Historical Data Retrieval in Relation to Screen Failure Rate at Central Rater Call: A Retrospective Comparative Analysis of Three Clinical Trials

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RESEARCH QUESTION

What is the effect of central rater interviews on screen failure rate in clinical trials for major depressive disorder compared to screen failure rate at on-site interview?

BACKGROUND

Clinical trials that investigate new medications to treat major depressive disorder (MDD) often employ central raters to screen candidates in order to increase the internal validity of their study. Central raters remotely evaluate the candidate to determine whether they are eligible for the study. Central rater evaluation of MDD severity may differ from on-site evaluation.

METHODS

Prior to each clinical trial, health information was gathered in detail for each participant. Data from a 12-lead ECG, a urine sample, and fasting blood samples were collected. A trained professional administered baseline or screening scales per study protocol and determined whether the participant met the study's inclusion or exclusion criteria. If the participant was deemed eligible after their on-site interview, they would undergo a site-independent qualification assessment with a central rater in order to assess the validity of the participant's diagnosis for inclusion in the study. This assessment was conducted via telephone in all three studies. If at participant is deemed to be ineligible during the screening process, they are said to have failed screening or are a "screen fail." Both on-site physical documentation and electronic documentation were maintained during this process.

Data retrieval during the retrospective comparative analysis was conducted through review of de-identified physical documentation for each study. The data were verified through review of de-identified electronic records. Data collected included demographic data (age, gender, ethnicity), on-site scale scores, central rater interview scale scores, current antidepressant, and, if applicable, the reason why the participant failed screening.

Statistical analysis was conducted on site by experienced members of the North Texas Clinical Trials team. Chi-squared analysis was used to determine significance of demographic variables

Those who failed screening prior to central rater interview were most likely to fail due to inclusion and exclusion criteria other than MDD severity. Those who failed screening at central rater interview were most likely to fail due to MDD severity, despite on-site SCID results, or treatment response measured by the MGH-ATRQ scale.

Study	Study participants	Gender	Average Age (Years)	Race	Ethnicity	Enrolled	Failed before CR interview	Failed at CR interview
1	N=12	Male: 6 Female: 6	37.9	White: 11 Other: 1	Not H/L*: 9 H/L: 1	5	5	2
2	N=15	Male: 4 Female: 11	48	White: 13 Black or African American: 1 Asian: 1	Not H/L: 15 0 H/L: 0	5	5	5
3	N=39	Male: 10 Female: 29	48.6	White: 34 Black or African American: 3 Asian:1 Other: 1	Not H/L: 32 H/L: 6 Italian: 1	18	11	10
Total	N=67	Male: 20 Female: 47	46.2	White: 59 Black or African American: 4 Asian: 2 Other: 2	Not H/L: 57 H/L: 9 Italian: 1	28	21	17

Table 1. Patient demographics by study * H/L – Hispanic or Latino

21 study participants were excluded prior to central rater interview for the following reasons:

- Exclusion due to abnormal lab values (10 total; 3 participants had TSH values out of normal range, 3 had elevated HbA1c values, 2 had ECG abnormalities, 1 had proteinuria with abnormal GFR and creatinine, and 1 had LFTs out of normal range)
- Withdrew consent before screening scales were administered (5)
- Did not complete central rater interview (2)
- History or current diagnosis of a psychotic disorder, bipolar disorder (1)
- Enrolled in PTSD study in last 12 months (1)
- Active alcohol use disorder (1)

17 study participants were excluded due to central rater interview for the following reasons:

- HDRS score below threshold at time of central rater interview (7)
- HDRS score improved >20% from the first to second independent HDRS rating (4)
- MGH-ATRQ (3)
- Investigator determination (2)
- Remote history of substance abuse (1)

RESULTS

The demographic data, specifically age, gender, and antidepressant therapy, were statistically insignificant ($p = 0.912$, $p = 0.546$, $p = 0.887$) in relation to screen failure rate.

Study 1 (N=12)
- 58.3% of participants failed at screening
- 71.4% of those failed prior to central rater interview
- 28.6% of those failed due to central rater interview

Study 2 (N=15)
- 66.6%% of participants failed at screening
- 50% of those failed prior to central rater interview
- 50% of those failed due to central rater interview
- 60% of those who failed at to central rater interview did so due to results of MGH-ATRQ scale

Study 3 (N=39)
- 58.3% of participants failed at screening
- 52.4% of those failed prior to central rater interview
- 47.6% of those failed due to central rater interview
- 90% of those who failed at to central rater interview did so due to their absolute HDRS-17 score or a change of 20% or more in their HDRS-17 score

FUTURE DIRECTIONS

Remote interviews, especially those conducted via the telephone, may not readily capture a psychiatric patient's full gestalt. future research could establish how to leverage study participant perception and technological communication to decrease bias and increase internal validity when integrating site-independent qualification assessments into research protocol, such as in decentralized clinical trials.

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