An Analysis of the Number of Patients Screened, Approached and Enrolled in Randomized Controlled Trials

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OBJECTIVE

A randomized controlled trial (RCT) is the gold-standard study design to assess if there is a causal relationship between an intervention and an outcome. It is critical for RCTs to be representative of the study population for there to be external validity. The generalizability of several recent RCTs have been questioned due to a high ratio of participants assessed for eligibility compared to those ultimately enrolled in the RCTs.[1,2] While the challenges for recruiting patients for RCTs are established, it has been proposed that a high ratio of assessed to enrolled patients results in a study population that is not truly representative.[3,4] This study seeks to investigate the assessed-to-enrolled participant ratios in RCTs and determine whether this is impacted by the nature of the primary outcome of the study.

METHODS

During a one-year period (January 2021–December 2021), we identified all RCTs published in three journals (*NEJM, JAMA, Lancet*). The journals were manually reviewed by two co-authors (AA, KD) to ensure all RCTs were identified and abstracted accurately. Reported patient recruitment data, per CONSORT recommendations, was abstracted from each RCT.[5] For secondary outcomes, the purpose of the trial was categorized as preventative or therapeutic, and those classified as therapeutic RCTs were sub-categorized as a procedural versus non-procedural intervention. Medians were compared using Wilcoxon-rank sum testing and P <0.05 was considered significant.

Table 1. Recruitment Differences by Objective of Primary Outcome

	Prevention as primary outcome (N= 43)	Therapy as primary outcome (N= 141)	P
Median # assessed	**9624 (1591–28768)**	**771 (445–1931)**	**<0.01**
Median # Eligible	**3402 (708–10656)**	**503 (269–1019)**	**<0.01**
Median # declined	**148 (–458)**	**16.5 (1–89)**	**<0.01**
Median # Randomized	**2883 (676–10218)**	**411 (240–749)**	**<0.01**
# of Studies that did not meet enrollment target (Total Randomized < Sample Needed) – N (%)	**15 (34.9)**	**16 (11.4)**	**<0.01**
Median # Lost to follow-up	**122 (28–444)**	**33 (–87)**	**<0.01**
Median # Withdrew	11.5 (0–33)	7 (1–23)	0.63

Data presented as N (%) or median (interquartile)
Bolded if significantly different

Table 2. Recruitment Differences By Intervention

	Procedural Intervention (N= 41)	Nonprocedural (N= 137)	P
Median # assessed	**1093.5 (562–3496)**	**931 (363–5534)**	**0.04**
Median # Eligible	689 (374–1780)	421 (173–1182)	0.87
Median # declined	22.5 (2–148)	37 (1–186)	0.70
Median # Randomized	**583 (320–1251)**	**377 (163–1106)**	**0.02**
# of Studies that did not meet enrollment target (Total Randomized < Sample Needed) – N (%)	24 (17.5)	7 (17.1)	0.95
Median # Lost to follow-up	**48 (13–135)**	**22 (5–57)**	**<0.01**
Median # Withdrew	**9 (1–27)**	**2 (0–8)**	**<0.01**

Data presented as N (%) or median (interquartile)
Bolded if significantly different

RESULTS

Of 611 original research studies, 265 RCTs were identified. Of these,184 (69.4%) reported data on the number of individuals screened and recruited; 31 trials (16.9%) failed to reach their patient recruitment target.

The median number of individuals screened per preventative trial was 9,624, of which 3402 (35.3%) were eligible and 148 were randomized (1.53%). For trials with a therapeutic intervention, the median number of individuals screened was 771, of which 503 (66.5%) were eligible and 16.5 (3.28%) were randomized. Of note, significantly more studies did not meet their enrollment target in the therapeutic group compared to the prevention trial group (11.4% vs. 34.9%, p <.01). (See **Table 1.**)

The median number screened for procedural interventions was 1,093 participants, of which 689 (63.0%) were eligible and 22.5 (2.06%) were randomized. For non-procedural interventions, a median number of 931 individuals were screened, of which 421 (45.2%) were eligible and 37 (3.97%) were randomized. (See **Table 2.**)

CONCLUSION

This study demonstrates that a significantly higher number of individuals are screened for preventative trials compared to therapeutic trials. However, a greater proportion of screened individuals are eligible and subsequently enrolled in the trials that studied a therapy as the primary outcome. These results are encouraging that individuals are willing to participate in experimental trials for novel interventions. A trial that requires many patients to be screened to extract a sample size may not be as applicable and generalizable as a condition that is more prevalent and inclusion criteria that are less stringent. As such, these results may also call into question the generalizability of RCTs assessing prevention measures as their primary outcome, given the relatively high screened-to-enrolled ratios in that group. Further research is warranted to determine best practices to recruit and enroll participants in such trials to maximize the external validity of their results.

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