The Potential Benefits of Utilizing a Standard of Care Treatment Study to Prepare Participants for Enrollment in a Treatment-Resistant Depression (TRD) Clinical Trial

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Introduction

- Participants must demonstrate non-response to at least one antidepressant (ADT) in their current major depressive episode to enroll in clinical trials of second-line or third-line ADTs. Over 90% of potential participants at our site fail to meet this criteria due to inadequate dosing, ADT burnout, and low adherence for this class of drugs.[1] As a result, second-line and third-line antidepressant trials enroll much more slowly than first-line trials.
- One trial design to address this issue is a prospective lead-in (PLI) in which the otherwise excluded participants are provided standard of care ADTs, with non-responders ultimately becoming eligible for randomization. This design has been shown to not significantly impact drug-placebo differentiation.[2]
- Adams Clinical developed a standalone, self-sponsored PLI, the Treatment Response Associated with Intervention Trial (TRAIT), in part as a method to speed enrollment. TRAIT has the following goals:
  1. Increase the pool of potential participants for industry-sponsored trials of second-line and third-line antidepressants.
  2. Characterize the clinical trial seeking population and identify predictors of study performance.
  3. Create a research platform to validate novel outcome measures and trial procedures.

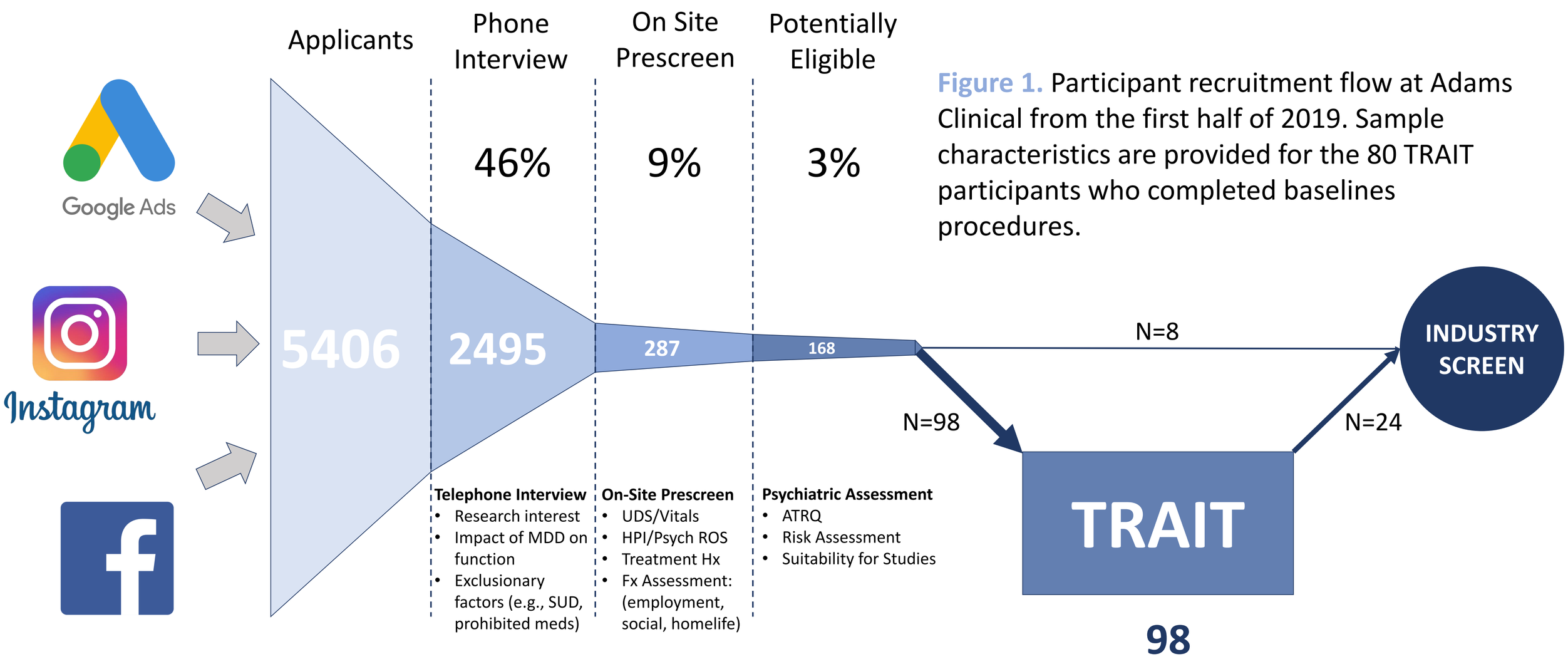

Figure 1. Participant recruitment flow at Adams Clinical from the first half of 2019. Sample characteristics are provided for the 80 TRAIT participants who completed baselines procedures.

Results

Between January and June of 2019, 98 participants completed TRAIT screening procedures, 80 of which enrolled and were and prescribed an ADT. Approximately half (39/80) completed all study procedures, with 11 "responders" discontinued due to stable improvement, and 28 "non-responders" who failed to improve. The average study duration was 77 and 47 days, respectively. 24 non-responders chose to screen for an industry trial, accounting for 75% of all screens for second-/third-line ADT studies at Adams Clinical during this time period.

Sample Characteristics
Gender = 54% Female
Age = 41.8 (15.1)
BMI = 28.8 (6.4)
Past ADTs = 1.8 (1.4)
- 24% Tx Naïve

BSL MADRS = 33.3 (4.7)

Antidepressants
- 29% Duloxetine
- 19% Sertraline
- 19% Citalopram
- 17% Escitalopram
- 16% Other

Screening
- Informed Consent
- Vitals and Urine Drug Screen
- Clinical Assessment
  - Diagnostic Interview (MINI)
  - History of Presenting Illness

-14 to 0 Days

Baseline / Visit 1
- Vitals, Con Meds, AEs, UDS
- Symptom Assessment
  - Self-Report (QIDS-SR16)
  - SIGMA
  - C-SSRS
- Prescribe ADT

14 +/- 2 Days

Visit 1
- Vitals, Con Meds, AEs, UDS
- Symptom Assessment
  - Self-Report (QIDS-SR16)
  - SIGMA
  - C-SSRS
- (Updates to ADT)

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Visit 7/EOS
- Vitals, Con Meds, AEs, UDS
- Symptom Assessment
  - Self-Report (QIDS-SR16)
  - SIGMA
  - C-SSRS
- Continuity of Treatment Plan

80 → 60 → 39

Responders / Non-responders

N=11

No significant differences in BSL characteristics

N=28
24 Screen
4 D/C

Conclusion

TRAIT resulted in a 4-fold increase in industry screens compared to expected screenings without a prospective lead-in. Of those prescribed an ADT, 30% went on to screen for an industry study. Study attrition was high at 50%, but this may improve with greater oversight and tighter operating procedures through a collaboration with Cronos CCS. Data from TRAIT will be leveraged to better characterize trial participants and to validate new measures through collaborations with AiCure and others.

Methods. Individuals interested in participating in a TRD clinical trial who met all eligibility criteria except for current and past ADT history were offered the opportunity to participate in TRAIT. After consenting participants completed a screening assessment with a psychological rater, which included the Mini-International Neuropsychiatric Interview (MINI),[3] Structured Interview Guide for the Montgomery-Asberg Depression Rating Scale (SIGMA),[4] Columbia Suicide Severity Rating Scale (C-SSRS),[5] and the Quick Inventory of Depressive Symptomatology Self Report (QIDS-SR16).[6] Participants with a primary diagnosis of MDD then met with prescribing clinician to review relevant medical history, and an ADT is prescribed consistent with standard of care.
Participants completed bi-weekly assessments of depression symptoms and met with a medical doctor as needed for updates to study medication. Participants were discontinued from the trial if they demonstrated non-response (defined as <50% response for least 4 weeks) to an ADT, or showed response (defined as >50% reduction in symptoms at 2 consecutive visits while taking the same ADT). At the final study visit (Visit 7/EOS) participants were either provided with details regarding potential clinical trial participation or provided follow-up resources as appropriate.

Research Platform

Comprehensive participant assessment
- Extensive demographics
- Travel information (e.g., Uber, distance from site)
- Coherence between clinician, self-report, and at-home assessment

Validation of new measures
- Computational Diagnostics (CDx) – AiCure
- Cognitive assessment – Pending

Strategic partnership
- Protocol compliance and rater training – Cronos
- Rx management and tracking – trialcard

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References:
1. Sansome & Sansome, Innov Clin Neurosci. 2012 May-Jun; 9(5-6): 41–46
2. Iovieno & Papokostas, J Clin Psychiatry. 2012 May;73(5):676-83.
3. Sheehan et al, J Clin Psychiatry. 1998;59 Suppl 20:22-33;quiz 34-57.
4. Williams & Kobak, Br J Psychiatry. 2008 Jan;192(1):52-8.
5. Rush et al, Biol Psychiatry. 2003 Sep 1;54(5):573-83.
6. Posner et al, Am J Psychiatry. 2011 Dec;168(12):1266-77.