Author’s response to reviews

Title: Developing Substance Use Programming for Person-Oriented Recovery and Treatment (SUPPORT): Protocol for a pilot randomized controlled trial

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Author’s response to reviews:

Thank you for your thoughtful and detailed review of our protocol. We found the comments extremely helpful for improving the manuscript. We have provided a detailed response to each of the concerns below. We have made changes where appropriate in the document using track changes.

Response to Reviewers

Reviewer #1

Comment: One comment concerns the value-laden language of the text: While I may share many of their views, they do not necessarily do their text a service by using language that so strongly communicates their views (e.g., calling drug courts "paternalistic" or stating that a strength-based comprehensive recovery network makes long-term recovery more likely). I'd rather have the authors describe the existing system in more neutral terms, concerning the helpfulness of recovery-based approaches, simply describe the evidence, limited as it is, and expand on the underlying logic - this is, after all, a protocol for a feasibility study in a field that is notoriously difficult to research for legal reasons.
Response: We have changed language on pg. 3 related to Reviewer 1’s concerns. We removed paternalistic so the sentence now reads: “The vast majority of criminal justice interventions for SUD are aimed at offenders prior to incarceration (e.g., drug treatment courts) and do not fit within a recovery paradigm in that they are abstinence-focused and have limited client choice”.

We have also made the following additions to the text on p. 3 to provide some better framing related to the recovery paradigm: “The vast majority of criminal justice interventions for SUD are aimed at offenders prior to incarceration (e.g., drug treatment courts) and do not fit within a recovery paradigm [5, 9, 11]. Recovery-oriented service models emphasize such factors as empowerment and consumer choice [12, 13], and there is evidence that behavioral health services emphasizing these factors lead to positive outcomes for clients [14–17]. Compatible with the recovery paradigms, though not well tested to date, the recovery-oriented system of care (ROSC) approach for returning inmates offers a choice of services and aims to strengthen both internal and external aspects of recovery capital [18, 19].”

Comment: Some mention of self-determination theory might be in order as well, especially as the authors make use of an instrument that (to my memory) is based on said theory.

Response: While we understand the reviewer’s request, we do not feel it is appropriate to highlight self-determination theory in this manuscript, as the theory itself does not underlie the SUPPORT intervention and may thus confuse readers. We are using the self-determination scale as an approach to measure the construct of agency, which is part of the pragmatic theory guiding the intervention. Due to the lack of availability of instruments to measure agency, we chose the closely-related concept of self-determination. Therefore, our use of the measure is because it has been demonstrated to be a valid and reliable instrument, not because it is attached to a specific theory.

Comment: Similarly, the authors describe improved outcomes in relation to the IN-ATR program, but do not make clear, if these improvements can reasonably be attributed to the program, or if they may just as well simply have coincided with the running of the program. If outcomes deteriorated after the closing of the program, it would provide some evidence to support the view that the improvements may be attributable to IN-ATR, but regardless, the point is that the evidence is definitely sufficiently weak to warrant spending an effort on research.

Response: There was a statement at the end of the introduction on pg. 6 critiquing previous studies of ATR as being “post-hoc and observational”, we have reworded to clarify this includes the IN-ATR evaluation: “While this is encouraging, these studies—including the evaluation of IN-ATR [25]—were post-hoc and observational in their approach, making it difficult to determine the extent to which ATR was directly responsible for outcomes.”

Comment: The description of the differences between the SUPPORT program and the IN-ATR program confused me a bit - are these differences important for my appreciation of the study, once the results of the pilot (and later, hopefully, of the full study) come out? If these differences are important to the protocol, it would be because they describe how the treatment has been adapted to a new and more narrow target group.
Response: We have included a sentence on p. 5 to clarify the reason behind the modifications: “These modifications are based on both the need to develop SUPPORT without government backing and lessons learned from the evaluation of IN-ATR.”

Comment: Under the description of TAU, the authors state: "Clients in the TAU group will have few options than those in SUPPORT;" I suspect this should be "fewer"?

Response: Thank you for pointing this out. We corrected this to “fewer.”

Comment: The abbreviation RC is used under "Data collection" but never written out, as far as I could see. Is it "Recovery coaches?"

Response: Thank you for pointing this out; we had not previously defined this abbreviation. While this paper was under review, we modified our data collection procedures so that a trained research assistant will enroll and collect data with all participants, rather than having the recovery coach collect data with the SUPPORT group. Thus, we have changed the description of these procedures on pg. 13 in our text, and the paragraph no longer refers to “RCs”.

Comment: A practical question: How will data be collected, if the client has poor reading skills?

Response: Thank you for this question. Similar to our response above, while this paper was under review, we modified our data collection procedures. The research assistants will now read all data collection questions to the participants. We believe this will remove barriers related to illiteracy and also decrease the time it takes to collect data. We believe research assistants will receive more valid and reliable answers than recovery coaches, as they are not involved in the delivery of services. We have changed the description of these procedures in the text on pg. 13.

Comment: In terms of recidivism, since the authors probably have access to the exact date of arrest, it is perhaps feasible to do a time-to-event model (such as Cox regression) rather than Fisher's test. The Cox regression model would be much more powerful, because it includes time in the model.

Response: We had previously indicated that we would be using event history but have changed the text to specify that we will use Cox Regression. Please see pg. 16: “We will also estimate event history models using Cox Regression survival analysis to model the time to recidivism while controlling for covariates and repeated measures of various intermediate and collateral outcomes to, and will consider the impact of participation in the program and of treatment characteristics on the likelihood of and length of time to recidivism.”

Comment: In terms of the mixed effects regressions, I assume that these will be conducted on the recovery-related outcomes. However, a more precise description of the analysis would be an improvement - e.g., will time be modelled as a categorical variable that interacts with randomization, or as a continuous variable that interacts with randomization? Will the baseline values be controlled for, or will the baseline assessment be included in the analysis? I would prefer if the authors write out a line of code from their statistics program to clarify this.
Response: Additional clarification has been added on pg. 15. Mixed effect models will be conducted to analyze recovery related outcomes, where measures of the outcomes at follow-up visits are a dependent variable and the baseline outcome measure is included as a covariate. Time will be modeled as a categorical variable that interacts with the treatment group. We are not to a point in this study where we can provide any code.

Reviewer #2

Comment: Please add "Protocol for" before "a pilot randomized controlled trial" in the title of the manuscript.


Comment: It would be helpful to add two sections to the end of the "Background": firstly relating to the study "Hypothesis" and secondly the "Aims and Objectives" of the study. There may be primary and secondary objectives, which would link to the primary and secondary outcomes of the study (see next point). The primary objectives of a pilot study should relate to the demonstration of feasibility/acceptability/deliverability/safety etc of the interventions/outcome assessments/recruitment/randomisation, etc or to provide reliable estimates for sample size calculation for a future definitive trial.

Response: We have added this information in the beginning of the methods section on pg. 6: “The primary goals of the pilot are to: (a) establish feasibility of instruments and protocols and (b) obtain more accurate effect sizes to estimate the sample size for future work than was possible through our prior evaluation of IN-ATR through comparisons between SUPPORT and TAU client outcomes. Our primary hypotheses are: (a) SUPPORT clients will have measurably better treatment outcomes than TAU clients and (2) we will be able to identify specific program elements and processes driving these outcomes by understanding SUPPORT clients’ program experiences.”

Comment: Please clarify the primary and secondary outcomes. The primary outcomes of a pilot study should link directly to the pilot/feasibility objectives; therefore, there should be primary "feasibility" outcomes as well as primary (and/or secondary) "patient-centered" (or "efficacy") outcomes of interest. Please label your primary and secondary outcomes accordingly (eg as primary feasibility outcomes, primary efficacy outcomes, secondary efficacy outcomes, etc).

Response: Our primary outcomes are substance use and abstinence. We have clarified this in the “outcome measures” section of the manuscript on pg. 9.

Comment: The description of the randomisation process (using a pre-established list) suggests that there is no allocation concealment. Allocations must be concealed in order to prevent selection bias; can you provide information on how this will be achieved (e.g. through the use of sealed opaque envelopes or telephone randomisation)?
Response: We have updated these details within the procedure description on pg. 12. “Prior to meeting clients for enrollment, research assistants will receive data collection packets labelled with a pre-established identification number and containing a concealed card with the group assignment that has been randomly reassigned to the identification number. After the baseline assessment to determine eligibility, the client will be asked to consent to participate in the study; if they consent, the research assistant will open the envelope containing the card and notify the client of their group assignment.”

Comment: Analysis of a pilot study should focus on confidence interval estimation, rather than hypothesis testing or statistical modelling, as the limited sample sizes used in pilot studies mean that they are typically underpowered for statistical testing. Although it is interesting to explore possible outcomes, inferential statistics should be used with great caution. As such, please could you rephrase the statistical analysis section, clarifying that the analysis will focus on confidence interval estimation, and that any hypothesis testing will be considered entirely exploratory in nature.

Response: We agree that pilot studies generally do not focus on hypothesis testing and statistical modeling should be exploratory. We originally included this because it was a request of our grant reviewers. We have made revisions on pg. 15 to indicate that the analyses will be exploratory.

Comment: Please could you clarify the sample size statement? Pilot studies are not usually powered to detect significant differences between randomised groups, as the purpose of pilot studies is not to provide definitive results in terms of powered statistical comparisons. Instead, sample sizes are usually justified in terms of providing sufficient precision for estimation of parameters to inform sample size estimation for future definitive clinical trials. The authors may be interested in the following additional references in relation to this issue:

Response: We agree that pilot study is usually justified for precision instead of power. We have made modifications in the sample size section of the draft. We had included the power calculation due to grant reviewer’s requests. We have corrected this in the manuscript on pg. 11.

Comment: You have quoted a minimum clinically important difference (MCID) of 10 days between groups (after 1 year of treatment) in your sample size calculation - and the justification for this is an average of 7 days observed after 6 months of IN-ATR treatment. This would suggest that you expect the treatment effect to increase from (at least) 7 days after 6m to (at least) 10 days after a year’s treatment - is this realistic? Also, the power calculation suggests in excess of 99% power, using the parameters provided in the sample size section - please could you clarify the MCID on which the power calculation has been based?

Response: As we have modified our sample size statement to focus on precision over power, this comment is no longer relevant and the corresponding text has been removed.

Comment: Pilot studies should be assessed in terms of progression criteria related to the feasibility objectives of the study. Please could you describe the feasibility criteria on which the pilot study will be assessed (eg recruitment/consent rate > 50%, acceptability or retention > 70%)
with threshold values for each criterion, which would inform the readers if a future study is indeed feasible.

Response: We have added the following clarification on p. 18: “Assessment of the feasibility of protocols to advance to the subsequent trial will hinge on our ability to obtain a study recruitment rate above 60% and a participant retention rate above 70% (goals based on our prior experience the IN-ATR program, as well as our expectation that potential modifications to improve participant satisfaction with the study and intervention protocols will be needed based on learning during the pilot).”

Comment: I understand that the CAPI interviews at 15m are carried out in the SUPPORT group only, "to understand retention of treatment effects three months post discharge". Is it not equally important to assess treatment effect retention in the TAU group, to allow comparison with the SUPPORT group?

Response: We initially did wish to include interviews with both groups at this time point; however, funding limitations will prevent us from conducting these interviews with both groups. For the purposes of the pilot, we feel it is only necessary to get this information from the treatment group to assist us in estimating effect sizes for the larger study.

Comment: When follow up data are missing due to incarceration, would it be possible to use this information ("negative" reason for missingness) to inform meaningful interpretation of the missing results (eg imputing a poor outcome for these patients in a sensitivity analysis)?

Response: Our previous pilot work with this location has suggested that there will be minimal reincarceration during the follow-up period; however, in those cases when individuals are rearrested we will be collecting information on the cause and outcome of the arrest. This will inform the reason for the “missingness” and of particular importance, we will be examining the cause of the arrest and especially in those cases where failure was the result of technical violation and whether this was the result of substance use.

Comment: The data monitoring section refers to "preliminary analyses of the data (at 6, 12 and 15 months)”: please can you specify what these analyses will involve, to ensure transparency relating to multiple testing of outcome data? For example, will these analyses relate only to safety outcomes, or will there be between-group interim analyses conducted prior to the end of the study? If the latter, do you have stopping rules on which to base any decisions in relation to stopping the trial early, which will account for the impact of multiple testing on subsequent interpretation of the final analyses?

Response: These analyses are not intended to stop the trial early but rather to ensure that data are being collected correctly and that participants are being randomized correctly. Thus, preliminary analysis will be looking for issues concerning missing data or group differences. We have clarified the text to show that these preliminary analysis are intended to “monitor client withdraws and complaints to ensure participant safety and to identify any significant negative outcomes or unintended consequences associated with SUPPORT involvement or the research protocols”. 
Comment: p8 line 12: add a full stop after coach
Response: Corrected.

Comment: p8 line 31: put a semi-colon (rather than comma) between "vouchers" and "rather"
Response: Corrected.

Comment: p8 line 41: replace "few" with "fewer"
Response: Corrected.

Comment: p11 line 12/14: please check this sentence for meaning ("attendance at self-report attendance...")
Response: Corrected.

Comment: p12 line 41: add a comma after "eligibility"
Response: Corrected.

Comment: p12 line 53: add closed bracket ")" after "technology"
Response: Corrected.

Comment: p17 line 17: add "and" between "organizations" and "a more diverse group..."
Response: Corrected.

Comment: p30 line 39: add apostrophe after "subjects" (ie subjects') and comma after "date of birth"
Response: Corrected.

Additional Response:

During the paper review period, while we were planning study implementation, we modified additional data collection procedures based on organizational needs and mock enrollment experiences. These changes are described below:

- The available voucher funding for clients was reduced from $1,400 to $700, with an additional $300 available upon request (pg. 7): “The SUPPORT program will provide clients with up to $700 worth of vouchers (depending on client’s stated goals and identified barriers) to cover the cost of additional flexible support services over the 12 months of program enrollment. Additional voucher funding, up to $300, will be available to the client at the request of the
recovery coach should additional resources be deemed necessary for them to meet the goals of their recovery plan.”

• To simplify data collection procedures and prevent participant confusion, we modified the time points at which the social network data is collected. Rather than only collecting this data at baseline and 12 months, we will now collect this data at all CAPI data collection time points, which include baseline, 6 months, 12 months, and 18 months (SUPPORT group only) (pg. 14).

• The participant incentive amount changed from $20 to $30 for each CAPI interview completed. Additionally, due to the changes in the timing of the social network data collection, participants will receive an additional $30 at the 6 month and 18 month (SUPPORT group only) time points. Thus, participants may receive $60 total for completing all data at baseline, 6 months, 12 months, and 18 months (SUPPORT group only) (pg. 13, 14).

We have also added an additional author, Huiping Xu. Dr. Xu is the biostatistician on the project, and she assisted us in responding to Reviewer 2’s questions related to the sample size and analysis.