhancing care management, (2) adding stepped psychotherapeutic options, (3) using clinical registries to guide treatment; and (4) centralizing implementation coordination (see Table 1).

2.3.1. Care management enhancements

Care managers received added patient engagement training (behavioral activation, problem solving, and motivational interviewing). These skills helped care managers to provide patient support, to keep patients active and engaged in their care, and to help patients examine treatment options and develop preferences. Care managers reviewed treatment options using one-page guides with patients, helping them consider medications, psychotherapies, or both.

Care management was expanded beyond primary care to other service delivery sectors and contexts (e.g., mental health clinics, TRICARE, VA, other civilian medical care, deployments, field exercises, change of station, departing military service). Remote care management was available by phone for patients following location changes or as a substitute for local care managers when unavailable.

2.3.2. Stepped psychotherapies

To enhance patient access to psychotherapies beyond basic support from the care manager, patients were afforded stepped psychotherapy options. These included web-based cognitive behavioral self-management [40,41], psychologist-delivered telephone CBT [42], and face-to-face specialist delivered psychotherapy. Care managers discussed with patients their preferences for web, phone, or face-to-face therapy repeatedly over time. Central STEPS-UP team psychologists delivered phone CBT using a flexible, modularized protocol.

2.3.3. Clinical registries

A web-based decision support tool was used to track patients' PTSD and depression symptom severity, to drive treatment changes, to create registries for STEPS-UP team review, and to populate site-level performance tracking reports. Care managers enter data online during phone conversations with patients. The online platform guides the care manager through visits and insures appropriate questions are covered. Data entered include depression (PHQ-9) [43] and PTSD (PCL-C) [44–46] symptom severity, symptom-related difficulty, medication and psychotherapy adherence, suicide risk, behavioral activation strategies and goals, alcohol use (AUDIT-C) [47] and bipolar disorder (MDQ) [48] screening, and military transitions.

2.3.4. Centrally coordinated implementation

Psychiatric consultation and review were centralized in STEPS-UP. STEPS-UP at each site was coordinated and overseen by a central mental health team comprised of a psychiatrist, psychologist, care manager and administrative support. Care manager specific registries were centrally disseminated, and flags were generated for patients with (1) symptoms that had not shown improvement (less than 5 point improvement in the 8 weeks since the last treatment change or 50% overall improvement on PCL-C and PHQ-9); (2) recent missed care manager follow-up contacts; and (3) impending health care or military transitions (e.g., specialty care referral, deployment).

The central team and care managers met weekly for two types of phone conferences. One involved individual care managers to review patient specific data. Management recommendations were developed for patients' primary care providers and care manager engagement strategies reformulated for patients transitioning or at risk of dropping out of care. New and acute patients were reviewed first, followed by unimproved patients, and then patients in transition. The central STEPS-UP psychiatrist insured patients on medication received therapeutic doses and treatment duration or changed treatment if unimproved after six to eight weeks or if side effects occurred. Remaining time was used to discuss patients in web or phone therapy or to discuss site-level service system problems. Care managers conveyed STEPS-UP team recommendations to primary care providers and STEPS-UP team members charted notes for the electronic health record.

The central team and care managers weekly for a second phone conference. In this meeting, site performance metrics were reviewed, discussed and lessons learned; didactic training was delivered; and peer-support and lessons were shared among care managers to improve their care management skills. When system-level problems emerged at a site, the central team would consult with relevant site leaders seeking resolution.

2.4. Participants

Participants were active duty military members attending one of the 18 participating primary care clinics who were referred by their primary care provider for care management within UCPC. All primary care visits routinely involved initial depression and PTSD screening (PHQ-2, PC-PTSD). PHQ-2 and PC-PTSD items were dichotomous (yes/no) questions. Either or both PHQ-2 items endorsed 'yes' is a positive depression screen. Two or more of the four PC-PTSD items endorsed 'yes' is a positive PTSD screen. Patients with positive screens routinely then receive the PCL-C and PHQ-9 to as "diagnostic aids", tools that the providers use to guide assessment, diagnosis, and treatment planning. Involving the care manager is a clinical decision left to the discretion of the provider and patient. Patients referred to care management were contacted within a week by a UCPC care manager. After insuring the patient (1) had private access to computer and Internet and (2) anticipated residing nearby for at least six months, the UCPC care manager would ask if the patient would like to be contacted regarding "research studies related to ongoing efforts to improve the quality" of UCPC. If the patient assented to contact, a STEPS-UP trial research site coordinator would contact them for a second level screen, research informed consent, and eligibility assessment. Any patient declining to participate in or excluded from the trial was continued in UCPC with their previously assigned care manager.

2.5. Inclusion and exclusion criteria

For inclusion participants (1) were on active duty at enrollment; (2) met DSM-IV-TR criteria for PTSD using the PCL-C or depression using the PHQ-9 (explained below); (3) reported computer, Internet, and e-mail access; and (4) provided informed consent to participation. At first deployment since 2001 was required for inclusion but was dropped after the first month. The rationale for dropping this inclusion criterion was that participants with PTSD and depression could benefit from collaborative care whether or not symptoms followed deployment. Furthermore, assuming effectiveness, benefits summed over a larger proportion of patients would yield more favorable cost–benefit calculation given the system-level intervention.

Military members meeting inclusion criteria were excluded if they had (1) recently participated in UCPC; (2) active alcohol dependence; (3) active, unstable suicidal ideation or an attempt within the prior month; or (4) anticipated deployment, demobilization, change of station, or separation from military service within six months. Initially, those undergoing medical retirement proceedings ("medical board") were excluded. The exclusion was dropped in the first month of recruitment because it was frequent and inclusiveness was important for sample generalizability. Instead the plan is to eventually assess this as a potential modifier of intervention effect.

2.6. Eligibility screening and informed consent

A web-based research reporting system was used to administer research assessments and establish trial eligibility. Following informed consent, simple eligibility items and demographics, the following instruments establish study suitability:

(1) the PTSD Checklist-Civilian Version (PCL-C) where PTSD was operationalized as a "moderate" or greater severity level on 1 re-experiencing, 3 avoidance, and 2 hyperarousal symptoms, consistent with the DSM-IV-TR criteria (Civilian Version of the PCL was used rather than the Military Version because the latter is used in UCPC and because enrollment for PTSD due to any trauma (not solely military trauma) was the focus [44–46]; (2) the Patient Health Questionnaire-9 (PHQ-9) where depression was operationalized as endorsement of at least 5 of the 9 symptoms experienced "more than half the days" and at least one of those symptoms including either "little interest or pleasure in doing things" or "feeling down, depressed or hopeless, consistent with DSM-IR-TR criteria [43]; (3) the Mini International Neuropsychiatric Interview (MINI)-Plus—Suicidality Module (C1–C6) where individuals scoring greater than 9, regarding suicidal ideation during the past 2 months, were excluded from the participation (details below) [49]; and (4) the Alcohol Use Disorders Identification Test (AUDIT) where individuals scoring ≥15 were excluded consistent with ICD-10 definitions of potential alcohol dependence symptoms [47]. Research site coordinators oversaw eligibility assessment in their offices. UCPC care managers were informed for ineligibles and acute care was obtained as indicated to those with active suicide risk or alcohol dependence. A study mental health specialist was on call at all times for psychiatric emergencies.

2.7. Randomization and research follow-up procedures

In most cases once the site coordinator informed participants that they were eligible, they continued directly into the questionnaire (some finished later or from home). On completing the baseline assessment, the automated system randomized participants (stratified by site) to STEPS-UP or UCPC. Participants were told that their care manager would contact them within a week and reminded of future study team contacts for the 3-, 6-, and 12-month research assessments. The latter were completed using direct computer entry over the Internet from a location of their choice, eliminating the need for blinded assessors.

Research follow-up assessment reminders began 30 days prior to the 3-, 6-, and 12-month mark and continued for 60 days past that mark. Thus, participants were in each follow-up window for a total of 90 days. Initial contact was made via automated emails generated from the project control system. The emails linked to the project website and encouraged participants to log on and complete the follow-up assessment. If there was no response to the original notification email, the following additional notification methods were used on a predetermined schedule: (1) reminder telephone calls by site coordinators, (2) reminder emails from the automated system, (3) contacts by a telephone interviewer, (4) reminder texts from site coordinators, and (5) mailing of a paper and pencil questionnaire.

2.8. Research and clinical intervention assessments

This trial compares two interventions, each featuring measurement-based care. It was anticipated that administration rates of clinical status assessments would differ across the interventions during the 12-month follow-up period. The differential impact of STEPS-UP versus UCPC was assessed with different research status assessments than the ones STEPS-UP and UCPC used to track patients' clinical status. This was done to reduce the possibility that learning effects due to differential rates of repeated clinical assessment administration across study arms would confound research trial results, In the clinical setting, the PCL-C and PHQ-9 were used to track symptoms over time, the same measures used to determine intervention eligibility (as described earlier).

The following measures were used to examine primary outcomes across the two arms of the trial:

Posttraumatic Diagnostic Scale (PDS). The PDS is a self-report measure that assesses both severity of PTSD symptoms related to a single identified traumatic event and probable diagnosis of PTSD [50]. In this study, the first section of the PDS was replaced with the other two trauma checklists (see Table 2). Respondents were asked to identify the trauma that currently bothering them the most and the frequency of 17 PTSD symptoms was assessed. The PDS shows high sensitivity (.89) and specificity (.75) as compared to the SCID-IV interview for PTSD, with a high degree of concordance in diagnosis (kappa = .65). It also shows high internal consistency (.92) and also high correlations with other related constructs and test-retest reliability over 2–3 weeks (.78–.84 for each symptom cluster) [51].

Depression Symptom Severity: Hopkins Symptom Checklist Depression Scale-20 Item Version (HSCL-20). The HSCL-20 is a self-report scale comprising the 13 items of the Hopkins Symptom Checklist Depression Scale plus 7 additional items from the Hopkins Symptom Checklist-90-Revised. The additional 7 items were added to better represent all diagnostic symptoms of major depression and improve the instrument's sensitivity to clinical change [52].

Several other secondary outcomes and descriptive variables were assessed as described in Table 2. In addition administrative data on service utilization were obtained for cost analysis and qualitative interviews performed to understand the process of care (see Sections 2.11 and 2.12 below).

2.9. Target and revised sample size

Given uncertainty regarding final data distributions, the a priori approach to sample size calculation was conservative. Specifically, the sample size required to compare 12-month changes in the outcomes was determined, ignoring the intervening time points and the correlation between repeated measurements on the same subjects. The treatment difference was defined to be $D = (\overline{X}_{22} - \overline{X}_{21}) - (\overline{X}_{12} - \overline{X}_{11})$ where $\overline{X}_{ij}$ is mean PDS or HSCL-20 score in treatment arm i at time j (j = 0, 12). If the sample size, N, and standard deviation, σ, are the same in both treatment arms at both time points, then the standard error of D is $2\sigma/\sqrt{N}$.

Dietrich et al. [34] and Dobscha et al. [61] obtained standard deviations of 0.65–0.80 for the HSCL-20 at the various time points in their prospective studies. This is the standard deviation for the average score on the 20 items on the HSCL-20; the corresponding standard deviations for the sum of the 20 scores

Table 2
List of research assessment constructs, the research measures used to assess them, and research measurement time points at which they were assessed.

Research construct	Research measure(s)	Time points
Demographics	Adapted versions of previously tested questions to assess basic demographics, military and deployment history, branch of service, and beneficiary status	BL[a] only
Military traumatic stressors	Deployment Risk and Resilience Inventory [53]—Unit Support and Post-Deployment Life Events scales	BL only
PTSD criterion a trauma exposures	DoD Survey of Health Related Behaviors Among Active Duty Military Personnel Survey—Combat Exposure Scale [54] National Comorbidity Survey—Revised—PTSD Traumatic Events Scale [55]	BL only
Social support	Medical Outcomes Study Social Support Survey Items [56]	BL only
Traumatic brain injury (TBI)	TBI items from Land Combat Study [2]	BL only
Primary outcome		
PTSD symptom severity	Posttraumatic Diagnostic Scale (PDS) [50]	BL, 3-, 6-, and 12 months
Depressive symptoms	HSCL-20 [52]	BL, 3-, 6-, and 12 months
Secondary outcomes		
Somatic symptoms	PHQ-15 [57]	BL, 3-, 6-, and 12 months
Alcohol abuse	AUDIT-C [47] — Bush K, Kivlahan D, McDonell M, Fihn S, Bradley K. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Archives Of Internal Medicine [serial online]. September 14, 1998;158(16):1789-1795.	BL, 3-, 6-, and 12 months
Health-related functioning	SF-12 [58]	BL, 3-, 6-, and 12 months
Work presenteeism and absenteeism	WHO Health & Work Performance Questionnaire (HPQ) Short Form [59]	BL, 3-, 6-, and 12 months
Pain	Adapted Numeric Rating Scale for Pain [60]	BL, 3-, 6-, and 12 months
Health service use	Adapted versions of previously used questionnaires to assess formal and informal health service use frequency and type	BL, 3-, 6-, and 12 months

[a] BL = baseline.

were 13–16. Assuming that the item variances and covariances for the HSCL-20 and PDS are similar, 13–16 is the upper limit for the standard deviation on the PDS; i.e., the sum of 17 items should be less variable than the sum of 20 similar items.

With 2 endpoints of equal interest, a Type I error rate of 0.025 was assumed for the sample size calculations. Using this information, a target sample size of 600 subjects per arm was proposed, inflating this to 750 per arm on the assumption that 20% of subjects would fail to provide follow-up data. If $\sigma = 16$, then the study will have power = 0.80 to detect a difference of D = 5.7 between average 12-month changes in PDS scores in the two treatment arms. At $\sigma = 0.8$, power = 0.80 is anticipated to detect a difference of D = 0.29 on the HSCL-20.

As the study progressed baseline and follow-up data were obtained, allowing a re-examination of the assumptions underlying these early sample size calculations. Interim analysis indicated that the standard deviations at all time points were substantially less than those used in the original calculations. It was also found that the correlation between repeated measurements was approximately 0.5. Therefore, the sample size required to have power = 0.80 to detect the treatment differences above was determined to be substantially less than the originally planned total of 600 subjects with complete data. A sample size of 200 subjects per arm with complete data would provide power of approximately 0.90 to detect the treatment effects described above. The reduction in the sample size from the initial target was due to our ability to use less conservative assumptions about the within-group standard deviations and correlations.

2.10. Analysis plan

Two approaches to data analysis are under consideration. If a parametric model can be identified that accurately describes the relationship between outcome score and time on study, then this model will be used to evaluate the treatment effect. If such a model cannot be identified, then repeated measures analysis will be employed. Under the repeated measures approach, time is treated as an ordinal categorical variable. Under both approaches, the treatment effect is evaluated by adding an indicator for treatment group and the interaction between treatment group and time to the model. The interaction provides a test for a difference between rates of change in outcome score in the two treatment arms. If the interaction is not statistically significant, then it will be dropped from the model. The indicator for treatment effect will then provide a test for differences in outcome score, averaged over time points, between treatment arms. Because statistical power to detect interactions is more limited than power to detect main effects, this step may identify a treatment effect that is missed in the first part of the analysis. Because the two outcomes, PDS and HSCL-20, are of equal interest, a critical p-value of 0.025 will be used to evaluate the treatment effect for each one.

The effects of baseline characteristics on treatment responses will be evaluated by adding these characteristics to the model in secondary analyses. The three-way interaction among time, treatment arm and a baseline trait provides a test for variation in the treatment effect among levels of the baseline characteristic.

2.11. Cost analyses

In addition to assessing the impact of the program on patient outcomes, this study includes cost-effectiveness analysis (CEA) completed from health system perspective. CEA is a method that compares the economic desirability of alternative health interventions by calculating the marginal cost of a unit of improved health [62,63]. Our measure of cost-effectiveness will be the incremental cost-effectiveness ratio (ICER), defined as the difference in the per capita cost of the treatment and comparison groups divided by the difference in the average effectiveness of the interventions. Measurement of costs will account for all treatment costs (e.g. medications, nurse and physician salaries, building rents and maintenance, equipment costs) as well as personal costs that accrue to intervention participants. At each wave of follow-up research assessment, automated and self-report data on health care use will be used to understand the process of care, including number and type of medical and mental health services, telephone care, and use of Internet resources. Analyzing these data will allow a test of whether patients randomized to STEPS-UP care will have significantly lower direct and indirect care costs and more favorable cost-effectiveness ratio compared to participants randomized to UCPC.

2.12. Qualitative analyses

To assess patient, clinician, and care manager perceptions of collaborative care interventions, qualitative interviews were conducted and analyzed.

To assess acceptability, satisfaction, and effectiveness of interventions from the patient perspective, patients were randomly selected from the enrolled sample so as to include 6 from each site—3 from STEPS-UP and 3 from UCPC. They were selected early, mid-way, and late into the enrollment period at each site to account for any maturation of the interventions within site over time. To understand experience with services over time, interviews were attempted 3 times per patient, once after enrollment, 3-months later and 6-months later. Specifically, patients were interviewed about their satisfaction with their health care, the various services offered to them and used, adherence to services, any barriers or challenges to receiving care, and their recommendations for how to improve the system.

To understand the perceived effectiveness of the interventions from the provider perspective, interviews were conducted mid-way through the trial with 5–7 randomly selected primary care providers from each site. Interviews included their views on managing PTSD and depression in primary care, their training regarding these conditions, challenges within their system, and their direct experience with the two interventions, including facilitators and barriers hours spent on each program, and their perceptions of patient views of the interventions.

Finally, each site-located and centralized care manager was interviewed twice—once early in implementation and a second time towards the end of the study. Interviews focused on their perceptions of the various elements of the STEPS-UP intervention (engaging patients, coordination of care, use of telephone therapy and on-line intervention tools), comfort level with the role, and challenges in their roles. As part of the second interview, chart-assisted review of 5 randomly chosen patients the care manager had followed during the trial was discussed. The focus was on how the intervention went for these specific patients.

3. Results (sample characteristics)

Fig. 1 displays the number and flow of potential study participants into the study. Specific reasons for ineligibility or not entering the study are noted. Recruitment was conducted at six large military installations located nationwide. At the end of the enrollment period (August 31, 2013), UCPC care managers reported receiving 2592 collaborative care referrals. Of those, 1320 (51%) gave permission for research team contact, had Internet access, and anticipated remaining in the area for at least six months. After research team contact for informed consent and first level inclusion screen, 1041 of potential participants remained (40% collaborative care referrals across the six sites). Of the 60% of UCPC referrals (1551) excluded before the eligibility assessment, 922 (59%) declined research participation and 355 (23%) anticipated moving from the area in six months or less, the latter figure highlighting the mobility of the active duty population and a major challenge to providing them with sound health services.

Of the 1041 consenting participants, 666 (64%) met eligibility criteria and were enrolled and randomized, 332 to STEPS-UP and 334 to UCPC. Among the 375 (36%) that were excluded, the large majority (236, 63%) did not meet the trial's inclusive clinical definition for either PTSD or depression. Another large portion (107, 29%) were essentially too severe, meeting criteria for active suicidal ideation or alcohol dependence. Compared to those randomized, those excluded were similar with regard to gender (18% female versus 19%; $p = 0.78$), younger in age (30% less than 25 versus 22%; $p = 0.03$), lower in rank (56% junior enlisted versus 46%; $p = 0.002$), and less likely to have deployed (73% versus 83%; $p = 0.005$). Clinically, compared to those randomized, those excluded were less likely to meet study diagnostic criteria for PTSD (40% versus 90%; $p < 0.0001$), depression (23% versus 65%; $p < 0.0001$), or both (29% versus 59%; $p < 0.0001$) and reported higher mean AUDIT-C scores (3.5 ± 2.9 versus 2.9 ± 2.4; $p = 0.02$).

Table 3 presents basic information about the sociodemographic and military characteristics of the study participants along with data for selected screening and baseline assessment measures for the overall sample and for those randomized to STEPS-UP and UCPC. As shown and expected, the sociodemographic and military characteristics of the participants were highly similar in the two study arms.

Of the 666 enrolled in the study, 629 (94%) screened positive on the PC-PTSD scale. Those 629 were then asked the PCL-C items and 90% of them ($n = 566$) met criteria for PTSD (1 or more items were met for Criterion A, 3 or more for Criterion B, and 2 or more for Criterion C). For the PHQ-9, 432 (65%) participants met criteria for depression. Of the 629 participants who answered both the PCL-C and the PHQ-9, 370 (59%) met criteria for both PTSD and depression. Participants in the STEPS-UP arm of the study were somewhat more likely to meet criteria for PTSD and depression on the PCL-C and PHQ-9 than those in UCPC, though differences were not statistically significant.

Table 3 also shows average scores from the baseline assessment for three outcome measures: (a) PTSD measured by the PDS scale, (b) depression measured by the Hopkins

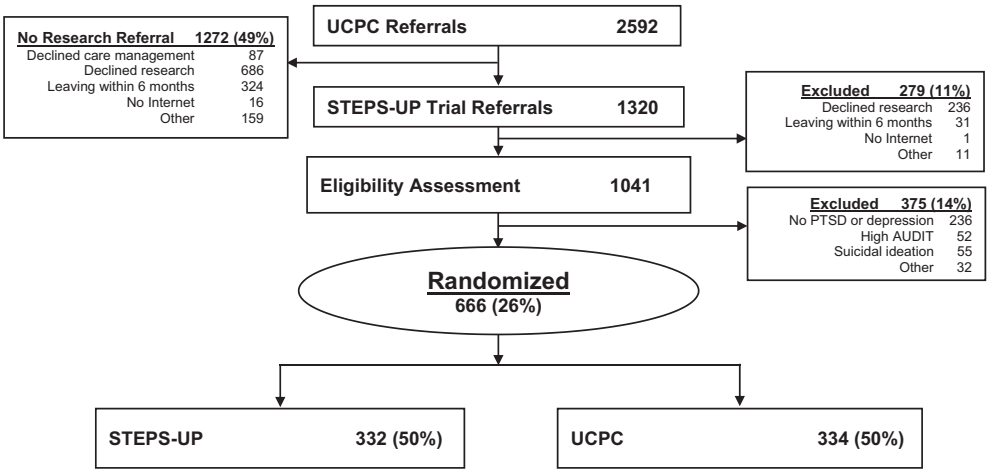

Fig. 1. CONSORT flow diagram for STEPS-UP Trial through the baseline assessment.

Symptom Checklist (HSCL-20), and (c) severity of somatic symptoms measured by the PHQ-15 [50,52,57]. For the PDS, the mean score of 29.2 indicated that on average participants had moderate to severe levels of PTSD. For the Hopkins Symptom Checklist (HSCL-20), average baseline scores were 2.1 out of a possible 4.0 suggesting that participants had

Table 3
Characteristics, screening, and assessment measures of STEPS-UP participants.*

Characteristic		Total $N = 666$ n (%) or mean (SD)	STEPS-UP $N = 332$ n (%) or mean (SD)	UCPC $N = 334$ n (%) or mean (SD)	P
Gender	Female	127 (19%)	68 (20%)	59 (18%)	0.35
Age	18–24	138 (22%)	73 (24%)	65 (21%)	0.74
	25–34	272 (44%)	135 (44%)	137 (45%)	
	≥35	205 (33%)	100 (32%)	105 (34%)	
Rank	E1–E4	306 (46%)	151 (46%)	155 (47%)	0.091
	E5–E6	274 (41%)	146 (44%)	128 (39%)	
	E7–O5	81 (12%)	32 (10%)	49 (15%)	
Installation	A	126 (19%)	63 (19%)	63 (19%)	>0.99
	B	26 (4%)	13 (4%)	13 (4%)	
	C	200 (30%)	100 (30%)	100 (30%)	
	D	18 (3%)	9 (3%)	9 (3%)	
	E	250 (38%)	124 (37%)	126 (38%)	
	F	46 (7%)	23 (7%)	23 (7%)	
Marital status	Married	446 (67%)	222 (67%)	224 (67%)	>0.99
Education	High school	203 (30%)	99 (30%)	104 (31%)	0.51
	Some college	325 (49%)	169 (51%)	156 (47%)	
	College degree	138 (21%)	64 (19%)	74 (22%)	
Race/ethnicity	White	318 (48%)	158 (48%)	160 (48%)	0.97
	Black	160 (24%)	82 (25%)	78 (23%)	
	Hispanic	117 (18%)	57 (17%)	60 (18%)	
	Other	70 (11%)	34 (10%)	36 (11%)	
Clinical indicators					
PC-PTSD	≥2	629 (94%)	310 (93%)	319 (96%)	0.23
PCL-C	DSM-IV	566 (90%)	285 (86%)	281 (84%)	0.54
PHQ-9	DSM-IV	432 (65%)	224 (67%)	208 (62%)	0.16
PTSD and depression	+PCL-C and PHQ-9	370 (59%)	193 (62%)	177 (55%)	0.18
AUDIT-C	score	2.8 (2.4)	3.0 (2.5)	2.7 (2.3)	0.15
Deployments after 2001	0	114 (17%)	59 (18%)	55 (16%)	0.89
	1	209 (31%)	102 (31%)	107 (32%)	
	2	159 (24%)	82 (25%)	77 (23%)	
	≥3	184 (28%)	89 (27%)	95 (28%)	
Research assessments					
PDS	Range, 0–51	29.2 (9.2)	29.4 (9.4)	28.9 (8.9)	0.55
HSCL-20 (range, 0–4)	Range, 0–4	2.1 (0.6)	2.1 (0.6)	2.0 (0.7)	0.0094
PHQ-15 (range, 0–30)	Range, 0–30	13.7 (4.8)	14.1 (4.7)	13.4 (4.8)	0.086
High combat exposure	CES score ≥ 10	452 (68%)	224 (67%)	228 (68%)	0.83

* Table includes completed data only. Missing items were rare, but result here in missing observations. Missing data imputation and intent-to treat analyses are planned for longitudinal data analyses.

moderate levels of depression. For the PHQ-15, the average score of 13.7 indicates medium somatic symptom severity.

4. Discussion

The STEPS-UP Trial is the first randomized effectiveness trial of mental health services conducted in the US Military Health System and represents a potentially important shift in the way new clinical programs are developed, tested and implemented for its 9 million beneficiaries to include military members, retirees, and their families. The design and baseline sample from this 6 installation randomized effectiveness trial was described, comparing the impact of collaborative care implementation on PTSD and depression outcomes across 18 military health system clinics.

A total of 666 participants were assigned to one of two arms and followed for 12 months. The comparison group received "usual collaborative primary care" as it has been widely practiced in US Army clinics since 2007, collaborative care in which implementation is managed largely at the installation level. STEPS-UP intervention participants received collaborative care using a centrally managed implementation process. STEPS-UP included central oversight of care managers trained in patient engagement techniques, availability of remote care managers for service members in transition, and stepped provision of both psychotherapeutic (web-based CBT self-management, telephone CBT from a central psychologist, and site-based face-to-face options) and pharmacologic treatment options. Of note, the most common reason for exclusion besides declining to participate in research was the expectation of relocating from the site within six months. The geographic mobility of military members with mental health needs underlines the important need to implement military health system strategies that enhance patient engagement and deliver safe and services to remote and highly mobile patients.

The STEPS-UP Trial may eventually serve as a model for future scientific assessments of system change on clinical outcomes in military and veteran service systems. Key by-products of the trial for posterity will be program manuals (primary care, mental health specialist, care manager, phone therapy, and central program monitoring and operations), a web-based clinical decision support tool, patient education tools, and other tools that will enhance the scalability of the intervention. If the STEPS-UP intervention proves effective, these tools may play an instrumental future role, given the virtual certainty that large numbers of the U.S. military will once again step into harm's way.

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Appendix B: Main Outcomes Manuscript (Under Review)

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Centrally assisted collaborative telecare for posttraumatic stress disorder and depression among military personnel attending primary care: A randomized controlled trial

Charles C. Engel, MD*[a,b], Lisa H. Jaycox, PhD[a], Michael C. Freed, PhD[b,c], Robert M. Bray, PhD[d], Donald Brambilla, PhD[d], Douglas Zatzick, MD[e], Brett Litz, PhD[f], Terri Tanielian, MA[a], Laura A. Novak, BS[c], Marian E. Lane, PhD[d], Bradley E. Belsher, PhD[c], Kristine L. Rae Olmsted, MSPH[d], Daniel P. Evatt, PhD[c], Russ Vandermaas-Peeler, MS[d], Jürgen Unützer, MD[e], Wayne J. Katon, MD[e]

[a.] RAND Corporation, 1200 South Hayes Street, Arlington, VA 22202, USA

[b.] Department of Psychiatry, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814, USA

[c.] Deployment Health Clinical Center, 1335 East West Highway, Silver Spring, MD 20910, USA

[d.] RTI International, 3040 East Cornwallis Road, Post Office Box 12194, Research Triangle Park, NC 27709-2194, USA

[e.] Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, 2815 Eastlake Avenue East #200, Seattle, WA 98102, USA

[f.] VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130, USA

* Corresponding author: RAND Corporation, 1200 South Hayes Street, Arlington, VA 22202; Tel.: +1 703 413 1100 x5466; Email address: cengel@rand.org (C. Engel).

Disclosures:

Dr. Engel, Dr. Jaycox, Dr. Freed, Dr. Bray, Dr. Brambilla, Dr. Zatzick, Dr. Litz, Ms. Tanielian, Ms. Novak, Dr. Lane, Dr. Belsher, Ms. Rae Olmsted, Dr. Evatt, Mr. Vandermaas-Peeler, Dr. Unützer, and Dr. Katon report no competing interests.

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Key words: PTSD, depression, primary care, telemedicine, collaborative care, military, clinical trial

The full trial protocol is available from the authors upon request.

Abstract.

Objective: To determine the effectiveness of centrally assisted collaborative telecare (CACT) for PTSD and depression in military personnel attending primary care.

Methods: STEPS-UP (STepped Enhancement of PTSD Services Using Primary care) is a randomized trial comparing CACT to usual integrated mental health care for PTSD or depression. Patients were enrolled from 18 primary care clinics at six US sites from February 2012 to August 2013 with follow-up at three, six, and 12-months. Patients were randomly assigned (computer automated, within site) to CACT (n = 332) or usual care (n = 334). CACT patients received 12 months of stepped psychosocial and pharmacologic treatment with nurse telecare management of caseloads, symptoms, and treatment. Primary outcomes were severity scores on the PTSD Diagnostic Scale (PDS; scored 0-51) and Symptom Checklist depression items (SCL-20; scored 0-4).

Results: CACT and usual care patients had similar baseline PDS PTSD (29.4±9.4 vs. 28.9 ±8.9) and SCL-20 depression scores (2.1±0.6 vs. 2.0±0.7). CACT patients reported a greater 12-month decrease in PDS PTSD (-2.53; 95% CI=0.59-4.47) and in SCL-20 depression scores (-0.26; 95% CI=0.11-0.41). There were no study-related serious adverse events (emergency visits, hospitalizations or deaths) in either treatment group.

Conclusions: Central assistance for collaborative telecare including stepped psychosocial and pharmacologic management improves outcomes of PTSD and depression among military personnel and may offer an effective model of care for other PTSD populations.

Clinical Trials Registration Name: “Stepped Enhancement of PTSD Services Using Primary Care (STEPS UP): A Randomized Effectiveness Trial”

Number: NCT01492348

URL: https://clinicaltrials.gov/ct2/show/NCT01492348

Introduction

A recent Institute of Medicine report emphasized an urgent need for the U.S. Departments of Defense (DoD) and Veterans Affairs (VA) to expand their capacity for integrated, coordinated, and evidence-based PTSD care (1). The prevalence of post-deployment PTSD and depression in the U.S. military is estimated at 13%–18%, and 28% report severe symptoms of PTSD, anxiety, or depression (2, 3). These problems cause suffering and impairment and contribute to military attrition, absenteeism, misconduct, and sick call visits (4-6). Fewer than half of affected serving military personnel receive military mental health services and many accessing services do not receive adequate care (2, 3, 5). While there is variation across Western nations in the magnitude of these problems (7) and in the ways that care is provided, mental health services for military personnel are an international priority.

Collaborative care is an increasingly evidence-based method of extending the reach, quality and outcomes of care for common mental disorders in medical settings (8, 9). Randomized trials of collaborative care have demonstrated improved outcomes among patients with depression and anxiety (9-11), depression related suicidal ideation (12, 13), depression and chronic health conditions (e.g., diabetes, asthma, 14), and chronic pain (15, 16). For PTSD specifically, however, there have been only two randomized trials of collaborative care, one demonstrating improvements in PTSD (17) while the other did not (18). Thus, there is a need for additional work in the development and study of collaborative care models for PTSD.

Recent U.S. military efforts to address mental health services have sought to better integrate them into primary care, with the first U.S. Army integration approach beginning in 2007 (19, 20). Despite the implications for current and future wartime health care, no controlled trials investigating these integration efforts have been completed. In the meantime, access to and quality of mental health services for military personnel has been a recurring public policy concern (1, 21). We now report the results of a large multisite randomized trial of centrally assisted collaborative telecare (CACT) for PTSD and depression among military personnel

attending primary care. The STEPS-UP trial (STepped Enhancement of PTSD Services Using Primary Care) compares CACT to the U.S. Army's preexisting program that integrates behavioral health into primary care.

Methods

Design

The study design is published elsewhere in detail (22). The study was reviewed and approved by institutional research review boards at Walter Reed National Military Medical Center (primary), six participating Army installations (i.e., military base/post, each of which may hosted multiple participating clinics), RTI International, RAND Corporation, University of Washington, and Boston VA, and the Human Research Protection Office, U.S. Army Medical Research Command. All participants provided written informed consent.

Briefly, a two parallel arm randomized design was used to evaluate the effectiveness of a 12-month primary care treatment program for military personnel with PTSD and/or depression. An effectiveness design was chosen to enhance the external validity of the findings (22). The primary hypothesis was that CACT delivered with stepped psychosocial and pharmacologic management would be superior to usual integrated mental health care (defined immediately below) for improving PTSD and depression in primary care.

Intervention

Usual Care**.** In 2007 Army primary care clinics began using an integrated mental health approach called RESPECT-Mil (20, 23) based on a "three component model" (24, 25). This program constituted usual care for trial participants. In this model, efforts to improve primary care for PTSD and depression (1) equip and train clinics to screen each visit and use symptom severity tools for diagnosis and assessment; (2) use nurse care managers to contact patients monthly and provide symptom status to primary care clinicians; and (3) increase access to a non-primary care clinic based mental health specialist. All 18 participating primary care clinics at

six Army installations (and 97 worldwide clinics at 39 Army installations) practiced this model. A detailed comparison of usual care and CACT components is published elsewhere (22).

Centrally Assisted Collaborative Telecare (CACT). PTSD treatment, relative to the treatment of major depression, panic disorder or generalized anxiety disorder alone, is complex: (1) pharmacotherapies are useful for PTSD comorbidities but relatively ineffective for PTSD per se and (2) involves greater emphasis on the delivery of psychosocial interventions, particularly those involving trauma and non-trauma focused cognitive behavioral therapies (CBT). CACT was therefore developed to better assist busy primary care settings with the delivery of CBT-related and other psychosocial support strategies. CACT added to usual care in four ways: (1) care management enhancements; (2) stepped psychosocial treatment options (web, phone, in person); (3) electronic symptom registry for measurement-based treatment planning (symptoms are measured at regular intervals and care is intensified for patients with recurrent or persistent PTSD and/or depression) and for telecare manager caseload and site performance monitoring; and (4) routine assisted review of patient, telecare manager, and site performance by a central psychiatrist and psychologist.

Care Management Enhancements: Care managers were nurses trained in behavioral activation, problem solving, and motivational interviewing to enhance patient engagement, to assist treatment planning, and to offer patients basic psychosocial support. Care managers contacted patients by phone and encouraged patients to adhere to treatment and remain in care.

Stepped Psychosocial Treatment Options: In addition to supportive assistance from the care manager, CACT participants had access to online cognitive behavioral self-management (26, 27), telephonic cognitive behavioral therapy using a modularized, flexible protocol offered with a central team psychologist (28), and face-to-face psychotherapy with a specialist in either a primary care site or specialty care clinic. Stepped pharmacologic treatments were available in CACT and usual care.

Electronic Symptom Registry: An electronic symptom registry tracked PTSD and depression symptoms, identified patients in need of central specialist review (less than 5 point change in the previous 8 weeks on clinical severity indicators [PCL for PTSD, PHQ-9 for depression] or PCL >30 or PHQ-9 >10) to recommend treatment change, and provided aggregate site- and program-level data for performance monitoring (29, 30). The electronic symptom registry helps guide care managers through each patient contact and insures appropriate questions are asked and areas assessed. Clinical data entered during telecare contacts included depression (PHQ-9) (31) and PTSD severity (PTSD Checklist, Civilian Version; PCL-C) (32).

Central Assistance and Review: Central specialist consultation, caseload review, and patient review were performed in CACT. The central team included a psychiatrist, psychologist, and nurse care manager. The team assisted care by (1) monitoring patient data and using the electronic record to recommend when primary care providers should increase patients' treatment intensity (psychosocial or pharmacologic); (2) reviewing care manager caseloads and discussing their patients; and (3) identifying, assessing and addressing emerging installation barriers to specialty care.

Participants and Data Collection

Six hundred sixty-six patients were randomized from February 2012 through September 2013 at 18 troop medical clinics located at six large Army installations in the continental U.S. Interested service members were referred by their primary care clinician to nurse care managers and then contacted by a study research assistant to assess eligibility and obtain informed consent. Eligible patients (a) were serving on active duty at enrollment; (b) met DSM-IV-TR criteria for probable PTSD on the PTSD Checklist-Civilian Version (PCL-C) or probable depression on the Patient Health Questionnaire-9, or both; and (c) reported having Internet and e-mail access. Study assessments were web-based with participant entry (in a few cases by phone interviewers or paper and pencil questionnaire).

Potential participants were excluded for (a) recent participation in usual care management; (b) current alcohol dependence (Alcohol Use Disorders Identification Test, AUDIT≥15) (33); (c) active suicidal ideation in the prior two months (Mini International Neuropsychiatric Interview (MINI)-Plus Suicidality Module score >9) (34); (d) expected permanent geographic relocation over the next six months (e.g., change of station, deployment, demobilization, separation); or (e) current duties in a participating clinic.

Randomization

After completing the baseline assessment, participants were randomized to CACT or usual care. This was accomplished centrally in real time using a computer-automated system with results delivered direct to patients and care managers. Randomization was stratified by clinic and automated emails were used to initiate follow-up research assessments. In the absence of response to initial emails, additional methods were used on a predetermined schedule: (a) reminder telephone calls, (b) reminder emails, (c) telephone interviewer contacts, (d) reminder texts, and (e) paper questionnaire mailing. Patients provided research assessments using a direct entry computer interface at baseline, three, six, and 12 months.

Outcomes

Primary. Primary outcomes were the Posttraumatic Diagnostic Scale (PDS) (35, 36) for PTSD symptoms and the Symptom Checklist Depression Scale (SCL-20) for depressive symptoms (37). PDS (17 items) assesses severity of PTSD symptoms over the prior four weeks with high internal consistency and test-retest reliability (36); scores are summed and range from 0 to 51; scores $\leq$ 10 are considered mild, $\geq$11 and $\leq$ 20 moderate, $\geq$21 and $\leq$ 35 moderate to severe, and $\geq$36 severe. SCL-20 is comprised of 13 Hopkins Symptom Checklist Depression Scale items plus seven additional depression items from the Symptom Checklist-90-Revised. The latter items better covered all diagnostic symptoms of depression

and improve sensitivity to clinical change. Scores are a mean of item scores and range from 0 to 3 (37).

Secondary. Secondary outcomes were suicidality, somatic symptoms, pain intensity and interference, alcohol misuse, and physical and mental health related quality of life. Suicidality was assessed with three items from the SCL-20 (37) that measured hopelessness, thoughts about death, and thoughts about suicide. Physical symptom severity was assessed with the PHQ-15, a 15-item scale with scores ranging from 0 to 30 (38). Health related quality of life was assessed with the Short Form – 12 (SF-12) (39), with two subscales measuring physical health and mental health related functioning. Each subscale is normed against the general population such that mean and standard deviation are approximately 50 and 10 respectively (40). Pain intensity and interference were assessed with the Adapted Numeric Rating Scale for Pain (41); each item is rated on a 0 to10 Likert scale. Alcohol outcomes were measured using the AUDIT Alcohol Consumption Questions (AUDIT-C), three items that sum to scores of 0 to 12 (42). Patients reported amount and type of health care and medication use at each assessment. Counts of key intervention components were derived: number of individual patient visits with a mental health specialist and number of telephone contacts with a health care provider such as a care manager or other telephone assistance (e.g., crisis or helpline). Psychoactive medications were coded for type and duration, and used to derive a count of months on a guideline concordant depression medication (i.e., antidepressant) or PTSD medication (i.e., SSRI, prazosin).

Safety and Adverse Events. Serious adverse events were defined as participant death from any cause; or psychiatric emergency or hospitalization related to study participation. The study data and safety monitoring board (DSMB) chair and the site-specific independent study monitor reviewed and collated all reported adverse event reports to insure safe study implementation.

Statistical analyses

For the sample size calculations, we focused on the effect size, Δ/σ, for 12-month changes in scores in the two treatment groups, where Δ is the expected value of the difference between mean 12-month changes and σ is the within-group standard deviation at each time point. Initially, we assumed, conservatively, zero correlation between repeated measurements on the same subject reflecting that a study with 600 subjects per arm and a Type I error rate of 0.025 to account for two endpoints of interest would have power=0.80 to detect an effect size of Δ/σ=0.252. Previous studies have reported similar effect sizes (36, 43). The sample size was inflated to 750 subjects per group to account for an anticipated attrition rate of 20%. We reevaluated the sample size calculations after 129 subjects had completed 12-month assessments. Correlations between repeated measurements were nearly all >0.50. A correlation of 0.50 reduced the required sample size for the same power and effect size to 300 subjects per treatment group.

Analysis of scores on the PDS and SCL-20 was based on an exponential model of score vs time: $s_{ijk} = \beta_{j1} + b_{ij} + \beta_{j2}e^{-\beta_{j3}t_{ijk}} + d_{ijk}$ where s_{ijk} is score (PDS or SCL-20) for subject i in treatment arm j (j=1,2) at assessment k (k=1,..,4), β_{j1}, β_{j2} and β_{j3} are fixed parameters, b_{ij} is a normally distributed random parameter with mean zero, t_{ijk} is time on study at assessment k and d_{ijk} is a normally distributed error term with mean zero. This model accurately described changes both in mean scores and the variance of scores at each assessment. Under this model, $\Delta = \left(\beta_{12}e^{-12\beta_{13}} - \beta_{12}\right) - \left(\beta_{22}e^{-12\beta_{23}} - \beta_{22}\right)$. Under the null hypothesis that Δ=0, $\Delta/\mathrm{SE}(\Delta)$ has approximately a standard normal distribution.

To determine whether responses were clinical significant, we compared the proportions of subjects achieving at least a 50% reduction in a score at the three follow-up time points, using a generalized linear model with GEE invoked to account for correlations between repeated observations on the same subjects.

Changes in the secondary endpoints were compared using repeated measures linear models because the exponential model did not fit the data. Predictors included treatment group, time and the interaction of time and group, with the interaction included to provide a test for differences between trends over time in the two groups. Changes in health care use were compared using Poisson regression with GEE. Baseline use was treated as a covariate. Other predictors included treatment group, an ordinal categorical variable for time and their interaction.

For scores on the PDS and SCL-20, we tested for differences between changes in the two treatment arms over the first three months and the first 6 months to determine whether differences that were identified over 12 months were apparent earlier. We repeated this for the proportion with at least a 50% reduction in score. We did not perform these additional tests for the secondary endpoints or health care use, so we only report the overall p-values for comparing treatment arms for these outcomes.

The main analysis was done at the end of the trial and included all randomized participants with usable outcome data according to the intention-to-treat principle. The number needed to treat for a binary outcome was one divided by the absolute difference between groups. Data analyses were conducted using SAS/STAT software Version 9.3 of the SAS System for Windows.

Results

Sample

Figure 1 presents the study flow diagram. Follow-up rates were high with assessments completed by 93% of patients at three months, 90% at six months, and 86% at 12 months. Of the 666 randomized patients, 332 were assigned to CACT and 334 to usual care. Complete follow-up data were obtained for 273 (82.2%) CACT and 280 (83.8%) usual care participants. There was only baseline data for 9 (2.7%) CACT participants and 21 (6.3%) usual care participants. CACT and usual care groups were balanced on baseline characteristics (Table 1).

Mean PDS PTSD score was 29.2 indicating moderate to severe PTSD and mean SCL-20 depression score was 2.1, indicating moderate depression severity.

PTSD and Depression Outcomes

Compared with usual care, patients in CACT reported significantly greater reductions in PTSD and depression symptoms over 12-months of follow-up (Table 2). Differences in effects were statistically significant at 12-months for PTSD and at six and 12 months for depression. Reductions were clinically significant for both PTSD and depression, with significantly more CACT patients achieving at least a 50% reduction in symptoms. At 12-month follow-up, numbers needed to treat were 12.5 (95% CI, 6.9-71.9) for PTSD and 11.1 (95% CI, 6.2-50.5) for depression.

Secondary Health Outcomes

Significant improvements in CACT versus usual care groups were noted for physical symptoms (PHQ-15) and mental health functioning (SF-12 mental component). Significant differences between intervention and control were not found for alcohol consumption (AUDIT-C), physical health function (SF-12 physical component) or pain (intensity and interference; Table 3). Of note, repeated measures analysis (treatment group, by time, and their interaction) revealed statistically significant reductions in suicide-related SCL-20 items in the CACT arm (versus no change in usual care) for “hopelessness about the future” ($p=0.04$), “thoughts of death and dying” ($p=0.003$), and in “thoughts of ending one’s life ($p=0.04$).

Process of Care

We examined four key aspects of the process of care expected to differ between the CACT and optimized usual care arms: individual psychotherapy, telephone contacts with the care manager, and use of appropriate PTSD or depression medications (Table 4). No treatment by time interactions were detected on these measures, but CACT participants reported significantly more telephone contacts and more months on an appropriate PTSD and

depression medication. No differences were detected on the number of individual visits with a mental health specialist.

Adverse Events

There were no participant deaths and no psychiatric emergencies or hospitalizations determined to be study related.

Discussion

This is the first randomized trial to assess the impact of a collaborative care approach for serving military personnel, and one of the few primary care trials to examine a collaborative care model for PTSD. Military personnel attending primary care with PTSD or depression who were referred to 12 months of centrally assisted telecare with stepped psychosocial and pharmacologic management (CACT) reported significant improvements in PTSD and depression severity, physical symptom severity, and mental health function compared to those referred to usual integrated mental health care in primary care. Differences were clinically significant, with numbers needed to treat for 50% improvement of PTSD and depression of 12.5 and 11.1 respectively. The effects were somewhat smaller than those often observed in collaborative care trials for depression and anxiety (9), perhaps due to the fact that usual care, while largely untested, was a long-standing program of mental health integration that included nurse care management (20). The effects on PTSD were similar in size to those for depression, though a statistically significant PTSD response occurred later than for depression. Telephone contacts were greater in CACT than in usual care, but corresponding increases in evidence-based medication and psychotherapy use appeared relatively small. Greater implementation of active treatments may result in larger symptom improvements.

There are other potential explanations for the size of the observed intervention effect. First, to maximize the generalizability of study findings, we included patients undergoing medical retirement or administrative military separation at time of randomization, and these severely ill patients constituted 14% of the study sample. Second, military personnel, especially in time of

war, are a highly mobile group. Many left the military over the course of their follow-up, and helping them to remain engaged in treatment during this transition was difficult. Additionally, unlike most previous studies involving collaborative care, our trial participants were mainly young men in their twenties, a demographic group that is among the least likely to attend mental health treatment. In this group, confidentiality concerns may further erode willingness to attend or remain engaged in mental health care. While service members were often willing to discuss problems with a nurse care manager, many expressed concerns about seeing a mental health specialist. Third, even though participating primary care clinics were staffed with mental health specialists, obtaining evidence-based psychotherapy was difficult. Finally, the usual care intervention featured a potentially active form of integrated care employed across the health system at the time of the study and therefore this study is likely to offer a conservative estimate of intervention benefit.

Longer time to significant improvement for PTSD as compared to depression is perhaps a function of the greater complexity and comorbidity associated with PTSD, the lower efficacy of pharmacologic PTSD treatments (44, 45), and the fact that many primary care clinicians considered PTSD to be outside their scope of clinical comfort (20). We did not observe significant improvements in alcohol misuse or in pain outcomes per se; however we observed significant improvements in mental health related function and overall physical symptom severity, suggesting intervention impact went beyond the targeted disorders. Of note, CACT was associated with reductions in suicidal ideation, preliminary findings consistent with a previous randomized trial of collaborative care showing long-term reductions in suicidal ideation (12, 13). These findings, though preliminary, are important in the face of recent rises in the U.S military suicide rate. Indeed, recent research in serving military personnel has reinforced the importance of mental disorders and substance misuse as key risk factors (46).

Two previous collaborative care trials have reported primary care PTSD outcomes. Schnurr and colleagues (18) found no benefit associated with a model that mainly focused on

psychiatrist-supervised care managers, measurement-based clinical assessments of symptom severity, and stepped pharmacologic management. More recently, Fortney and colleagues (17) successfully improved PTSD outcomes using a collaborative care approach to PTSD designed to extending the reach and increasing the use of evidence-based cognitive processing therapy. Our trial offered stepped psychosocial and pharmacological intervention, suggesting that greater emphasis on psychotherapeutic approaches may be an instrumental component for successful primary care approaches to collaborative care for PTSD, though more research in this regard is needed.

Limitations should be considered when interpreting study findings. First, the intervention included multiple components and efforts were not made to control for nonspecific factors such as contact time. Hence, we are unable to parse the specific impact of intervention components. Finally, important information about cost and cost-effectiveness of this intervention is not yet available but will ultimately help inform decisions about these enhancements and their overall value to improving mental health among military personnel. Our forthcoming work will explore experiences of patients and clinicians from a qualitative perspective as well as cost-effectiveness analyses to help policy-makers weigh the value of this intervention.

In summary, we conclude that greater central assistance for collaborative telecare and use of stepped psychosocial and pharmacologic management is likely to improve primary care outcomes of PTSD and depression among affected military personnel and offers a promising approach for other populations with similar problems. These data also add to the emerging literature on the effectiveness of collaborative care treatment models for PTSD more generally.

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Table 1. Baseline characteristics of 666 randomized study patients.

Characteristic		CACT N=332 n (%) or mean (SD)	Usual Care N=334 n (%) or mean (SD)
Demographic	***Group(s)***		
Gender	Male	264 (80%)	275 (82%)
Age	Years	28.7 (10.9)	28.9 (11.4)
Rank	E1-E6	297 (89%)	283 (85%)
Marital Status	Married	222 (67%)	224 (67%)
Education	≥ High School	233 (70%)	230 (69%)
Race/Ethnicity	White, non-Hispanic	158 (48%)	160 (48%)
	Other, non-Hispanic	116 (35%)	114 (34%)
	Hispanic	57 (17%)	60 (18%)
Deployments after 2001	0	59 (18%)	55 (16%)
	1	102 (31%)	107 (32%)
	2	82 (25%)	77 (23%)
	≥ 3	89 (27%)	95 (28%)
Baseline Clinical Status			
High Combat Exposure[1]		224 (67%)	228 (68%)
PTSD	DSM-IV/ PCL-C[2]	285 (86%)	281 (84%)
Depression	PHQ-9[3]	224 (67%)	208 (62%)
PTSD and Depression		193 (58%)	177 (53%)
PTSD Severity	PDS	29.4 (9.4)	28.9 (8.9)
Depression Severity	SCL-20	2.1 (0.6)	2.0 (0.7)

Characteristic		CACT N=332 n (%) or mean (SD)	Usual Care N=334 n (%) or mean (SD)
Alcohol Consumption	AUDIT-C	3.0 (2.5)	2.7 (2.3)
Somatic Symptoms	PHQ-15	14.1 (4.7)	13.4 (4.8)
Physical Health Function	SF-12, PCS	37.7 (10.0)	36.8 (10.6)
Mental Health Function	SF-12, MCS	32.7 (9.6)	34.4 (10.9)
Pain Intensity	BPI	5.7 (2.3)	5.7 (2.4)
Pain Interference	BPI	5.0 (2.6)	5.0 (2.7)

[1] High combat exposure = 10+ points on Combat Exposure Scale.

[2] Meets PCL-C criteria if 1 or more items are endorsed for Criterion A, 3 or more for Criterion B, and 2 or more for Criterion C. A total of 37 participants were not asked the PCL because they did not meet criteria on the PC-PTSD and were assumed not to meet PTSD criteria

[3] Meets PHQ-9 criteria if 5 or more items were endorsed for “more than half the days” and one of those items was “little interest or pleasure in doing things” or “feeling down, depressed or hopeless”.

AUDIT-C=Consumption items of the Alcohol Use Disorders Identification Test

PCL-C=PTSD Checklist, Civilian Version

PDS=PTSD Diagnostic Scale

PHQ-9=Patient Health Questionnaire depression severity score

PHQ-15=Patient Health Questionnaire somatic symptom severity score

SCL-20=Hopkins Symptom Checklist, 20 item depression screen

SF-12, MCS=SF-12 Mental Component Summary score

SF-12, PCS=SF-12 Physical Component Summary score

Table 2. PTSD and depression related outcomes among study patients.

Outcome	CACT (n=332)	Usual Care (n=334)	Measure (95% CI)	p-value
PTSD (PDS) Severity				
0 to 3 months	-2.95[1] (0.53)	-2.73 (0.54)	-0.23 (-1.72,1.26)	0.59
0 to 6 months	-4.86 (0.61)	-3.42 (0.60)	-1.43 (-3.11, 0.25)	**0.057**
0 to 12 months	-6.07 (0.68)	-3.54 (0.72)	-2.53 (-4.47,-0.59)	**0.0029**
Depression (SCL-20)				
0 to 3 months	-0.29[1] (0.04)	-0.20 (0.04)	-0.08 (-0.19, 0.03)	0.062
0 to 6 months	-0.44 (0.05)	-0.25 (0.05)	-0.19 (-0.32, -0.06)	**0.0007**
0 to 12 months	-0.56 (0.05)	-0.31 (0.05)	-0.26 (-0.41, -0.11)	**<0.0001**
≥50% Improvement, PTSD				**0.023**
0 to 3 months	11.5[2] (36)	9.5 (29)	1.25[3] (0.74, 2.09)	0.40
0 to 6 months	19.3 (58)	13.4 (40)	1.55 (0.99, 2.40)	0.0510
0 to 12 months	25.0 (73)	17.0 (49)	1.62 (1.08, 2.43)	**0.0194**
≥50% Improvement, Depression				**0.014**
0 to 3 months	12.2[2] (38)	10.8 (33)	1.14[3] (0.70, 1.88)	0.60
0 to 6 months	21.3 (64)	13.8 (41)	1.70 (1.11, 2.61)	**0.0149**
0 to 12 months	29.7 (86)	20.6 (59)	1.65 (1.13, 2.42)	**0.0100**

[1] mean (SE)

[2] percent improved (number improved)

[3] odds ratio (95% confidence limits)

PDS=PTSD Diagnostic Scale

SCL-20=Hopkins Symptom Checklist, 20 item depression screen

Table 3. Changes in secondary outcomes among study patients from baseline to each follow-up assessment.

	CACT (n=332)	**Usual Care (n=334)**	**Measure (95% CI)**	**Overall P Value**
AUDIT-C, mean (SE)				0.24
0 to 3 months	-0.26 (0.12)	-0.29 (0.12)	-0.04 (-0.28, 0.36)	
0 to 6 months	-0.34 (0.13)	-0.33 (0.12)	-0.001 (-0.35, 0.35)	
0 to 12 months	-0.54 (0.14)	-0.20 (0.14)	-0.33 (-0.72, 0.06)	
PHQ-15, mean (SE)				**0.0252**
0 to 3 months	-1.12 (0.25)	-0.58 (0.25)	-0.53 (-1.22, 0.15)	
0 to 6 months	-1.56 (0.26)	-0.69 (0.29)	-0.88 (-1.64, -0.11)	
0 to 12 months	-2.29 (0.33)	-0.92 (0.31)	-1.37 (-2.26, -0.47)	
SF-12, mean (SE)				
Physical (PCS)				0.65
0 to 3 months	-1.02 (0.41)	-1.16 (0.44)	0.14 (-1.04, 1.31)	
0 to 6 months	-0.64 (0.45)	-1.10 (0.46)	0.46 (-0.80, 1.72)	
0 to 12 months	-1.11 (0.47)	-1.25 (0.55)	0.14 (-1.29, 1.57)	
Mental (MCS)				**0.014**
0 to 3 months	4.31 (0.65)	4.13 (0.65)	0.18 (-1.62, 1.98)	
0 to 6 months	5.78 (0.74)	3.51 (0.74)	2.28 (0.23, 4.33)	
0 to 12 months	8.10 (0.80)	4.93 (0.82)	3.17 (0.91, 5.42)	
Pain Intensity, mean (SE)				0.32
0 to 3 months	-0.17 (0.13)	0.02 (0.11)	-0.19 (-0.51, 0.14)	
0 to 6 months	-0.18 (0.13)	0.08 (0.13)	-0.26 (-0.61, 0.10)	

0 to 12 months	-0.25 (0.15)	0.08 (0.12)	-0.33 (-0.74, 0.07)	
Pain Interference, mean (SE)				0.36
0 to 3 months	0.09 (0.19)	0.27 (0.13)	-0.17 (-0.54, 0.20)	
0 to 6 months	-0.05 (0.15)	0.18 (0.14)	-0.23 (-0.63, 0.18)	
0 to 12 months	-0.19 (0.16)	0.20 (0.17)	-0.39 (-0.85, 0.07)	

AUDIT-C=Consumption items of the Alcohol Use Disorders Identification Test

PHQ-15=Patient Health Questionnaire somatic symptom severity score

MCS=SF-12 Mental Component Summary score

PCS=SF-12 Physical Component Summary score

Table 4. Patient reported mental health service use by treatment group (mean, SE).

			Treatment Effect	
	CACT (n=332)	**Usual Care (n=334)**	**Measure (95% CI)**	**P****
Individual Therapy Visits				0.49
3 months prior to enrollment	2.66* (0.27)	2.68 (0.45)	-0.02 (-1.06, 1.01)	
0 to 3 months	2.94 (0.26)	2.86 (0.26)	0.08 (-0.62, 0.79)	
3 to 6 months	2.82 (0.29)	2.32 (0.24)	0.50 (-0.24, 1.24)	
6 to 12 months	3.66 (0.47)	3.55 (0.41)	0.11 (-1.11, 1.33)	
Telephone Contacts				**<0.0001**
3 months prior to enrollment	1.53 (0.14)	2.56 (0.63)	-1.03 (-2.30, 0.25)	
0 to 3 months	3.05 (0.22)	1.76 (0.13)	1.·29 (0.80, 1.79)	
3 to 6 months	2.72 (0.31)	1.46 (0.13)	1.26 (0.59, 1.92)	
6 to 12 months	3.30 (0.35)	1.99 (0.22)	1.31 (0.51, 2.12)	
Months of Depression Medication[1]				**0.0129**
3 months prior to enrollment	0.67 (0.06)	0.77 (0.06)	-0.10 (-0.26, 0.07)	
0 to 3 months	1.30 (0.07)	1.13 (0.08)	0.16 (-0.05, 0.37)	
3 to 6 months	1.37 (0.08)	1.22 (0.08)	0.15 (-0.07, 0.37)	
6 to 12 months	2.42 (0.16)	2.02 (0.16)	0.40 (-0.05, 0.84)	
Months of PTSD Medication[2]				**0.0122**
3 months prior to enrollment	0.47 (0.05)	0.51 (0.06)	-0.04 (-0.18, 0.11)	
0 to 3 months	1.05 (0.07)	0.85 (0.07)	0.20 (-0.003, 0.39)	
3 to 6 months	1.20 (0.08)	0.88 (0.08)	0.32 (0.10, 0.53)	
6 to 12 months	2.03 (0.16)	1.60 (0.15)	0.43 (0.003, 0.86)	

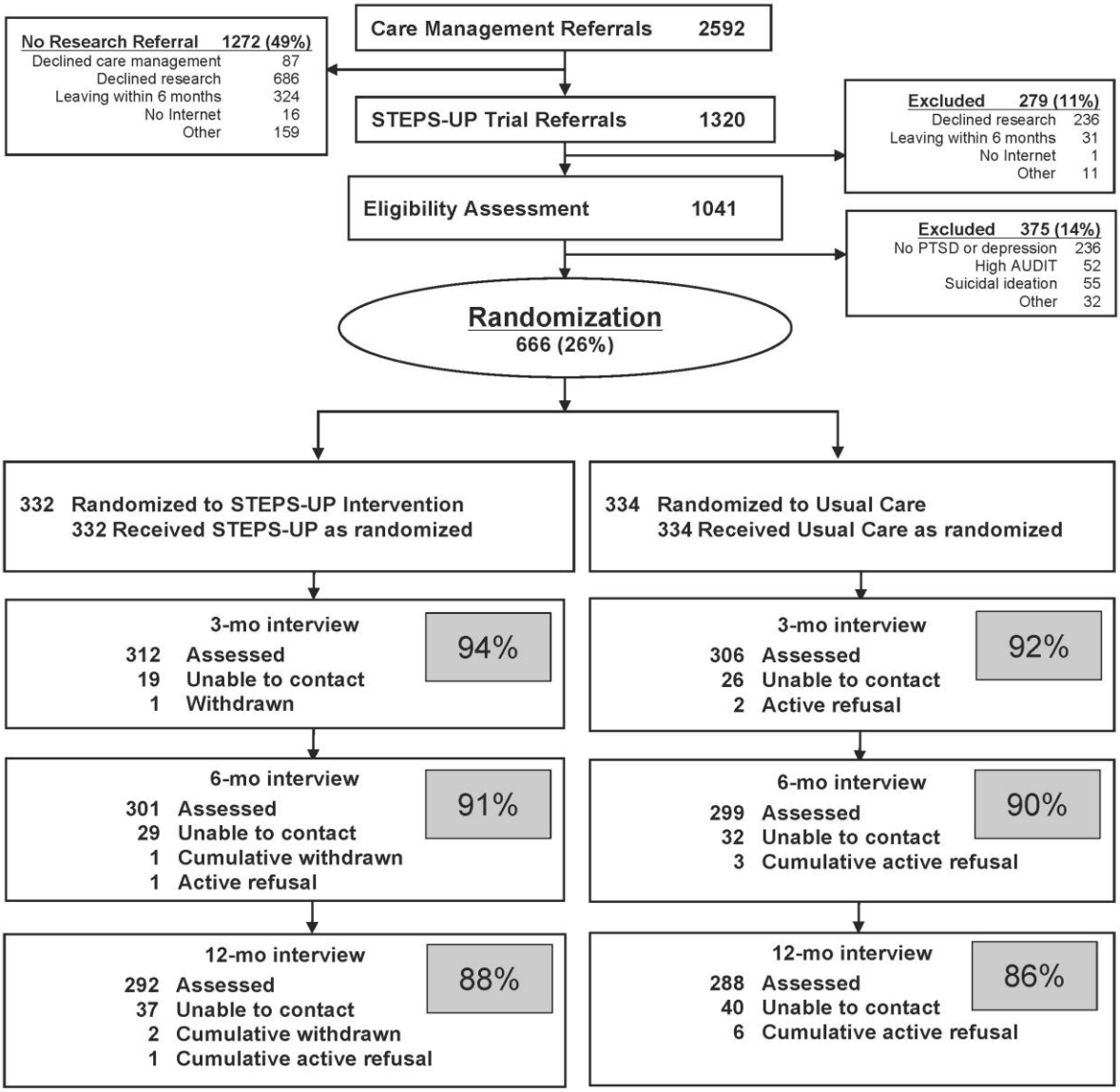
[1] Any antidepressant medication

[2] Any selective serotonin reuptake inhibitor or prazosin

* mean (standard error)

** p for treatment difference averaged over 3-, 6-, and 12-month assessments

Figure 1. Study flow diagram. Percentage in gray box is response rate by follow-up assessment and treatment arm.



Stepped Enhancement of PTSD Services Using Primary Care (STEPS UP): A Randomized Effectiveness Trial

DR080409/P1/P2, DoD Deployment Related Medical Research Program

PI: Michael C. Freed, PhD (Initiating PI)[1]; Robert M. Bray, PhD (Partnering PI)[2]; Lisa Jaycox, PhD (Partnering PI)[3]
Org: [1]Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF; Please note – Dr. Freed is a federal employee); [2]RTI International; [3]RAND Corporation
Award Amount: $14,781K ($6,762K to HJF; $4,928K to RTI; $3,091K to RAND)

Study/Product Aim(s)

• Primary Aim: To evaluate whether, relative to Optimized Usual Care (OUC), STEPS UP will lead to greater improvements in PTSD and/or depression symptom severity.
• Secondary Aims: To evaluate whether, relative to OUC, STEPS UP will lead to greater improvements in somatic symptom severity, alcohol problems, mental health functioning, work functioning, costs, and satisfaction with care.

Approach

This is a six-site, randomized controlled trial with follow-up assessments at 3, 6, and 12 months. Over a 2.5-year period, we enrolled 666 service members who screened positive for symptoms of PTSD and/or depression. This study will compare the STEPS UP intervention to OUC. OUC is RESPECT-Mil, a multi-site, primary care-based program where service members with symptoms of PTSD and depression are carefully screened, tracked, and treated within the primary care system, with the assistance and collaboration of a psychiatrist and an on-site nurse-level care manager. STEPS UP is testing possible enhancements to RESPECT-Mil, including:
1) Adding the option for centralized, telephone-based care management;
2) Adding care manager training in strategies to improve engagement in treatment and tools for early intervention;
3) Adding preference-based stepped care to existing options of pharmacotherapy that includes:
- Web-based therapy options for PTSD and depression;
- Telephone delivered therapy;
- Possibly faster connection to face-to-face therapy by a specialist

Outcome	STEPS-UP (n=332)	Usual Care (n=334)	Measure (95% CI)	p-value
PTSD (PDS) Severity				
0 to 3 months	-2.95[1] (0.53)	-2.73 (0.54)	-0.23 (-1.72,1.26)	0.59
0 to 6 months	-4.86 (0.61)	-3.42 (0.60)	-1.43 (-3.11, 0.25)	0.057
0 to 12 months	-6.07 (0.68)	-3.54 (0.72)	-2.53 (-4.47,-0.59)	0.0029
Depression (SCL-20)				
0 to 3 months	-0.29[1] (0.04)	-0.20 (0.04)	-0.08 (-0.19, 0.03)	0.062
0 to 6 months	-0.44 (0.05)	-0.25 (0.05)	-0.19 (-0.32, -0.06)	0.0007
0 to 12 months	-0.56 (0.05)	-0.31 (0.05)	-0.26 (-0.41, -0.11)	<0.0001
≥50% Improvement, PTSD				0.023
0 to 3 months	11.5[2] (36)	9.5 (29)	1.25[3] (0.74, 2.09)	0.40
0 to 6 months	19.3 (58)	13.4 (40)	1.55 (0.99, 2.40)	0.0510
0 to 12 months	25.0 (73)	17.0 (49)	1.62 (1.08, 2.43)	0.0194
≥50% Improvement, Depression				0.014
0 to 3 months	12.2[2] (38)	10.8 (33)	1.14[3] (0.70, 1.88)	0.60
0 to 6 months	21.3 (64)	13.8 (41)	1.70 (1.11, 2.61)	0.0149
0 to 12 months	29.7 (86)	20.6 (59)	1.65 (1.13, 2.42)	0.0100

[1] mean (SE)
[2] percent improved (number improved)
[3] odds ratio (95% confidence limits)
PDS=PTSD Diagnostic Scale
SCL-20=Hopkins Symptom Checklist, 20 item depression screen

Figure: PTSD and depression outcomes among study patients

Accomplishment: Investigators presented the main study findings at several conferences, including the American Psychiatric Association 168th Annual Meeting in Toronto in May 2015 and the 2015 MHSRS Conference in Ft. Lauderdale, FL in August 2015. Investigators continue to conduct analyses and prepare manuscripts. The table above shows the primary PTSD and depression outcomes among study patients in the STEPS UP intervention and usual care arms.

Timeline and Cost

Activities	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6 EWOF	Year 7 EWOF (to 2/29/16)
Intervention & protocol development/refinement							
Provider & expert panel interviews							
IRB submission/approval							
Hire staff & conduct training							
Recruit & consent participants							
Conduct data collection							
Analysis & writing							
Ongoing research team meetings							
Ongoing QA/QC procedures							
Submit reports							
Estimated Budget ($K)* *Amount Spent	$842K*	$1,289K*	$1,898K*	$2,829K*	$2,737K*	$1,990K*	$1,366

Updated: 30 September 2015

Goals/Milestones

Year 1 Goals (Sept 2009-Aug 2010)
☑ Develop protocol, tools, manuals
☑ Provider interviews and collaborate with expert panel
☑ Submit to IRBs/obtain IRB approval
☑ Hold research team meetings
☑ Implement QA/QC procedures
☑ Submit reports

Year 2 Goals (Sept 2010-Aug 2011)
☑Refine protocol, tools, manuals
☑Hire staff and conduct training
☑Submit to IRBs/obtain IRB approval
☑Ongoing research team meetings
☑Ongoing QA/QC procedures
☑Continue to submit reports

Year 3 Goals (Sept 2011-Aug 2012)
☑Amend protocol, tools, manuals
☑Continue to hire staff and conduct training
☑Submit to IRBs/obtain IRB approval
☑Recruit and consent participants (began Feb 12)
☑Conduct data collection (began Feb 12)
☑Ongoing research team meetings
☑Ongoing QA/QC procedures
☑Continue to submit reports

Year 4 Goals (Sept 2012-Aug 2013)
☑Continue to recruit and consent participants
☑Continue data collection
☑Analysis and writing
☑Ongoing research team meetings
☑Ongoing QA/QC procedures
☑Continue to submit reports

Year 5 Goals (Sept 2013-Aug 2014)
☑Continue data collection for follow-up assessments
☑Continue analysis and writing
☑Ongoing research team meetings
☑Ongoing QA/QC procedures
☑Continue to submit reports

Year 6 EWOF Goals (Sept 2014-Aug 2015)
☑Complete follow-up data collection
☑Continue analysis and writing
☑Ongoing research team meetings
☑Ongoing QA/QC procedures
☑Continue to submit reports

Year 7 EWOF Goals (Sept 2015-Feb 2016)
☐Complete analysis and writing
☐Ongoing research team meetings
☐Ongoing QA/QC procedures
☐Submit reports

Comments/Challenges/Issues/Concerns

- IRB approval delays were impediments in starting up sites and beginning recruitment/enrollment, setting back the entire study timeline.
- Due to multiple start-up delays, investigators will need an extension without funds (EWOF) to meet current deliverables. Obtaining MRMC approval of the 1-year EWOF and revised budgets was a challenge, but approval was received in January 2015. MRMC approved a second 6-month EWOF (through February 2016) in August 2015.

Budget

Expenditures to Date (Year 1 – Year 6 EWOF): TOTAL: $11,585K (HJF: $4,673K; RTI: $4,655K; RAND: $2,257K)
Projected Expenditures Year 7 EWOF (through 2/29/16): TOTAL: $1,366K (HJF: $522K; RTI: $273K; RAND: $571K)
PLEASE NOTE: The HJF and RAND total budgets were reduced from their original award amounts for the Year 6 & 7 EWOFs.