A. OVERALL COVER PAGE

Project Title: Internet-based Psychotherapies for PTSD Symptoms in WTC Responders	
Grant Number: 5U01OH010729-03	**Project/Grant Period:** 09/01/2016 - 08/31/2019
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Human Subjects: NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Specific Aim 1:
1a. To evaluate the efficacy of Internet-based CBT (IBCBT) in treating WTC rescue and recovery workers with clinically significant WTC-related PTSD symptoms. We hypothesize that, compared to Internet-based supportive counseling, IBCBT will be associated with a clinically significant and moderate-to-large magnitude reduction in WTC-related PTSD symptoms, most notably intrusion symptoms, and alterations in arousal and reactivity (based on results from our pilot study).
1b. To evaluate the efficacy of IBCBT in improving functioning and quality of life, and promoting posttraumatic growth in WTC workers with clinically significant WTC-related PTSD symptoms. We hypothesize that, compared to Internet-based supportive counseling, IBCBT will be associated with a significantly greater and moderate-to-large magnitude improvement in mental functioning, quality of life, and posttraumatic growth.
1c. To examine whether IBCBT-related increases in therapeutic alliance mediate improvement in PTSD symptoms in WTC workers with clinically significant PTSD symptoms. We hypothesize that greater treatment-related increases in therapeutic alliance will be associated with greater reductions in WTC-related PTSD symptoms.

Specific Aim 2:
2a. Exploratory aims include evaluating baseline genetic and epigenetic predictors of treatment response and changes in epigenetic regulation of genes implicated in risk for PTSD from pre- to post-treatment. We expect that cumulative genetic and epigenetic risk factors for PTSD throughout the genome will predict response to treatment. We will (i) construct polygenic risk scores (PRS) from the largest available PTSD genome-wide association study (GWAS) dataset, and test for association with treatment outcome, and (ii) perform an epigenome-wide association study (EWAS), test for differential percent methylation, and identify specific differentially methylated positions (DMPs) between treatment responders and non-responders.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

B.2 (Final Report Narrative.pdf)

Final Progress Report

A Randomized Controlled Trial of Internet CBT for PTSD in WTC Responders and Survivors

(U01 OH010729)

Centers for Disease Control and Prevention

9/1/2016 – 8/31/2021

Final Report

(DATE)

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List of Terms and Abbreviations

These are included in the text for ease of reading.

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Abstract

Background: The 9/11 terrorist attacks on the WTC were unprecedented in scope and impact, affecting hundreds of thousands of individuals of who lived, worked, or were passersby in the areas surrounding the WTC, as well as tens of thousands of workers who were involved in rescue, recovery and clean-up efforts following the attacks. Recent studies conducted in the second decade following 9/11/2001 have shown that rates of PTSD remain elevated in these populations, ranging from 14.3 to 21.9%. While trauma-focused cognitive behavioral therapies (CBT) is the most effective and empirically supported of available treatments for PTSD, the provision of this treatment to symptomatic WTC workers is often limited by geographical distance, reduced availability of expertly trained therapists, and stigma associated with seeking formal treatment. This study aimed to address this gap by conducting a randomized controlled trial (RCT) of a therapist-assisted, internet-based CBT, *Integrative Testimonial Therapy (ITT)* compared to therapist-assisted, *Internet-based Modified Present-Centered Therapy (I-MPCT)* in WTC workers and survivors with persistent clinically significant WTC-related PTSD symptoms (syndromal or subsyndromal PTSD).

Methods: A total of 105 eligible participants (75% will syndromal PTSD, 25% with subsyndromal PTSD at screening) were randomized to ITT or I-MPCT, stratified by three groups: traditional responder (e.g., police), non-traditional responder (e.g., construction worker), and survivor. Participants completed self-report questionnaires at baseline, post-treatment, and 3 months following end of treatment. Of the 105 randomized participants, 85 (81%) completed treatment. A subsample provided saliva samples for genetic and epigenetic biomarker studies –67 (64%) at baseline, 56 (53%) at post-treatment. After comparing sociodemographic, trauma, and clinical characteristics of participants randomized to the two treatment groups, linear mixed-effects models were conducted to analyze treatment effects on all study outcome measures. Treatment (ITT vs. I-MPCT), Time (baseline, post-intervention), and Treatment x Time interaction were entered as fixed factors; baseline scores as a fixed covariate, subject as a random effect, and scores on primary (i.e., PTSD Checklist for DSM-5, PCL-5) and secondary (e.g., Beck Depression Inventory – Version II, BDI-II; PCL-5 PTSD symptom clusters) outcome measures as dependent variables in separate analyses. As per intention-to-treat principles, all participants who completed the pre-treatment assessment, regardless of whether any participants dropped out of the trial, were included in these analyses. Additional analyses evaluated whether a history of prior mental health treatment influenced response to ITT and/or I-MPCT.

Results: Significant main effects of time were observed for the primary outcome measure of PCL-5 scores as well as all PTSD symptom clusters, co-morbid depressive symptoms, quality of life (Q-LES-Q), and SF-8 mental health-related functioning, indicating that both ITT and I-MPCT yielded significant improvements in PTSD symptoms and additional, secondary outcomes. For the primary outcome measure of PCL-5 scores, the magnitude of this improvement was large (d=1.49, 95%CI=1.05-1.92). Magnitudes of improvements for secondary outcome measures were moderate-to-large, ranging from d=0.62 (95%CI=0.23-1.01) for quality of life (Q-LES-Q) to 1.33 (95%CI=0.91-1.75) for PTSD symptoms of alterations in arousal and reactivity. Main effects of treatment and interactions of treatment x time were not significant for any of the primary or secondary outcome measures. Additional analyses examining moderating effects of prior mental health treatment revealed significantly higher improvement in overall PTSD symptom severity in participants randomized to ITT who had a history of prior mental health treatment, and in those randomized to I-MPCT who did not have a history of prior treatment. Secondary analyses further revealed that lifetime treatment with psychotropic medication (but not psychotherapy) accounted for these effects.

Conclusion: Findings from this novel RCT of therapist-assisted, internet-based psychotherapies suggest that both ITT and I-MPCT are efficacious for the treatment of WTC responders and survivors who have continued to experience clinically significant PTSD symptoms two decades following the 9/11 terrorist attacks. Findings additionally suggest personalizing these treatment interventions –selection of ITT vs. I-MPCT– based on the affected individual's mental health treatment history. Provision of these therapist-assisted, internet-based psychotherapies to WTC responders and survivors with PTSD can greatly reduce barriers preventing access to effective interventions for this chronic and disabling condition

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Section 1

Significant or Key Findings

This was, to our knowledge, the first RCT to compare Integrative Testimonial Therapy (ITT), a therapist-assisted, internet-based cognitive-behavioral psychotherapy for individuals with PTSD, to an active comparison condition, therapist-assisted, internet-based Modified Present Centered Therapy (I-MPCT), and the first RCT of internet-based psychotherapies for WTC workers and survivors with persistent clinically significant WTC-related PTSD symptoms. Significant and key findings include the following:

1. Both ITT and I-MPCT are effective therapist-assisted internet-based psychotherapies for WTC workers and survivors with persistent clinically significant WTC-related PTSD symptoms, associated with large-magnitude improvements in PTSD symptom severity at post-treatment.
2. Both ITT and I-MPCT were additionally associated with moderate-to-large-magnitude improvements in all PTSD symptom clusters (intrusions, avoidance, negative mood and cognitions, and alterations in arousal and reactivity), as well as co-morbid depressive symptoms, quality of life, and mental health-related functioning.
3. Treatment-related improvements in PTSD symptom severity were found to generally persist 3 months after treatment completion, the study follow-up assessment time point.
4. ITT was associated with significantly higher improvement in PTSD symptom severity in patients who had a history of prior mental health treatment. This finding, driven by a history of lifetime treatment with psychotropic medication, suggests that ITT –which focuses on working through WTC-related traumas and on integrating these traumatic experiences in the WTC responder's or survivor's life– should be the psychotherapy of choice for these patients.
5. Conversely, I-MPCT was associated with significantly higher improvement in PTSD symptom severity in patients who had no prior history of mental health treatment. This finding suggests that I-MPCT –which focuses on generating potential solutions for current life stressors, previously linked to persistent PTSD symptom severity in WTC-exposed populations– might be the recommended first-line psychotherapy for WTC responders and survivors new to mental health treatment.
6. Preliminary biomarker analyses revealed that while global percent methylation (PCM) of DNA was slightly lower at post-treatment than pre-treatment, pre-treatment PCM did not significantly predict PTSD symptom improvement at post-treatment or 3-month follow-up in the subsample of participants who provided saliva samples for biomarker assays. Additional preliminary analyses revealed that pre-treatment PCM significantly predicted PTSD symptom improvement at the 3-month follow-up, only in the I-MPCT group. Additional genetic (polygenic risk scores, PRS) and epigenetic data analyses are currently in progress.

Translation of Findings

Findings from this novel RCT of therapist-assisted, internet-based psychotherapies suggest that both ITT and I-MPCT are efficacious for the treatment of WTC responders and survivors who have continued to experience clinically significant PTSD symptoms two decades following the 9/11 terrorist attacks. Findings additionally suggest personalizing these treatment interventions –selection of ITT vs. I-MPCT– based on the affected individual's mental health treatment history.

Research Outcomes/Impact

Provision of these therapist-assisted internet-based psychotherapies to WTC responders and survivors with PTSD can greatly reduce barriers preventing access to effective interventions for this chronic and disabling

condition, as these interventions are not limited by geographical distance or stigma associated with attending in-person mental health treatment sessions.

Additionally, the current COVID-19 pandemic has increased the need for effective treatment interventions that can be delivered remotely, such as the two psychotherapies evaluated in this study. Given the number of psychotherapists experienced in treating WTC workers and survivors across WTC Health Program locations, training therapists in the delivery of these internet-based psychotherapies to WTC-affected populations is highly feasible. Dissemination of these therapies across the WTC Health Program can improve access to effective treatment interventions for WTC-related PTSD, one of the most prevalent and persistent health conditions in WTC populations.

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Section 2

Scientific Report

Background

The 9/11 terrorist attacks on the WTC were unprecedented in scope and impact, affecting hundreds of thousands of individuals of who lived, worked, or were passersby in the areas surrounding the WTC, as well as tens of thousands of workers who were involved in rescue, recovery and clean-up efforts following the attacks [1]. Recent studies conducted in the second decade following 9/11/2001 have shown that rates of PTSD remain elevated in these populations, ranging from 14.3 to 21.9% [2-4]. Further, in a recent survey led by our research team, the prevalence of probable full and subthreshold WTC-related PTSD in police responders was 9.3% and 17.5%, respectively, and in non-traditional responders (e.g., construction workers) 21.9% and 24.1%, respectively [5]. Particularly high rates of persistent WTC-related PTSD are observed in those with highest exposure to the disaster or secondary stressors and, among WTC workers, those in occupations with low or no preparedness for disaster response [2, 4-6]. Among individuals with WTC-related PTSD, almost half report poor health-related quality of life and being dissatisfied with life, and one quarter report unmet mental health care needs [2]. Further, unmet mental health care needs despite receiving treatment were found to be associated with more severe PTSD symptom trajectories in WTC survivors [6]. Despite initiatives to expand access to mental health services to WTC cohort members via the WTC Health Program (WTC-HP), our research team has found that considerable barriers to treatment remain [7]. The prevalence and chronicity of WTC-related PTSD in populations exposed to the WTC disaster, including among those who have accessed mental health treatment, underscore the urgent need to develop and study the efficacy of new treatment interventions for PTSD in these populations.

While trauma-focused cognitive behavioral therapies (CBT) is the most effective and empirically supported of available treatments for PTSD [8], the provision of this treatment to symptomatic WTC workers is often limited by geographical distance, reduced availability of expertly trained therapists, and stigma associated with seeking formal treatment. Thus, there is an imperative need to enhance access to CBT while preserving the effectiveness of key aspects of this treatment, such as therapeutic alliance. This study aimed to address this gap by conducting a randomized controlled trial (RCT) of a therapist-assisted, Internet-based CBT, ***Integrative Testimonial Therapy (ITT)*** [9, 10], compared to therapist-assisted, ***Internet-based Modified Present-Centered Therapy (I-MPCT)*** [11, 12], in WTC workers and survivors with current, WTC-related full or partial PTSD. This RCT is the first of which we are aware to evaluate the efficacy of Internet-based CBT in mitigating WTC-related PTSD symptoms in WTC workers and survivors; and to compare this intervention to an active control condition. An emerging treatment for PTSD and clinically significant PTSD symptoms, ITT has demonstrated high treatment adherence, therapeutic alliance, and large magnitude reductions in PTSD and related symptoms in initial studies of other trauma survivors. If found to be effective in WTC workers and survivors, ITT has the potential to reach many WTC workers and survivors who remain symptomatic but have encountered obstacles to formal mental health treatment. In a complementary, exploratory aim, we will evaluate genetic and epigenetic predictors and correlates of treatment response, measured in saliva samples at pre- and post-treatment, an extension of our CDC/NIOSH-funded grants U01OH010407-01 and U01OH010986 to identify biomarkers of PTSD in WTC workers. We expect that cumulative genetic and epigenetic risk factors for PTSD throughout the genome will predict response to treatment.

Specific Aims

Specific Aim 1: 1a. To evaluate the efficacy of Internet-based CBT (IBCBT) in treating WTC rescue and recovery workers with clinically significant WTC-related PTSD symptoms. We hypothesize that, compared to Internet-based supportive counseling, IBCBT will be associated with a clinically significant and moderate-to-large magnitude reduction in WTC-related PTSD symptoms, most notably intrusion symptoms, and alterations in arousal and reactivity (based on results from our pilot study). ***1b.*** To evaluate the efficacy of IBCBT in improving functioning and quality of life, and promoting posttraumatic growth in WTC workers with clinically significant WTC-related PTSD symptoms. We hypothesize that, compared to Internet-based supportive counseling, IBCBT will be associated with a significantly greater and moderate-to-large magnitude improvement in mental functioning, quality of life, and posttraumatic growth. **1c.** To examine whether IBCBT-

related increases in therapeutic alliance mediate improvement in PTSD symptoms in WTC workers with clinically significant PTSD symptoms. We hypothesize that greater treatment-related increases in therapeutic alliance will be associated with greater reductions in WTC-related PTSD symptoms.

Specific Aim 2: 2a. Exploratory aims include evaluating baseline genetic and epigenetic predictors of treatment response and changes in epigenetic regulation of genes implicated in risk for PTSD from pre- to post-treatment. We expect that cumulative genetic and epigenetic risk factors for PTSD throughout the genome will predict response to treatment. We will (i) construct polygenic risk scores (PRS) from the largest available PTSD genome-wide association study (GWAS) dataset, and test for association with treatment outcome, and (ii) perform an epigenome-wide association study (EWAS), test for differential percent methylation, and identify specific differentially methylated positions (DMPs) between treatment responders and non-responders.

Methodology

Recruitment

For this study, participants were recruited in several ways: *(1)* collaborating with faculty and staff of the WTC-HP General Responder Data Center (GRDC), b*y* contacting WTC responders enrolled in the WTC-HP General Responder Cohort, who had screened positive for PTSD on the PTSD Checklist (PCL) at their most recent health monitoring visit and had provided signed consent to be contacted for future studies.; *(2)* collaborating with faculty and staff of the WTC Health Registry, who sent out emails to WTC responder and survivor Registry members who had screened positive for PTSD at their most recent survey, informing them about this study; *(3)* by community outreach, print and web advertising to groups with large cohorts of 9/11 responders or survivors (e.g, support groups, police departments), including the Feal Foundation and Voices of Resilience; and *(4)* by clinician referral for study participation, in particular clinicians at the WTC Mental Health Program at Mount Sinai.

Clinical Evaluation

Potential participants were directed to the project website, which included a link to a pre-screening questionnaire and the study online consent form. Potential participants had the option to ask any questions about the study by communicating with the clinical research coordinator via email or phone. After signing the consent form electronically, participants received a link to complete the study online screening questionnaire on the Research Electronic Data Capture (RedCap) platform, including questions about demographics, brief psychiatric and substance use history, current medical conditions and medications, and a brief question about their experience as WTC responder or survivor. Participants who were preliminarily eligible based on this screening questionnaire completed a psychiatric assessment over the phone, including administration of the Mini International Neuropsychiatric Interview (MINI) by trained study personnel. Eligible participants, who met criteria for full or subthreshold PTSD in the past month, had access to a desktop or laptop computer, and did not meet any of the exclusion criteria received a complete explanation of study procedures via telephone. Exclusion criteria were as follows: elevated suicidal or homicidal risk, psychotic symptoms/disorder or bipolar disorder, marked dissociative symptoms, alcohol/drug use disorder within the past three months, current uncontrolled medical illness, neurological disorder affecting the central nervous system or history of head injury, currently in psychotherapy, or currently taking antipsychotic medication or lithium or valproic acid. Ineligible individuals were provided with alternative treatment options or direct referrals when needed.

Brief Summary of Study Methods

Eligible participants were randomized to ITT or I-MPCT, stratified by three groups: traditional responder (e.g., police), non-traditional responder (e.g., construction worker), and survivor. Three randomization sequences were generated by MPI Dr. Pietrzak, and remained concealed to study personnel by using sequentially numbered opaque envelopes prepared by a research assistant not otherwise involved with the

study. Based on their randomization outcome, participants were assigned to one of two ITT therapists or two I-MPCT therapists. Therapists communicated with patients in writing via the REDCap platform, where therapists provided instructions for patients to write a total of 11 narratives, twice per week, as well as feedback on written narratives. Patients were considered to have followed protocol procedures if the completed all 11 narratives over a period of up to 12 weeks.

In ITT, a therapy focused on WTC-related traumas, written narratives include exploration of past and current challenges and coping strategies, narrative exposure therapy, and cognitive reappraisal. In I-MPCT, developed for this study by Drs. Presseau and Litz to match ITT's treatment dose and frequency of written interaction with the therapist, narratives include exploration of current circumstances, identification of current problems/stressors, and brainstorming about problem solving/potential solutions to current problems. Participant safety and concomitant medications were evaluated at baseline and periodically throughout the study via periodic self-report questionnaires, followed up by a phone call from the therapist if needed for further safety evaluation of a patient. Treatment fidelity (adherence to therapy protocols by the four study therapists) was examined in 20% of therapist-patient narrative exchanges for each therapist, randomly selected within each therapy phase.

Participants who additionally provided signed consent via mail to collect saliva samples for genetic and epigenetic biomarkers (optional study component) provided saliva samples at pre-treatment baseline and at post-treatment using Genotek's Oragene-DNA (DNA 500) collection kits, sent and returned via mail. Samples were genotyped using the Infinium Global Screening Array (GSA), and genome-wide DNA methylation was assessed using the Infinium Methylation EPIC BeadChip Kit, which includes over 850,000 methylation sites genome-wide.

Sample size calculations indicated that, assuming a minimum differential 0.80 standard deviation reduction in the primary outcome measure, PCL-5 scores and alpha=0.05, a total of 80 treatment completers (n=40 per treatment arm) would provide > 90% statistical power to detect differential effect size magnitude changes as small as d=0.32. We anticipated up to 20% dropout across conditions, and thus aimed to randomize at least 100 patients. For the exploratory aim, based on prior psychotherapy study of individuals with PTSD, we estimated that with this sample size we would detect moderate-to-large magnitude genetic and epigenetic biomarkers.

Table 1: Assessment Overview and Timeline of Primary and Secondary Outcome Measures

Measure	Pre-Tx	Post-Tx	3MFU
PTSD Checklist for DSM-5 (PCL-5) [21]	X	X	X
Beck Depression Inventory – Version II (BDI-II) [35]	X	X	X
Generalized Anxiety Disorder-7 (GAD-7) [36]	X	X	X
Medical Outcomes Study (MOS) Short Form 8 Health Survey (MOS-SF-8) [37]	X	X	X
Quality of Life Enjoyment and Satisfaction Scale-Short Form (Q-LES-SF) [38]	X	X	X
Posttraumatic Growth Inventory Short Form (PTGI-SF) [39]	X	X	X
Biomarkers	X	X	

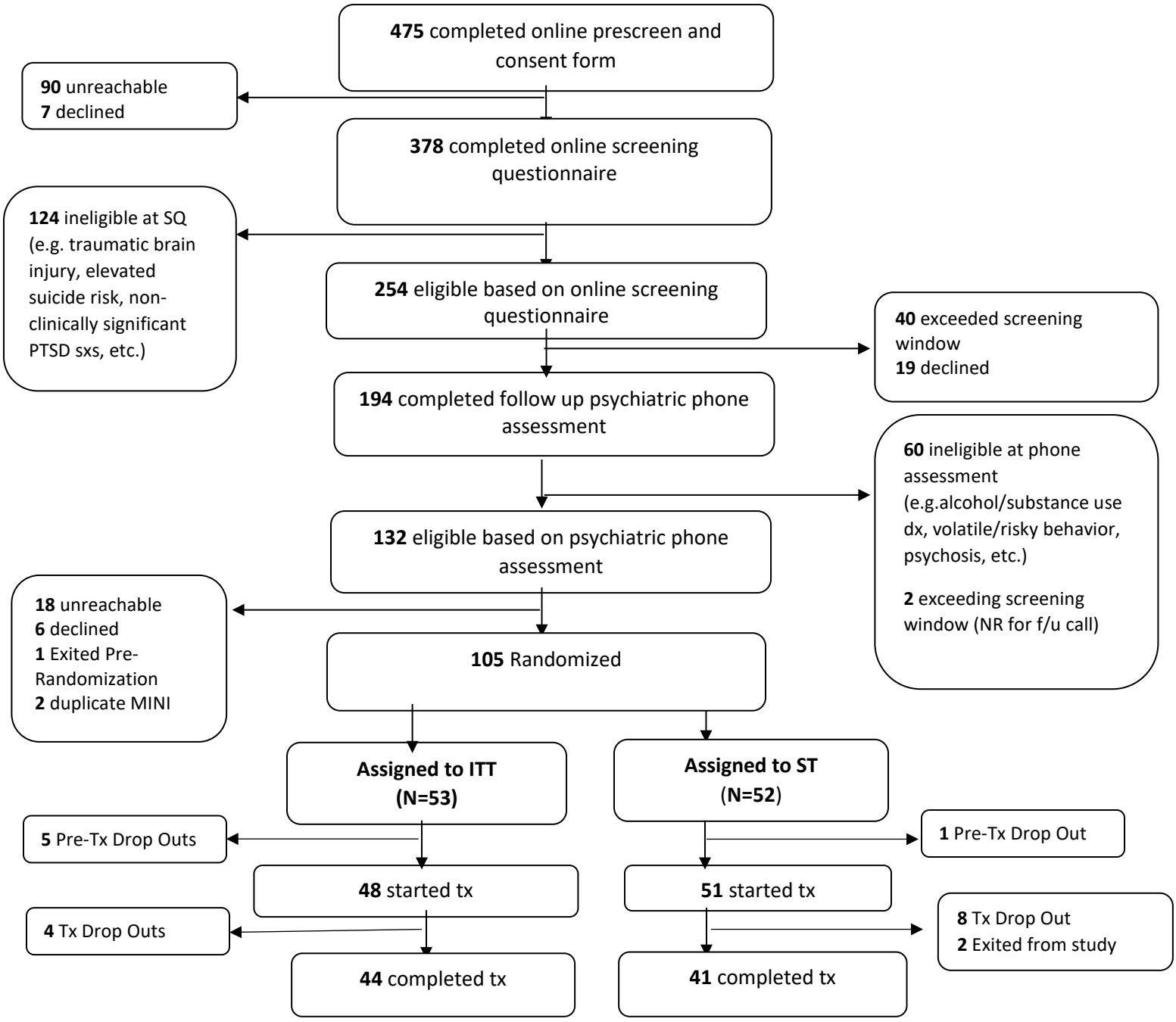
Note: Pre-Tx, Pre-treatment Questionnaire; Post-Tx, Post-treatment Questionnaire; 3MFU, Three-month Follow-up Questionnaire.

Data Analysis

Data analyses proceeded in three steps. First, sociodemographic, trauma, and clinical characteristics of participants randomized to ITT and I-MPCT conditions were compared using independent-samples t-tests and chi-square analyses. Second, linear mixed-effects models were conducted to analyze treatment effects on all study outcome measures. Treatment (ITT vs. I-MPCT), Time (baseline, post-intervention), and Treatment x Time interaction were entered as fixed factors; baseline scores as a fixed covariate, subject as a random

effect, and scores on primary (i.e., PCL-5) and secondary (e.g., BDI-II, PCL-5 symptom clusters) outcome measures as dependent variables in separate analyses. As per intention-to-treat principles, all WTC workers who completed the pre-treatment assessment, regardless of whether any participants dropped out of the trial, were included in these analyses. Third, in order to evaluate whether prior mental health treatment (i.e., psychotropic medication, psychotherapy) influenced response to ITT and/or I-MPCT, main effect of prior treatment and interaction terms of prior treatment x time, prior treatment x current treatment assignment, and prior treatment x current treatment assignment x time were incorporated in to the linear mixed-effects model for the primary outcome measure of PCL-5 scores. This third analytic step was conducted because prior mental health treatment (any vs. none) differed significantly between the two treatment groups. Effect sizes of statistically significant ($p<0.05$) effects were computed using Cohen's d.

Figure 1. Study Recruitment and Enrollment



RESULTS

Demographic and Clinical Characteristics

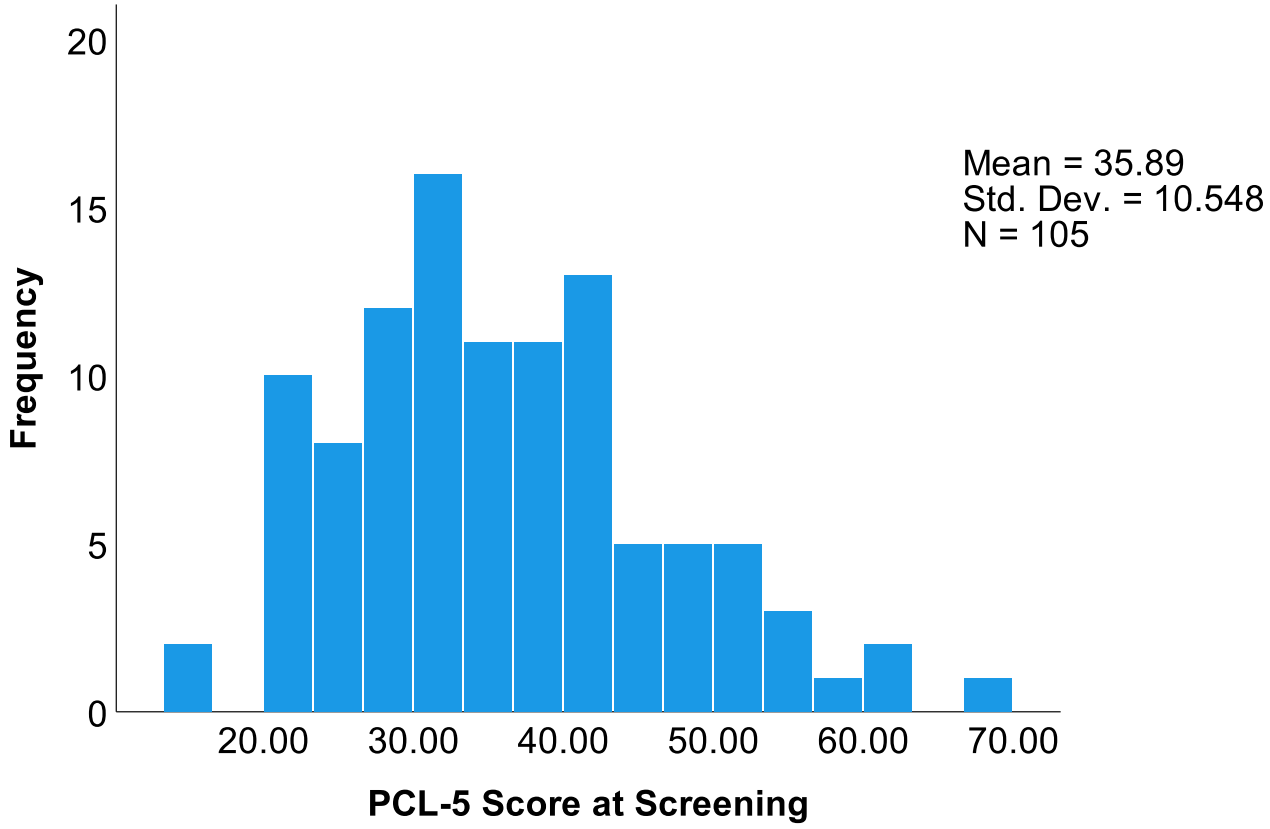
Demographic and clinical characteristics in the full sample of randomized participants are summarized in **Table 2**. Seventy-five % of participants met DSM-5 criteria for syndromal PTSD, assessed with the MINI, and the remaining had subsyndromal PTSD. **Figure 2** shows the distribution of total scores on the PTSD Checklist for DSM-5 (PCL-5) at study screening, administered about WTC-related PTSD symptoms over the prior month.

Table 2. Demographic and Clinical Characteristics

Demographic Characteristics				
Characteristic	**ITT (N=53)**	**I-MPCT (N=52)**	**t or X^2**	**p**
	Mean (SD)	**Mean (SD)**		
Age (years)	55.4 (10.1)	53.8 (9.6)	0.84	0.40
	N (%)	**N (%)**		
Male	29 (54.7%)	35 (67.3%)	1.75	0.19
Race/ethnicity			3.97	0.26
Non-Hispanic White	33 (62.3%)	38 (73.2%)		
Non-Hispanic Black	5 (9.4%)	6 (11.5%)		
Hispanic	14 (26.4%)	6 (11.5%)		
Other	1 (1.9%)	2 (3.8%)		
Education			1.60	0.21
≤ Some College/Associates Degree	31 (58.5%)	24 (46.2%)		
≥ College Graduate	22 (41.5%)	28 (53.8%)		
Work status			3.34	0.34
Employed (full or part time)	34 (64.2%)	30 (57.7%)		
Disabled from a WTC-related health problem	6 (11.3%)	3 (5.8%)		
Disabled from a non WTC-related health problem, unemployed, or student	4 (7.5%)	3 (5.8%)		0.61
Retired	9 (17.0%)	16 (30.8%)		
Marital status			0.99	0.61
Single	6 (11.3%)	7 (13.5%)		
Married or partnered	41 (77.4%)	36 (69.2%)		
Separated, divorced or widowed	6 (11.3%)	9 (17.3%)		
Participant type			0.03	0.98
Traditional responder	25 (47.2%)	25 (48.1%)		
Non-traditional responder	13 (24.5%)	12 (23.1%)		
Survivor	15 (28.3%)	15 (28.8%)		
Clinical Characteristics				
Characteristic	**ITT**	**I-MPCT**		
	Mean (SD)	**Mean (SD)**		
PCL score at screening (past month)	34.6 (10.5)	37.2 (10.6)	1.29	0.2
PCL score at pre-treatment baseline (past week)	25.2 (14.0)	31.3 (13.0)	2.31	0.023
BDI-II score at pre-treatment baseline (past week)	10.6 (8.0)	15.4 (9.0)	2.91	0.004
GAD-7 score at pre-treatment baseline (past week)	7.1 (5.1)	8.7 (5.8)	1.5	0.14
SF-8 MCS score at pre-treatment baseline (past week)	45.3 (9.5)	43.1 (10.5)	1.13	0.26
SF-8 PCS score at pre-treatment baseline (past week)	45.5 (9.4)	44.7 (9.2)	0.46	0.64
Q-LES-Q-SF at pre-treatment baseline (past week)	48.6 (9.9)	45.9 (10.0)	1.43	0.16
PTGI-SF at pre-treatment baseline (past week)	21.5 (12.1)	23.3 (11.4)	0.81	0.42
Number of comorbid health conditions	5.2 (2.7)	5.1 (3.2)	0.29	0.77
Number of lifetime trauma types	4.6 (2.7)	4.8 (3.0)	0.3	0.77
	N (%)	**N (%)**		
Syndromal PTSD diagnosis (MINI)	39 (73.6%)	40 (76.0%)	0.16	0.69
Current MDD diagnosis (MINI)	10 (18.9%)	14 (26.9%)	0.97	0.33
Recurrent MDD diagnosis (MINI)	6 (11.3%)	10 (19.2%)	1.27	0.26
Current Panic Disorder (MINI)	3 (5.7%)	3 (5.8%)	0.00	0.98
Current Agoraphobia	4 (7.5%)	4 (7.7%)	0.00	0.98
Current Social Anxiety Disorder	4 (7.5%)	5 (9.6%)	0.14	0.70
Current OCD	3 (5.7%)	4 (7.7%)	0.17	0.68
Current GAD	8 (15.1%)	10 (19.2%)	0.32	0.57

Lifetime (past) Alcohol Use Disorder	2 (3.8%)	2 (3.8%)	0.00	0.98
Lifetime (past) Substance Use Disorder	0 (0%)	1 (1.9%)	1.03	0.31
Concomitant treatment with psychotropic medication	14 (26.4%)	12 (23.1%)	0.16	0.69
Standing medication(s)	9 (17.0%)	8 (15.4%)	0.05	0.82
History of treatment	7 (13.2%)	5 (9.6%)	0.33	0.56
Any history of mental health treatment	45 (84.9%)	35 (67.3%)	4.48	**0.03**
Past one-to-one psychotherapy or counseling	39 (73.6%)	23 (44.2%)	9.35	**0.002**
Lifetime treatment with psychotropic medication	34 (64.2%)	23 (44.2%)	4.20	**0.040**
History of psychiatric hospitalization	0 (0%)	1 (1.9%)	1.03	0.31
History of suicide attempt	1 (1.9%)	1 (1.9%)	0.00	0.99
History of alcohol of substance use disorder treatment	1 (1.9%)	1 (1.9%)	0.00	0.99
Characteristics pertaining to the study treatment period				
Characteristic	**ITT**	**I-MPCT**		
	Mean (SD)	**Mean (SD)**		
Treatment duration (days)	62.8 (24.1)	66.9 (19.7)	0.86	0.39
Reported at 3-Month Follow-up				
Number of additional lifetime trauma types	0.8 (1.2)	0.4 (0.7)	1.69	0.095

Figure 2. Distribution of PTSD Symptom Severity (Total PCL-5 Scores) at Screening



Clinical Outcomes

As shown in **Table 3**, significant main effects of time were observed for the primary outcome measure of PCL-5 scores (Figure 3), as well as all PTSD symptom clusters, BDI-II, Q-LES-Q, and SF-8 MCS scores. These findings indicate that both ITT and I-MPCT yielded significant reductions in PTSD and depressive symptoms, and improvements in QOL and mental functioning. For the primary outcome measure of PCL-5 scores, the magnitude of this improvement was large (d=1.49, 95%CI=1.05-1.92). Magnitudes of improvements for secondary outcome measures were moderate-to-large, ranging from d=0.62 (95%CI=0.23-1.01) for quality of life (Q-LES-Q) to 1.33 (95%CI=0.91-1.75) for PTSD symptoms of alterations in arousal and reactivity. Main effects of treatment and interactions of treatment x time were not significant for any of the primary or secondary outcome measures.

Table 3. Primary and Secondary Outcomes

	Treatment	**Time**	**Treatment x Time**
Outcomes	**F, p-value**	**F, p-value**	**F, p-value**
PTSD Checklist for DSM-5 (PCL-5) total *(primary outcome)*	1.72, 0.191	**58.04, p<.001**	0.15, 0.70
Intrusions	0.61, 0.44	**30.78, p<.001**	0.00, 1.00
Avoidance	3.89, 0.050	**46.38, p<.001**	1.52, 0.22
Negative mood and cognitions	1.12, 0.29	**43.44, p<.001**	0.01, 0.94
Alterations in arousal and reactivity	1.65, 0.20	**46.58, <.001**	0.11, 0.73
Beck Depression Inventory – Version II (BDI-II)	2.87, 0.092	**28.52, p<.001**	0.08, 0.78
Generalized Anxiety Disorder-7 (GAD-7)	0.61, 0.43	3.49, 0.063	1.57, 0.21
Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)	0.09, 0.76	**10.19, 0.002**	0.18, 0.67
SF-8 Health Survey Mental Component (MCS)	1.92, 0.17	**16.47, <.001**	0.76, 0.39
SF-8 Health Survey Physical Component (PCS)	0.04, 0.84	1.61, 0.21	0.01, 0.93
Posttraumatic Growth Inventory (PTGI)	0.00, 0.99	3.27, 0.072	0.06, 0.81

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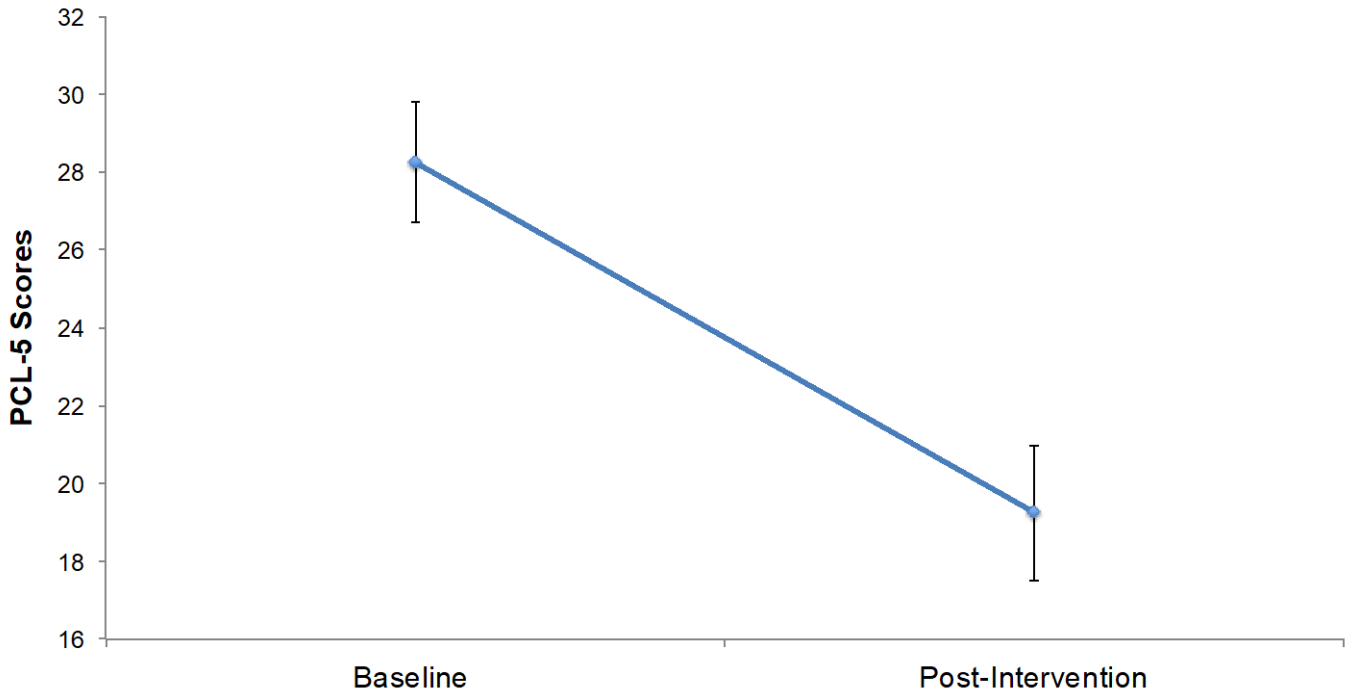
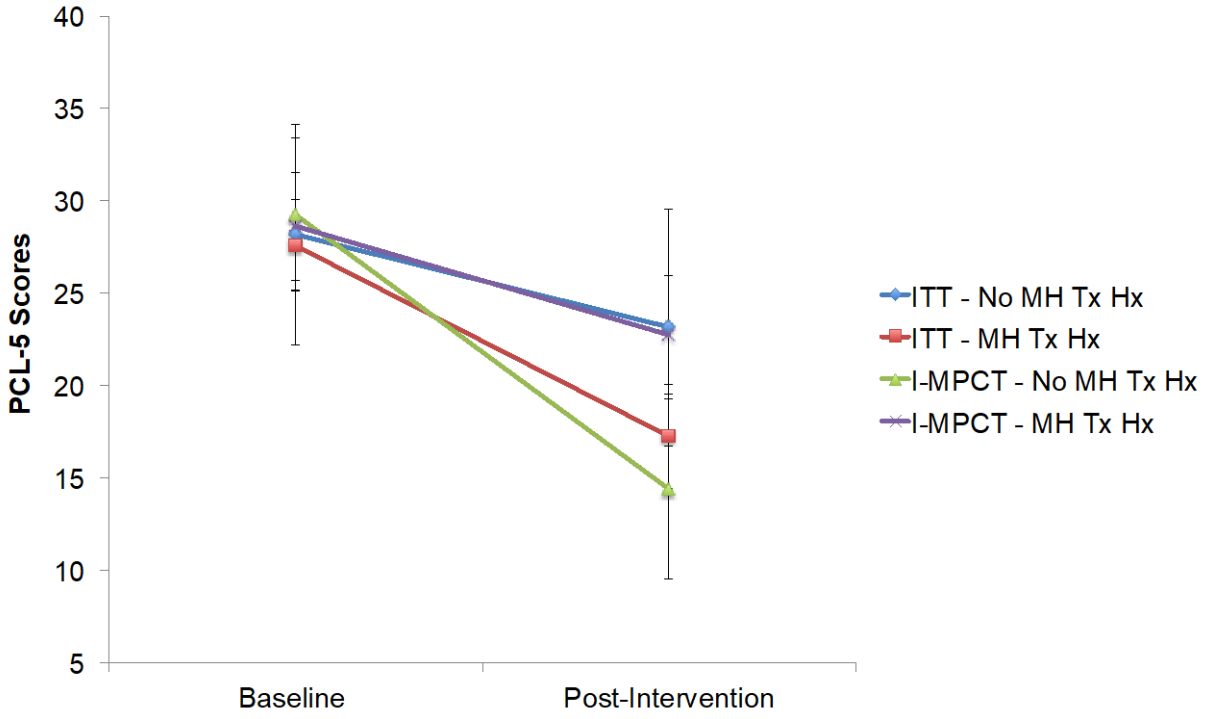
Figure 3. Main Effect of Time (Both Treatments Combined) on PCL-5 Scores



Note. Error bars represent 95% confidence intervals.

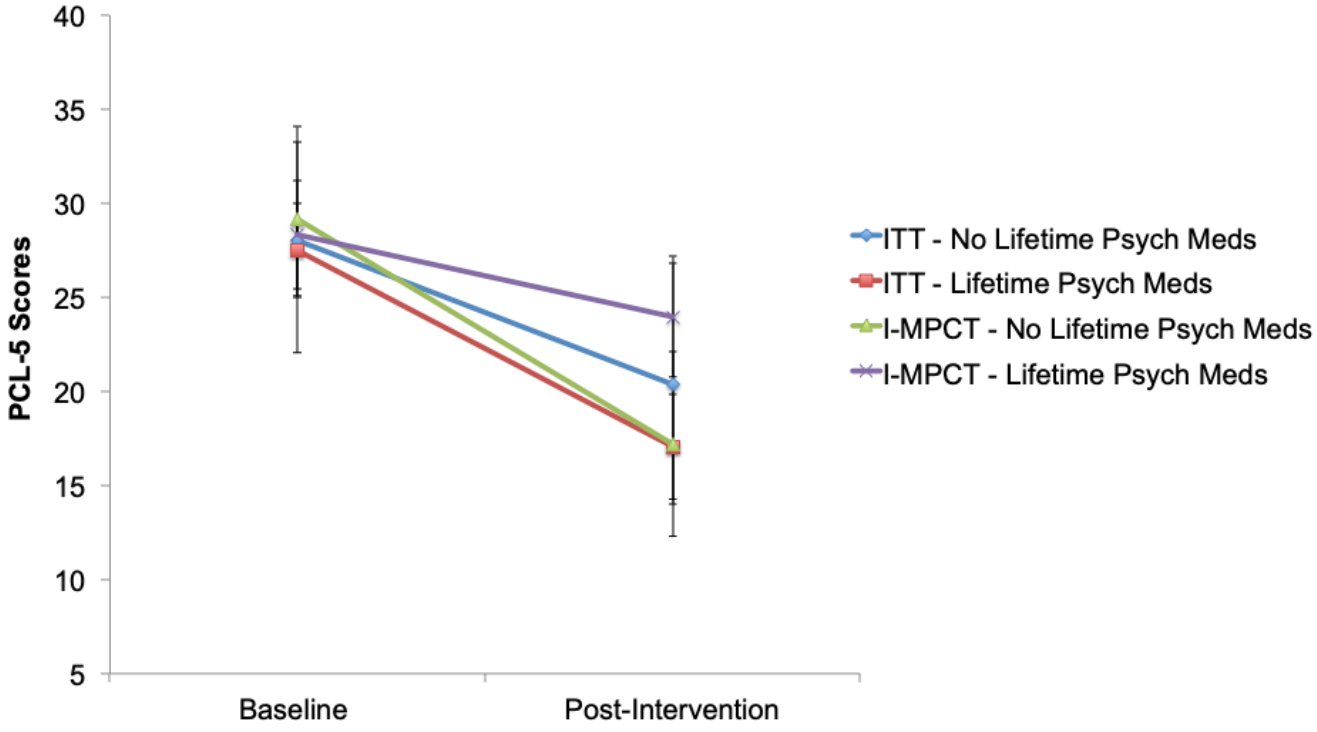
As shown in **Figure 4** below, incorporation of prior mental health treatments into the linear mixed-effects model for the primary outcome measure revealed a significant prior treatment x current treatment assignment x time interaction ($F_{[1,179]}$=6.32, p=0.013). The most pronounced reductions in PCL-5 scores were observed for those who were randomized to ITT and had prior treatment and those who were randomized to I-MPCT and did not have prior treatment, followed by those who were randomized to ITT and did not have prior treatment, and those who were randomized to I-MPCT and had prior treatment. Secondary analyses further revealed that history of treatment with psychotropic medication ($F_{[1,179]}$=4.66, p=0.032) but not psychotherapy ($F_{[1,179]}$=1.24, p=0.27) accounted for these effects (**Figure 5**).

Figure 4. Interaction between Treatment Group and Lifetime Mental Health Treatment



Note: PCL-5, PTSD Checklist for DSM-5; ITT, Integrative Testimonial Therapy; I-MPCT, Internet-based Modified Present-Centered Therapy; MH Tx Hx, prior history of mental health treatment; No MH Tx Hx, no prior history of mental health treatment.

Figure 5. Interaction between Treatment Group and Lifetime Treatment with Psychotropic Medication



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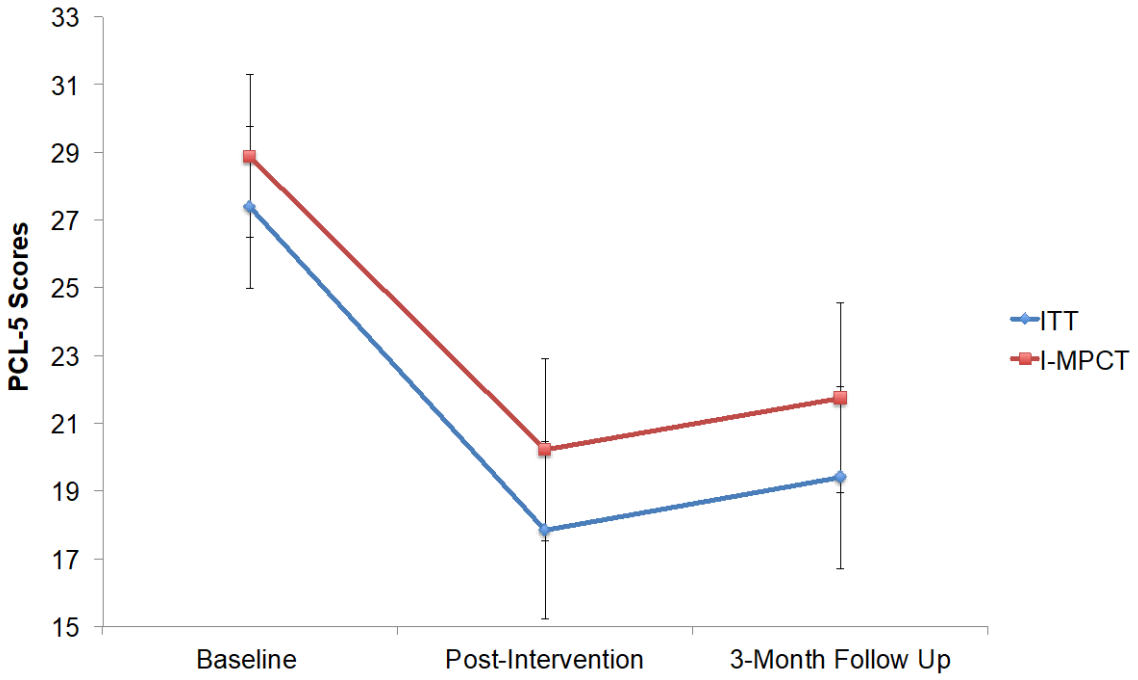
Note: PCL-5, PTSD Checklist for DSM-5; ITT, Integrative Testimonial Therapy; I-MPCT, Internet-based Modified Present-Centered Therapy; Lifetime Psych Meds, lifetime treatment with psychotropic medication; No Lifetime Psych Meds, no lifetime treatment with psychotropic medication.

Figure 6 shows results of a linear mixed-effects analysis that included baseline, post-intervention, and 3-month follow-up data. Results revealed a significant main effect of time ($F_{[1,184]}$=37.42, p<0.001), but not treatment ($F_{[1,106]}$=2.49, p=0.12) or treatment x time ($F_{[1,184]}$=0.09, p=0.91).

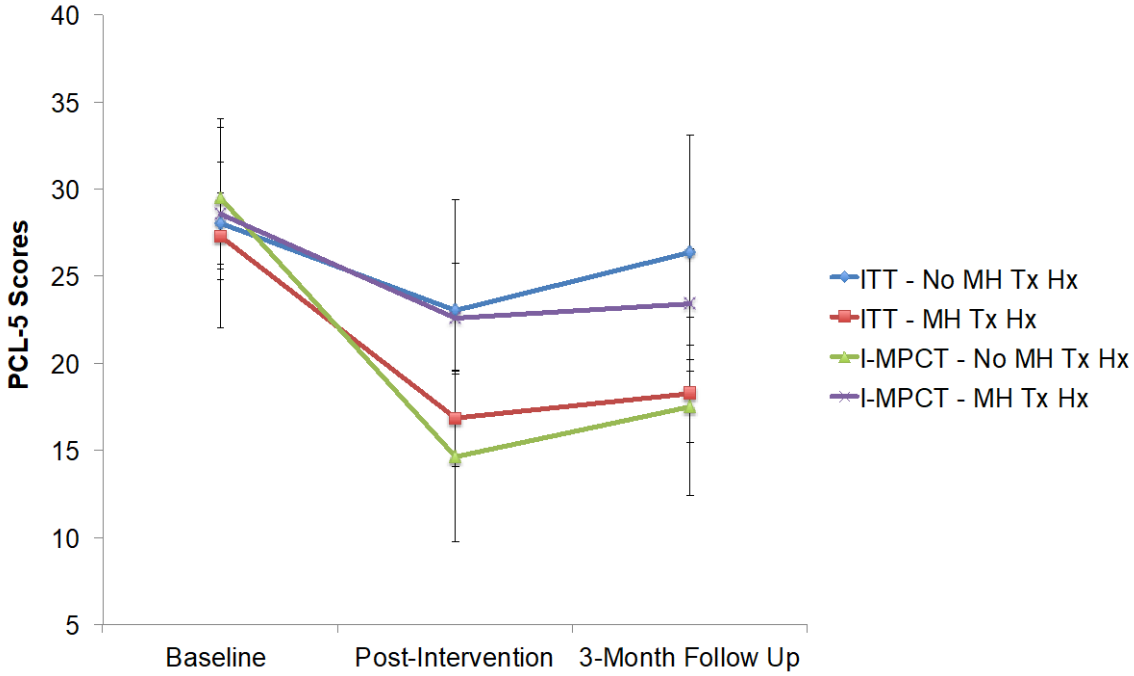
Figure 6. Effect of Treatment Group by Time at post-intervention and 3-month follow-up assessments



Note: PCL-5, PTSD Checklist for DSM-5; ITT, Integrative Testimonial Therapy; I-MPCT, Internet-based Modified Present-Centered Therapy.

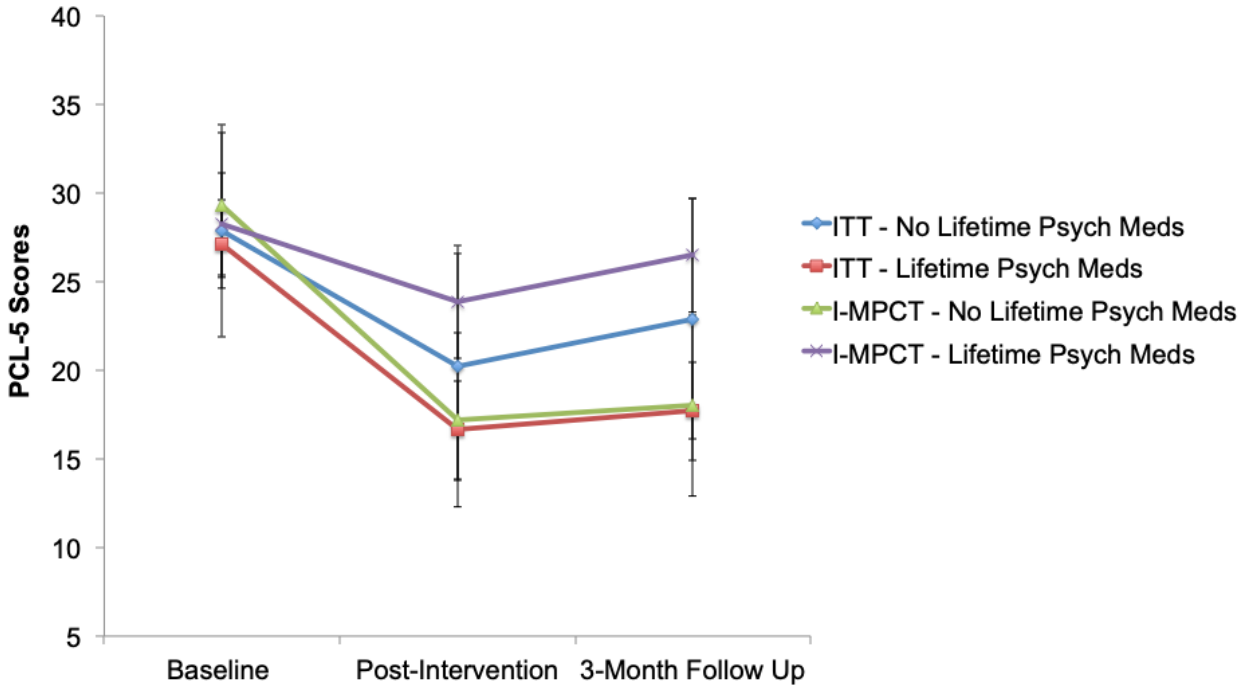
Figure 7 shows results of an analysis that examined the role of prior mental health treatment in moderating treatment effects with 3-month data additionally included in the model. A significant interaction of treatment x time x history of mental health treatment was observed ($F_{[1,181]}$=4.42, p=0.013), with the most pronounced reductions in PCL-5 scores were observed for those who were randomized to ITT and had prior treatment and those who were randomized to I-MPCT and did not have prior treatment. Secondary analyses further revealed that history of treatment with psychotropic medication ($F_{[1,180]}$=5.17, p=0.007) but not psychotherapy ($F_{[1,179]}$=0.68, p=0.51) accounted for these effects (**Figure 8**).

Figure 7. Interaction between Treatment Group and Lifetime Mental Health Treatment (including post-intervention and 3-month follow-up assessments)



Note: PCL-5, PTSD Checklist for DSM-5; ITT, Integrative Testimonial Therapy; I-MPCT, Internet-based Modified Present-Centered Therapy; MH Tx Hx, prior history of mental health treatment; No MH Tx Hx, no prior history of mental health treatment.

Figure 8. Interaction between Treatment Group and Lifetime Treatment with Psychotropic Medication (including post-intervention and 3-month follow-up assessments)



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Note: PCL-5, PTSD Checklist for DSM-5; ITT, Integrative Testimonial Therapy; I-MPCT, Internet-based Modified Present-Centered Therapy; Lifetime Psych Meds, lifetime treatment with psychotropic medication; No Lifetime Psych Meds, no lifetime treatment with psychotropic medication.

Genetic and Epigenetic Predictors and Correlates of Treatment Response (Preliminary Findings)

DNA Methylation Quality Control and Processing

A subsample of participants provided saliva samples for biomarker assays: baseline (pre-treatment) DNA was available from 67 randomized participants, and post-treatment DNA was available from 56 participants. We used probe and sample quality control recommendations outlined by the Psychiatric Genomics Consortium (PGC) PTSD Epigenome Wide Association Study (EWAS) working group [13]. Briefly, we visually inspected signal intensity of quality control probes for bisulfite conversion, specificity, negative and positive controls and removed samples with mean intensity <50% of experiment wide mean or <2000 arbitrary units. Using a probe detection p-value based on distribution of negative control probes at a threshold of 0.05, samples with <90% probe detection rate and probes missing in more than 10% of samples were excluded. Raw IDAT files were processed with default parameters of the openSesame pipeline in the R package SeSAME [14], which includes a mask for underperforming probes [15], an out-of-band probe detection p-value mask (pOOBAH; $p<0.05$), background subtraction (noob) [16], dye-bias correction (dyeBiasNL), and calculation of betas. Proportion of leukocytes were estimated with estimateLC function (R package: ewastools [17]) using a saliva methylation reference panel [18].

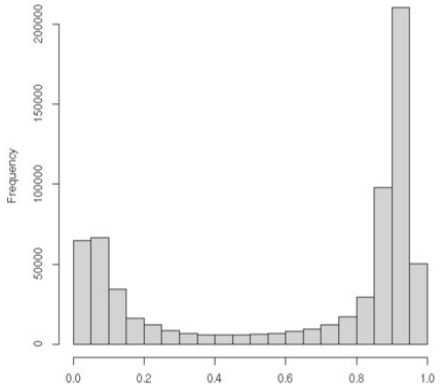

Figure 9. Distribution of beta values for a representative sample.

Statistical Analysis

Percent methylated probes per sample (PCM) were defined as the percentage of probes with beta > 0.8 (**Figure 9**). Associations of % methylation with demographic (**Figure 10**) and clinical outcome variables were assessed using a two-sided Student's t-test for categorical variables and linear regression for continuous variables in R statistical software.

We identified three variables that were associated with pre-treatment PCM: Age ($p=0.029$), proportion of Leukocytes ($p=9.17\times10^{-15}$), and current MDD ($p=0.036$). We included correction for all three of these variables in our downstream analyses to avoid confounding.

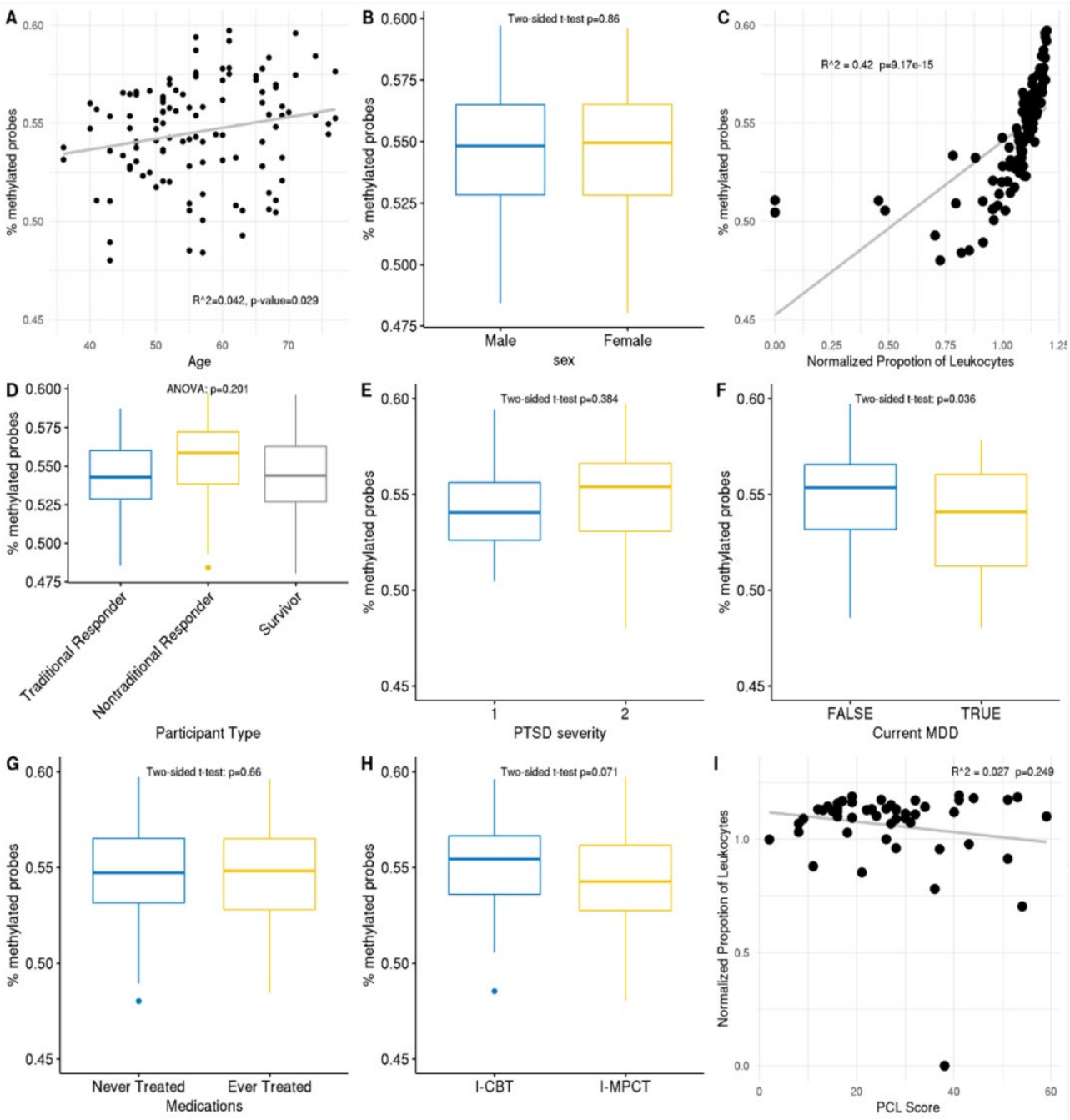

Figure 10. Association between % methylation and demographic factors.

DNA genotyping Quality Control and Processing

We assayed saliva samples on Illumina Global Screening Array 24 v3 Bead Chip for genotyping. Samples were genotyped in two batches. Using PLINK [19, 20], we applied standard genotyping quality control metrics to remove sex chromosomal variants, multiallelic variants, indels, variants failing Hardy-Weinberg Equilibrium expectations (HWE<1e-06), and variants with MAF<0.05 and low call rate (> 0.05). Samples with high missingness (>0.08) were removed. After genotype-level QC, we retained 346,813 variants and 55 individuals.

Samples were annotated for ancestry group by clustering in PCA space with 1000 Genomes superpopulation clusters (**Figure 11**) [21].

Finally, we performed a sex-check to confirm accurate assignment of study identifiers to genotyped data. Rate of sex-check failure in the first batch was high; therefore, to confirm that clinical, methylation and genotyping data all match accurately, we will perform an adapted version of DNA fingerprinting to match samples. First, we identified SNPs (1) that are common in the general population; (2) that can be confidently imputed from methylation data; (3) that are available and genotyped with high accuracy on the GSA genotyping chip. We selected 5 SNPs meeting all these criteria. Using these variants and the expected sex of participants should allow us to identify correct matches to a 1/486 accuracy, relatively quickly and without the need to re-genotype the first batch of samples. Since our second batch of samples did not suffer from any sex-check failures, we are confident that these samples are all correctly genotyped. We will apply the adapted DNA fingerprinting to this second batch first, to ensure that our assignments are correct. We will then use this approach to infer identity of all genotyped samples in batch 1.

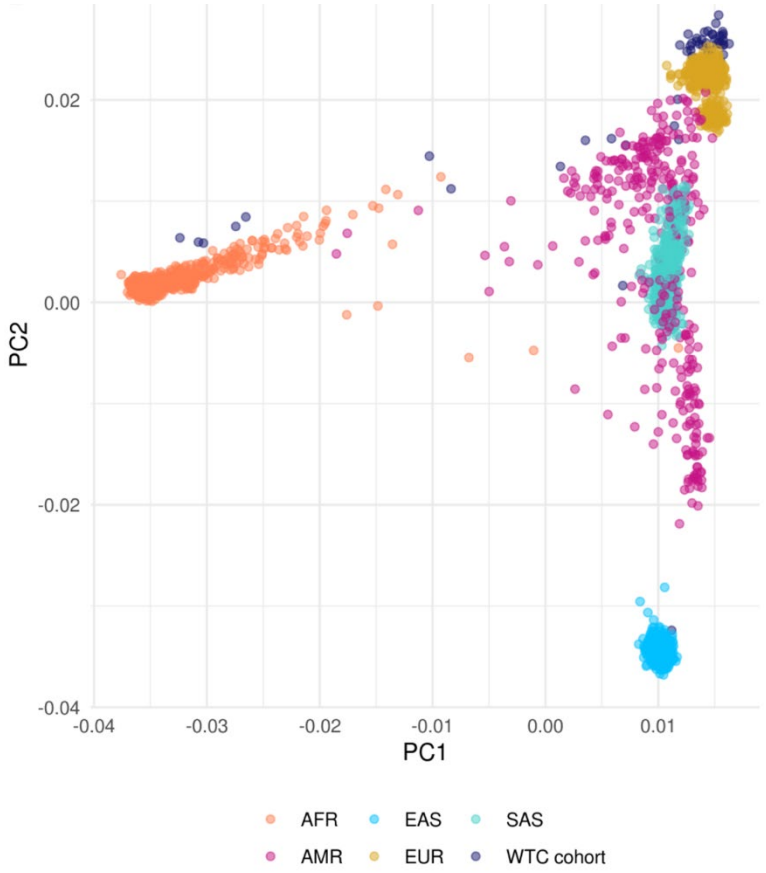

Figure 11. Principal Components analysis of WTC samples compared to 1000Genomes superpopulations.

Relationship between genome-wide methylation and therapy outcomes

First, we tested for associations between global % methylation (PCM) (defined as % of cpgs with beta values >=0.8) and a number of clinical outcomes. We found that PCM values were slightly lower post-treatment than pre-treatment (paired t-test, p=0.054, **Figure 12**); however, pre-treatment PCM values did not significantly predict overall improvement in PTSD symptom severity at post-treatment (p=0.52) or at the 3-month follow-up (p=0.14). Next, we partitioned our data according to treatment type, and again tested for a relationship between pre-treatment PCM and improvement in PTSD symptom severity at post-treatment and at the 3-month follow-up. While we did not observe any significant prediction of improvement post-treatment in either group (p=0.23,0.46), pre-treatment PCM significantly predicted improvement in PCL at the 3-month follow up in the I-MPCT group (p=0.048), but not in the ITT group (p=0.93). These analyses are still preliminary; notably, global percent methylation does not capture the effects of specific single cpg sites. Therefore, we will next test for relationships between single cpg methylation pre-treatment and improvement in PTSD symptom severity following treatment, both overall and in a treatment (group)-specific manner. We will also test for changes between methylation of specific cpg sites pre- and post-treatment and test whether these are associated with specific treatment outcomes.

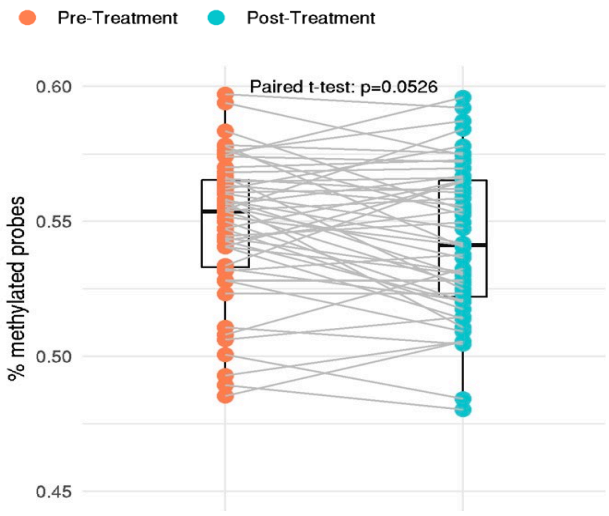

Figure 12: Change in global % methylation pre vs. post treatment.

Future work: Genotyping

We will construct a polygenic risk score (PRS) derived from the latest and largest genome-wide association studies (GWAS) statistics for PTSD, and test whether these predict (1) baseline pretreatment PTSD symptom severity or (2) improvement in PTSD symptom severity following treatment and/or at the 3-month follow-up. If either are significant, we will further test whether a joint model incorporating PRS and global % methylation can predict improvement in PTSD symptom severity following treatment.

Briefly, PRS are constructed for each individual as a weighted sum of risk alleles within the genome. Weights used to construct these scores may be derived directly from GWAS summary statistics (i.e., may simply be the observed effect size in a study), or may be shrunken or scaled to optimize performance. We will follow the latest gold-standard approaches to maximize predictive accuracy of our scores.We will correct for sex, birth year, and ancestry (both self-reported and genotype-derived). We will apply a nested modelling approach to calculate the phenotypic variance explained by our polygenic score, as follows:

$$R^2_{Full}: PCL \sim PRS + Sex + Birth\ Year + Ancestry$$

$$R^2_{Baseline}: PCL \sim Sex + Birth\ Year + Ancestry$$

$$R^2_{PRS} = R^2_{Full} - R^2_{Baseline}$$

DISCUSSION

This was, to our knowledge, the first RCT to compare Integrative Testimonial Therapy (ITT), a therapist-assisted, internet-based cognitive-behavioral psychotherapy for individuals with PTSD, to an active comparison condition, therapist-assisted, internet-based Modified Present Centered Therapy (I-MPCT), and the first RCT of internet-based psychotherapies for WTC workers and survivors with persistent clinically significant WTC-related PTSD symptoms. Our findings indicated that both ITT and I-MPCT yielded significant, large-magnitude reductions in PTSD symptom severity, the primary outcome in this study. Additionally, moderate-to-large-magnitude improvements were observed for PTSD symptoms of alterations in arousal and reactivity, depressive symptoms, quality of life, and mental health-related functioning. One possible explanation for why I-

MPCT worked as well as ITT is that it focuses on post-9/11/2001 life stressors, which we and others have previously found to be strongly linked to WTC-related PTSD symptom severity in WTC responders.

Additional analyses examining moderating effects of prior mental health treatment revealed significantly higher improvement in overall PTSD symptom severity in participants randomized to ITT who had a history of prior mental health treatment, and in those randomized to I-MPCT who did not have a history of prior treatment. Secondary analyses further revealed that lifetime treatment with psychotropic medication (but not psychotherapy) accounted for these effects. Analyses also including the 3-month follow-up assessment revealed that PTSD symptom improvements were generally maintained over time, with no significant difference between treatment groups. Consistent with the findings at post-treatment, PTSD symptom improvements at the 3-month follow-up assessment were highest in in participants randomized to ITT who had a history of prior mental health treatment, and in those randomized to I-MPCT who did not have a history of prior treatment.

These differences in treatment response between the two groups by prior mental health treatment history suggest that I-MPCT –focused on generating potential solutions for current life stressors– might be the recommended first-line psychotherapy for WTC responders and survivors with clinically significant PTSD symptoms who have not previously engaged in mental health treatment. Conversely, the exposure-based cognitive-behavioral therapy ITT –focused on WTC-related traumas and integrating these traumatic experiences WTC responders' and survivors' lives– suggest that ITT should be the psychotherapy of choice for WTC responders and survivors with clinically significant PTSD symptoms despite a prior history of mental health treatment, and in particular those with a lifetime history of treatment with psychotropic medication, including current treatment with medication. Additional analyses currently in progress will examine the potential moderating effect of therapeutic alliance between patient and therapist, reported by study participants on the Working Alliance Inventory.

Analyses of genetic and epigenetic predictors and correlates of treatment response are currently in progress. DNA methylation analyses will be corrected for age, proportion of leukocytes, and current co-morbid MDD diagnosis, as these three characteristics were found to differ significantly between the treatment groups in the subsample of participants who provided saliva samples for biomarker studies. Preliminary DNA methylation analyses revealed slightly lower global % methylation (PCM) at post-treatment than pre-treatment, but pre-treatment PCM did not significantly predict PTSD symptom improvement at post-treatment or 3-month follow-up. In further preliminary analyses, pre-treatment PCM significantly predicted improvement in PTSD symptom severity at 3-month follow-up, only in the I-MPCT treatment group. Additional analyses currently in progress include testing for relationships between methylation of specific cpg sites (pre-treatment and changes from pre- to post-treatment) and treatment outcomes.

Conclusion

Findings from this novel RCT of therapist-assisted, internet-based psychotherapies suggest that both ITT and I-MPCT are efficacious for the treatment of WTC responders and survivors who have continued to experience clinically significant PTSD symptoms two decades following the 9/11 terrorist attacks. Findings additionally suggest personalizing these treatment interventions –selection of ITT vs. I-MPCT– based on the affected individual's mental health treatment history.

Provision of these therapist-assisted internet-based psychotherapies to WTC responders and survivors with PTSD can greatly reduce barriers preventing access to effective interventions for this chronic and disabling condition, as these interventions are not limited by geographical distance or stigma associated with attending in-person mental health treatment sessions. As the current COVID-19 pandemic has increased the need for effective treatment interventions that can be delivered remotely, dissemination of ITT and I-MPCT across the WTC Health Program can improve access to effective treatment interventions for WTC-related PTSD, one of the most prevalent and persistent health conditions in WTC populations.

B.2 (Final Report Narrative.pdf)

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Other relevant recent publications

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Poster Presentations

1. Brinkman, H.R., Minaya, C., Hirschowitz, C., Brown, A.D., Pietrzak, R.H., & Feder, A. (2018). PTSD and Negative Self-Appraisal in World Trade Center Responders: Preliminary Findings from an Ongoing RCT of a Web-based Narrative Writing Therapy. Poster, International Society for Traumatic Stress Studies annual meeting, Washington, DC.
2. Kowalchyk, M., Torres, D., Brinkman, H., Bharadway, S., Brown, A., Pietrzak, R., & Feder, A (2020) Symptom Dimensions and Persistent Trauma Salience in World Trade Center Responders and Survivors with Chronic PTSD. Poster, Society of Biological Psychiatry (SOBP) annual meeting, New York, NY.
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4. Kowalchyk, M., Chernoff, E., Brinkman, H., Brown, A., Pietrzak, R., & Feder, A. (2021). Social Support Mediates the Relation between Perceived Ability to Cope with Trauma and PTSD Severity in World Trade Center Trauma Survivors. Poster, Anxiety and Depression Association of America annual meeting, virtual meeting.

Cumulative Inclusion Enrollment Table (see below)

Inclusion of Gender and Minority Study Subjects

For this study we recruited and enrolled WTC rescue, recovery and clean-up workers, as well as WTC survivors. The study sample is composed of WTC responders and survivors from both genders, and diverse ethnicity and racial background, broadly reflecting the composition of WTC-affected populations.

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Inclusion of Children

Children are not included in this study, completed 20 years after 9/11/2001. (Of note, some WTC survivors who participated in this study were children or adolescents when the 9/11 terrorist attacks took place).

Materials Available for Other Investigators

The final dataset from this study includes data regarding demographic characteristics, data from self-report questionnaires and clinical data from interviews with study participants; and outcome data from self-report questionnaires completed by participants at baseline, post-treatment, and 3-month follow-up assessments. Biomarker data includes genetic and epigenetic (DNA methylation) data obtained from saliva samples provided by a subsample of study participants. The final dataset is free of any identifiers that would permit linkages to individual research participants; however, the possibility exists that the variables collected could lead to deductive disclosure of individual subjects, particularly those with unusual characteristics. Thus, data and associated documentation from this study will only be made available to other users under a data-sharing agreement that is in compliance with existing polices of the WTC Health Program Data Center.

Cumulative Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title: A Pilot Randomized Controlled Trial of an Internet-based Psychotherapy for Posttraumatic Stress Disorder in Police World Trade Center

Comments:

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native										0
Asian	1									1
Native Hawaiian or Other Pacific Islander										0
Black or African American	7	2								9
White	22	48		3	1					74
More Than One Race	2	1								3
Unknown or Not Reported		2		6	10					18
Total	**32**	**53**	**0**	**9**	**11**	**0**	**0**	**0**	**0**	**105**

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C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Norbury A, Brinkman H, Kowalchyk M, Monti E, Pietrzak RH, Schiller D, Feder A. Latent cause inference during extinction learning in trauma-exposed individuals with and without PTSD. Psychological medicine. 2021 March 8:1-12. PubMed PMID: 33682653; DOI: 10.1017/S0033291721000647.
N/A: Not NIH Funded	Brinkman HR, Kowalchyk ML, Cahn L, Aaronson CJ, Bottche M, Presseau C, Markowitz JC, Litz BT, Huckins L, Yehuda R, Knaevelsrud C, Pietrzak RH, Feder A. Internet-based cognitive behavioral therapy vs. Internet-based modified present-centered therapy for World Trade Center responders and survivors with PTSD: Rationale and design of a randomized controlled trial. Int J Clin Trials. Forthcoming.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
FEDERADRI	Y	Feder, Adriana	MD	PD/PI	3.3	0.0	0.0			NA
PIETRZAK	Y	Pietrzak, Robert H		PD/PI	3.6	0.0	0.0			NA
AARONC10	Y	Aaronson, Cindy J	MOTH,PHD,OTH	Co-Investigator	3.3	0.0	0.0			NA
HBRINKMAN	N	Brinkman, Hannah	BA,PHD	Clinical Research Coordinator	12.0	0.0	0.0			NA
KOWALCHYKM	N	Kowalchyk, Mary		Clinical Research Coordinator	12.0	0.0	0.0			NA
	N	Greene, Andrea		Study Therapist	11.1	0.0	0.0			NA
	N	Hok, Julissa		Study Therapist	11.1	0.0	0.0			NA
	N	Cahn, Leah		Study Therapist	3.4	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Provision of these therapist-assisted internet-based psychotherapies to WTC responders and survivors with PTSD can greatly reduce barriers preventing access to effective interventions for this chronic and disabling condition, as these interventions are not limited by geographical distance or stigma associated with attending in-person mental health treatment sessions.

Additionally, the current COVID-19 pandemic has increased the need for effective treatment interventions that can be delivered remotely, such as the two psychotherapies evaluated in this study. Given the number of psychotherapists experienced in treating WTC workers and survivors across WTC Health Program locations, training therapists in the delivery of these internet-based psychotherapies to WTC-affected populations is highly feasible. Dissemination of these therapies across the WTC Health Program can improve access to effective treatment interventions for WTC-related PTSD, one of the most prevalent and persistent health conditions in WTC populations.

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

File(s) uploaded:
CumulativeInclusionEnrollmentReport.pdf

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

Cumulative Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title: A Pilot Randomized Controlled Trial of an Internet-based Psychotherapy for Posttraumatic Stress Disorder in Police World Trade Center

Comments:

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
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Total	**32**	**53**	**0**	**9**	**11**	**0**	**0**	**0**	**0**	**105**

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

Findings from this novel randomized controlled trial of therapist-assisted, internet-based psychotherapies suggest that both Integrative Testimonial Therapy (ITT), a trauma-focused cognitive-behavioral therapy, and Internet-based Modified Present Centered Therapy (I-MPCT), focused on current stressors, are efficacious for the treatment of WTC responders and survivors who have continued to experience clinically significant PTSD symptoms two decades following the 9/11 terrorist attacks. Findings additionally suggest personalizing these treatment interventions –selection of ITT vs. I-MPCT– based on the affected individual's mental health treatment history.

Provision of these therapist-assisted internet-based psychotherapies to WTC responders and survivors with PTSD can greatly reduce barriers preventing access to effective interventions for this chronic and disabling condition, as these interventions are not limited by geographical distance or stigma associated with attending in-person mental health treatment sessions.

Additionally, the current COVID-19 pandemic has increased the need for effective treatment interventions that can be delivered remotely, such as the two psychotherapies evaluated in this study. Given the number of psychotherapists experienced in treating WTC workers and survivors across WTC Health Program locations, training therapists in the delivery of these internet-based psychotherapies to WTC-affected populations is highly feasible. Dissemination of these therapies across the WTC Health Program can improve access to effective treatment interventions for WTC-related PTSD, one of the most prevalent and persistent health conditions in WTC populations.