Patient-Reported Outcomes are Frequently Incomplete in Randomized Controlled Trials Focused on Alcohol Use Disorder: a Meta-Epidemiological Analysis

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Introduction

- In 2019, the Substance Abuse and Mental Health Services Administration released data showcasing approximately 14 million people in the US were diagnosed with Alcohol Use Disorder (AUD)[1]
- Financial burden cost the US an estimated $249 billion in 2010[2]
- Excessive alcohol consumption contributes to over 200 disease processes and traumatic injuries[3]
- These burdens and effects tend to affect a patient's quality of life, mental health, social skills, and physical functioning[4]
  - Emphasizes importance of monitoring a variety of outcomes in AUD patients

- Patient-Reported Outcomes:
  - Health outcomes that are directly given by the patient without clinician interpretation
  - Valuable to better understand patient's perspective on daily activities and functioning
  - Randomized controlled trials (RCTs) involving AUD focus on consumption rather than quality of life[5]

- The Consolidated Standards of Reporting Trials (CONSORT) group created the CONSORT-PRO extension to provide trialists resources for identifying and properly reporting PROs as primary and secondary outcomes[6]

- Primary Objective: Mean completeness of reporting
- Secondary Objective: Factors associated with completeness of reporting

Methods

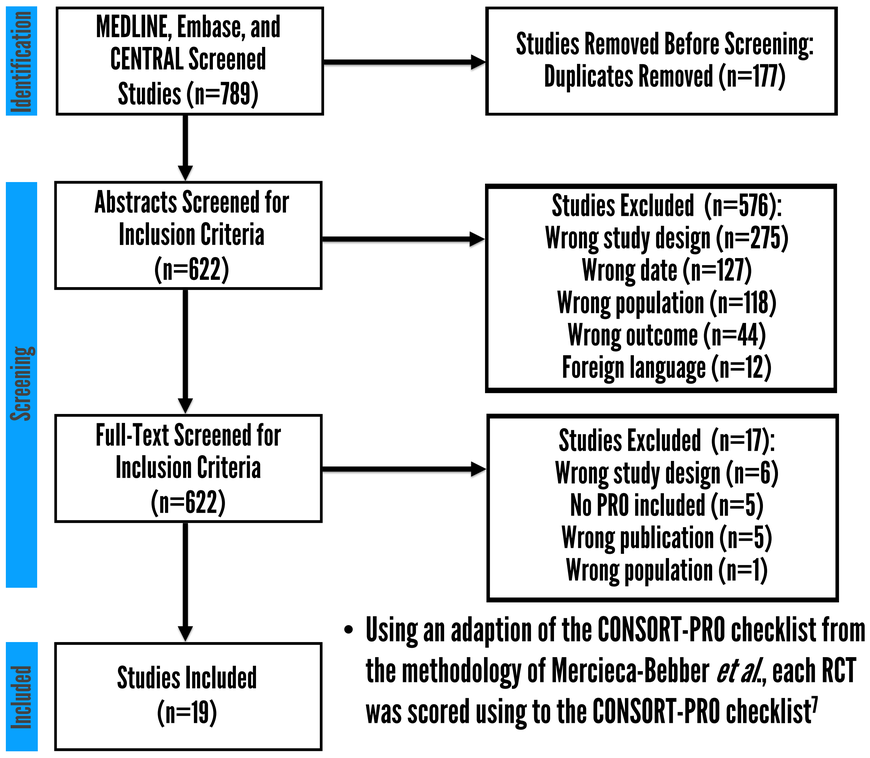

Figure 1: PRISMA Flow Chart

- Using an adaption of the CONSORT-PRO checklist from the methodology of Mercieca-Bebber *et al.*, each RCT was scored using to the CONSORT-PRO checklist[7]
- These trials were also evaluated for risk of bias (RoB) using the Cochrane RoB 2.0 tool
- An exploratory analysis was performed on the type of PROs used in each RCT and were assigned a Therapeutic Area according to the ePROVIDE™ classification[8]
- Performed in a blind, duplicate fashion

Results

Table 1: Characteristics of Randomized Controlled Trials and bivariate associations with CONSORT-PRO completion.

Characteristic	Total 19 (100)	Coef. (SE)	t	*P*
Year of publication, No. (%)				
< 2014	13 (68.42)	1 (Ref)	-	-
≥ 2014	6 (31.58)	15.07, (5.77)	2.61	**0.018**
Intervention of RCT, No. (%)				
Combination	2 (10.53)	1 (Ref)	-	-
Drug	14 (73.68)	-7.79, (10.89)	-0.72	0.486
Instrument	1 (5.26)	-12.5, (17.65)	-0.71	0.49
Psychotherapy	2 (10.53)	-8.93, (14.41)	-0.62	0.545
Includes COI statement, No. (%)				
No statement	10 (52.63)	1 (Ref)	-	-
Reports COI	3 (15.79)	2.18, (8.78)	0.25	0.807
Reports No COI	6 (31.58)	10.36, (6.89)	1.5	0.152
Journal Requirement of Reporting Guidelines, No. (%)				
Not Mentioned	3 (15.79)	1 (Ref)	-	-
Recommended	6 (31.58)	1.83, (10.05)	0.18	0.858
Required	10 (52.63)	3.13, (9.36)	0.34	0.742
Mention of CONSORT or CONSORT-PRO within RCT, No. (%)				
No	18 (94.74)	1 (Ref)	-	-
Yes	1 (5.26)	24.71, (12.89)	1.92	0.072
PRO as a primary or secondary outcome, No. (%)				
Primary	2 (10.53)	1 (Ref)	-	-
Secondary	17 (89.47)	2.84, (10.32)	0.28	0.786
Overall ROB, No. (%)				
High	5 (26.32)	1 (Ref)	-	-
Some Concern	10 (52.63)	-2.33, (7.71)	-0.3	0.766
Low	4 (21.05)	3.21, (9.44)	0.34	0.738
Length of PRO Follow-up				
3 months or less	5 (26.32)	1 (Ref)	-	-
3+ to 6 months	11 (57.89)	-0.79, (7.71)	-0.1	0.92
6+ months to 1 year	2 (10.53)	7.17, (11.97)	0.6	0.558
1 years +	1 (5.26)	-8.9, (15.67)	-0.57	0.578
Sample size,				
Mean (SD)	190.26 (174.56)	0, (0.02)	0.04	0.968

Table 2. Completion of CONSORT-PRO by primary and secondary objective designation.

	Primary Outcome 2 (10.53)		Secondary Outcome 17 (89.47)		Total 19 (100)	
	Complete	*Not Complete*	*Complete*	*Not Complete*	*Complete*	*Not Complete*
CONSORT-PRO item	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*
Introduction						
P1b. Abstract—PRO as primary/secondary Outcome	0 (0)	2 (100)	4 (23.53)	13 (76.47)	4 (21.05)	15 (78.95)
2a. Rationale for including PRO outcome	1 (50)	1 (50)	4 (23.53)	13 (76.47)	5 (26.32)	14 (73.68)
P2bi. PRO hypothesis present	0 (0)	2 (100)	3 (17.65)	14 (82.35)	3 (15.79)	16 (84.21)
P2bii. PRO domains in hypothesis	0 (0)	2 (100)	0 (0)	17 (100)	0 (0)	19 (100)
Methods						
P6ai. Evidence of PRO instrument validity	1 (50)	1 (50)	13 (76.47)	4 (23.53)	14 (73.68)	5 (26.32)
P6aii. Statement of the person completing the PRO questionnaire	0 (0)	2 (100)	4 (23.53)	13 (76.47)	4 (21.05)	15 (78.95)
P6aiii. Mode of administration (paper, e-PRO)	0 (0)	2 (100)	1 (5.88)	16 (94.12)	1 (5.26)	18 (94.74)
P7a. How sample size was determined (not required unless PRO is a primary endpoint)*	0 (0)	2 (100)	-	-	0 (0)	2 (100)
P12a. Statistical approach for dealing with missing data (imputation, exclusion, other)	0 (0)	2 (100)	8 (47.06)	9 (52.94)	8 (42.11)	11 (57.89)
Results						
13ai. Report no. questionnaires submitted/available for analysis at baseline	2 (100)	0 (0)	12 (70.59)	5 (29.41)	14 (73.68)	5 (26.32)
13aii. Report no. questionnaires submitted/available for analysis principle time point for analysis	2 (100)	0 (0)	9 (52.94)	8 (47.06)	11 (57.89)	8 (42.11)
15. Demographics table includes baseline PRO	1 (50)	1 (50)	7 (41.18)	10 (58.82)	8 (42.11)	11 (57.89)
16. Number of pts (denominator) included in each PRO analysis	0 (0)	2 (100)	9 (52.94)	8 (47.06)	9 (47.37)	10 (52.63)
17ai. PRO results reported for the hypothesised domains and time point specified in the hypothesis—OR—reported for each domain of the PRO questionnaire if no PRO hypothesis provided	1 (50)	1 (50)	3 (17.65)	14 (82.35)	4 (21.05)	15 (78.95)
17aii. Results include confidence interval, effect size or some other estimate of precision	2 (100)	0 (0)	14 (82.35)	3 (17.65)	16 (84.21)	3 (15.79)
18. Results of any subgroup/adjusted/exploratory analyses	1 (50)	1 (50)	2 (11.76)	15 (88.24)	3 (15.79)	16 (84.21)
Discussion						
P20. PRO study limitations	1 (50)	1 (50)	16 (94.12)	1 (5.88)	17 (89.47)	2 (10.53)
P21. Implications of PRO results for generalizability, clinical practice	1 (50)	1 (50)	2 (11.76)	15 (88.24)	3 (15.79)	16 (84.21)
22. PROs interpreted in relation to clinical outcomes	2 (100)	0 (0)	10 (58.82)	7 (41.18)	12 (63.16)	7 (36.84)

*Item P7a only applies to PROs identified as a primary outcome.

Conclusion & Discussion

- Almost two-thirds of our CONSORT-PRO items were underreported by over half of the RCTs in our sample
- RCTs published after the CONSORT-PRO extension in 2014 contained significantly more complete reporting than trials published before the CONSORT-PRO extension
- Underreported items of concern:
  1. Inappropriate handling of missing data
  2. Incomplete reporting of the implications of PRO generalizability in clinical practice
- Over 20 distinct PRO measures in the trials were found leading to substantial heterogeneity among the types of PRO measures used to assess the same PRO domain
  - Core Outcomes Measurement in Effectiveness Trials (COMET) Initiative has endorsed the use of a Core Outcomes Set (COS) to overcome such inconsistencies[9]

Recommendations:

1. Support the recommendation of Mercieca-Bebber *et al.* requiring, not simply recommending, publishing journals be more adherent to the requirements of the CONSORT-PRO checklist[10]
2. Provide education on proper methodological reporting to promote adherence to checklists
3. Development of a COS specific for AUD to provide consistency

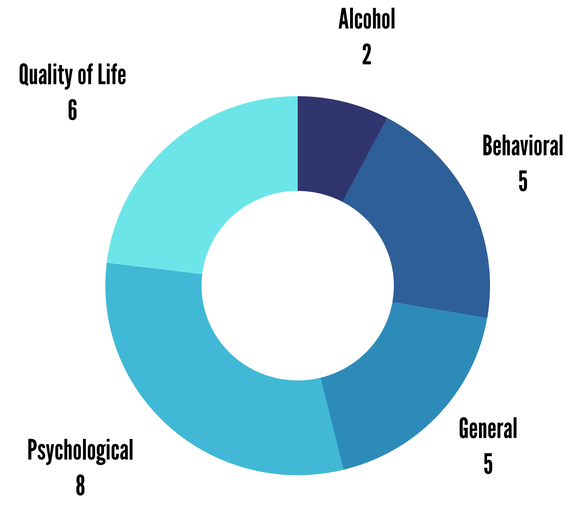

Figure 2: Number of different PRO measures used and their therapeutic area

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