Clinical Trial Discontinuation and Non-Publication for the Pharmacologic Treatment of Post-Traumatic Stress Disorder Among Military Veterans

Jonas Weygandt, BS, Morgan Moody, BS, Nicholas B. Sajjadi, BS, Benjamin Greiner, DO, MPH, Alicia Ford, PhD, Micah Hartwell PhD

COLLEGE OF OSTEOPATHIC MEDICINE at the Cherokee Nation

INTRODUCTION

Failures by researchers and clinicians to understand, confront, and overcome barriers in veteran-health research may result in the waste of finite resources. Research waste includes clinical trial (CT) discontinuation and non-publication which have been shown to be substantial among several fields of medicine. It is the ethical responsibility of researchers, as scientists, to contribute their findings to the existing literature as supported by the International Committee of Medical Journal Editors and the National Institute for Health Research and the Declaration of Helsinki regarding human subjects.

OBJECTIVES

Given the rates of discontinuation and non-publication of clinical trials among other fields of medicine and the lack of evidence demonstrating publication rates of clinical trials (CTs) among veterans, our primary objective was to determine rates of discontinuation and non-publication among post traumatic stress disorder (PTSD) focused CTs with pharmaceutical interventions specific to the veteran population.

METHODS

We performed a systematic search of registered trials using ClinicalTrials.gov for pharmaceutical interventions for the treatment of PTSD. Studies were screened in a duplicate masked fashion and extracted study characteristics including sample size, study design, trial status, phase, and funding source were completed. We then searched the trials designation ID and title to identify publications associated with the study. If no study was found, and the study was not prematurely terminated, the study's primary contact was emailed to identify potential publications. Studies were classified as completed or discontinued based on the status category provided from ClinicalTrials.gov. Descriptive statistics of trials will be reported and associations of trial termination and non-publication will be assessed using logistic regression.

Table 1. Associations of study characteristics and completion of trials.

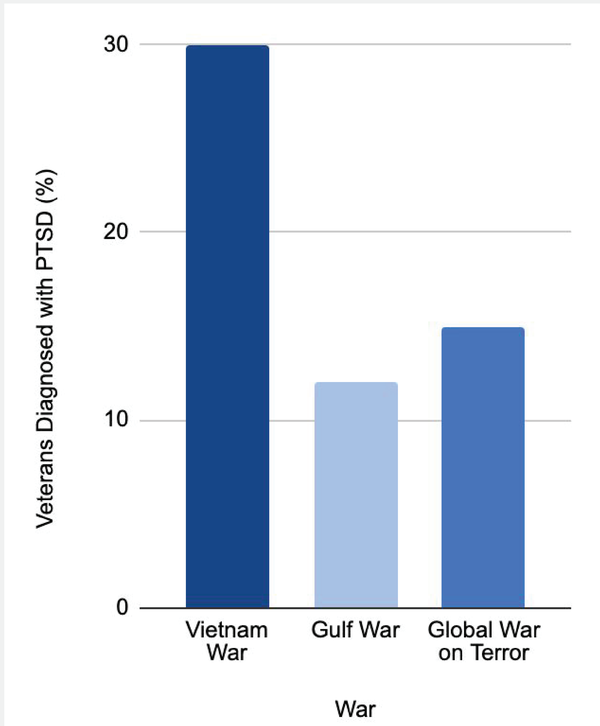
	Discontinued (n=11)	Complete (n=43)	Odds Ratios (95%CI)
Sample Size, Med. (IQR)[A]	0 (0-12)	49 (26-100)	1.04 (1.00-1.07)*
Study design, No. (%)			
Non-RCT	2	10	1 [Reference]
RCT	9	33	.733 (0.14-3.96)
Phase			
NA	3	8	1 [Reference]
1	1	3	1.25 (0.81-15.51)
2	3	11	1.78 (0.22-8.69)
3	0	4	1.59 (0.29-8.87)
4	4	17	2.67 (0.71-10.05)
Funding Sources			
Government	8	31	1 [Reference]
Other	3	6	
Industry	0	6	0.52 (.11-2.53)

Funding other includes universities and medical institutions. Not calculated due to collinearity. *Statistically significant: P<.05

			Odds Ratios (95%CI)
	Unpublished (n=15)	Published (n=37)	Unadjusted
Sample Size, Med. (IQR)[A]	12 (0-44)	49 (25-100)	1.01 (1.00-1.03)
Study design, No. (%)			
Non-RCT	6	6	1 [Reference]
RCT	10	32	3.2 (0.84-12.17)
Phase			
NA	3	8	1 [Reference]
I	1	3	1.13 (0.08-15.51)
II	5	9	.68 (.12-3.77)
III	0	4	1 -
IV	7	14	.75 (0.15-3.74)
Funding Sources			
Government	11	28	1 [Reference]
Industry	2	4	.79 (.13-4.92)
Other	3	6	.79 (0.17-3.71)

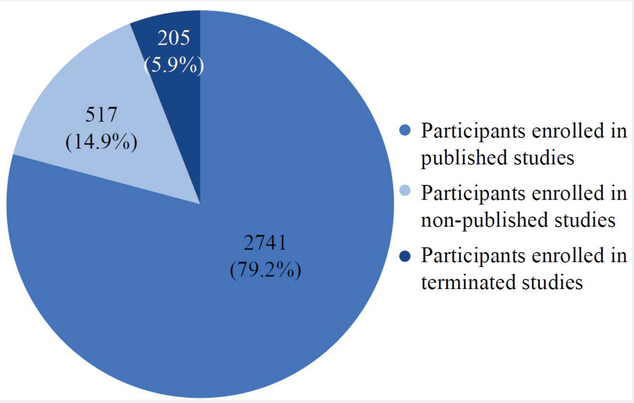
A.Enrollment wasnt listed for 2 studiesd. Funding other includes universities and medical institutions. *Statistically significant: P<.05

Figure 1: Rates of PTSD Diagnosis Among Veterans



Source: https://www.ptsd.va.gov/understand/common/common_veterans.asp

Figure 2:Enrollment in Clinical Trials



CONCLUSION

We found that a combined 29% of trials of medications for PTSD among veterans were either discontinued or not-published. It is not only the ethical responsibility of researchers to publish results, but a legal requirement under Section 801 of the FDA Amendments Act (FDAAA) of 2007 to report study results. which has been reaffirmed and strengthened in 2017 and the first preliminary litigation was announced. In light of the dedication of our service men and women to serving the United States, sometimes at great personal cost, it is the ethical responsibility of researchers to advance clinical knowledge via CT publication as it relates to improving treatments for veterans diagnosed with PTSD is greater than ever before.

Implications

Exposure and recognition of high rates of discontinuation and non-publication among veteran related PTSD trials can aid policy makers, clinicians, and scientists involved in CTs improve outcomes among such trials. This will allow government organizations such as the FDA, VA, and NIH to hold principal investigators accountable for the trials and funding they receive. Acknowledgement of wrongdoing by the scientific establishment in this matter will also help build trust among veterans seeking mental health services.

REFERENCES

1. PTSD: National center for PTSD. Accessed January 18, 2022. https://www.ptsd.va.gov/understand/common/common_veterans.asp
2. Cheney AM, Koenig CJ, Miller CJ, et al. Veteran-centered barriers to VA mental healthcare services use. *BMC Health Serv Res*. 2018;18(1):591.
3. Johnson AL, Fladie I, Anderson JM, Lewis DM, Mons BR, Vassar M. Rates of Discontinuation and Nonpublication of Head and Neck Cancer Randomized Clinical Trials. *JAMA Otolaryngol Head Neck Surg*. Published online December 26, 2019. doi:10.1001/jamaoto.2019.3967
4. Scott J, Cooper CM, Checketts JX, et al. An observational analysis of discontinuation and non-publication of osteoarthritis trials. *Osteoarthritis Cartilage*. 2018;26(9):1162-1169.
5. Pica N, Bourgeois F. Discontinuation and Nonpublication of Randomized Clinical Trials Conducted in Children. *Pediatrics*. 2016;138(3). doi:10.1542/peds.2016-0223
6. Chen R, Desai NR, Ross JS, et al. Publication and reporting of clinical trial results: cross sectional analysis across academic medical centers. *BMJ*. 2016;352:i637.
7. Roddick AJ, Chan FTS, Stefaniak JD, Zheng SL. Discontinuation and non-publication of clinical trials in cardiovascular medicine. *Int J Cardiol*. 2017;244:309-315.
8. Angelis CD, De Angelis C, Drazen JM, et al. Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors. *Annals of Internal Medicine*. 2004;141(6):477. doi:10.7326/0003-4819-141-6-200409210-00109
9. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194.