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Original Article

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Evaluating the underreporting of patient-reported outcomes in carpal tunnel syndrome randomized controlled trials

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Abstract

Context: In recent years, patient-centered healthcare has become a primary concern for researchers and healthcare professionals. When included in randomized controlled trials (RCTs), patient-reported outcome (PRO) measures serve a critical role in supplementing efficacy outcomes with a patient perspective.

Objectives: The goals of this study are to evaluate the reporting completeness of PROs within literature concerning carpal tunnel syndrome (CTS) utilizing the Consolidated Standards of Reporting Trials Patient-Reported Outcomes (CONSORT-PRO) extension.

Methods: We searched MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) for published RCTs relating to CTS with at least one PRO measure from 2006 to 2020. Two investigators screened all RCTs for inclusion utilizing Rayyan (https://rayyan.qcri.org/), a systematic review screening platform. In an independent, masked fashion, investigators then evaluated all RCTs utilizing the CONSORT-PRO adaptation and Cochrane Collaboration Risk of Bias (RoB) 2.0 tool. Bivariate regression analyses were utilized to assess relationships between trial characteristics and completeness of reporting.

Results: Our search returned 374 publications, yet only 31 unique RCTs met the inclusion criteria. The mean overall percent of adherence for CONSORT-PRO was 41%. Our secondary outcome—assessing study characteristics—indicated significantly higher completeness of reporting in the absence of a conflict of interest statement ($p<0.05$), 'some concerns' for bias ($p<0.005$), and when journals required the use of the CONSORT statement ($p<0.005$). The RoB assessment determined overall suspicion for bias among included RCTs, with 35% (n=11/31) being labeled as 'high,' 58% (n=18/31) as 'some concerns,' and 7% (n=2/31) as 'low.'

Conclusions: Our study indicated that the completeness of CONSORT-PRO reporting was deficient within CTS trials. Because of the importance placed on PROs in clinical practice, we recommend adherence to CONSORT-PRO prior to publication of RCTs to increase the understanding of various interventions on patients' quality of life (QoL).

Keywords: Carpal tunnel syndrome; CONSORT-PRO; patient-reported outcomes.

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Carpal tunnel syndrome (CTS) is the most common form of peripheral neuropathy in the United States, with prevalence estimates ranging from 5.1 to 6.2% in the general population [1, 2]. CTS is the leading cause for upper extremity disability, which may result in hand or wrist pain, paresthesia, and weakness [3]. Patients with CTS have reported decreased quality of life (QoL) due to loss of dexterity, reduced work performance, diminished quality of sleep, and depression [4, 5]. Regarding societal costs, CTS accounts for an estimated total loss of earnings of approximately $4.2 billion annually [6]. Owing to the increasing prevalence of CTS, the negative effects on QoL, and financial burden, research should focus

on identifying techniques to promote the use of patient perspectives to guide clinical practice.

Patient-reported outcomes (PROs) are becoming increasingly measured alongside efficacy in therapy trials. The outcomes help clinicians and patients better understand how these therapies affect daily life and function. According to the US Department of Health and Human services, PROs are important because they provide a unique perspective to treatment effectiveness and may be more reliable than an informal interview in a doctor's office [7]. For example, Damms et al. [8] reported that patients who underwent carpal tunnel release surgery showed higher reported QoL because of increased function and decreased pain. Thus, given the importance of PROs in randomized controlled trials (RCTs), efforts are needed to ensure that PROs are thoroughly and adequately reported in published reports.

The variability within RCT reporting in general led to the creation of the Consolidated Standards of Reporting Trials (CONSORT) Statement [9]. The CONSORT Statement set standards for RCTs to allow for greater transparency and to minimize systematic reporting errors [10]. The original CONSORT Statement did not include items for complete PRO reporting—which are often inadequately reported [11] —thus, an extension, Consolidated Standards of Reporting Trials Patient-Reported Outcomes (CONSORT-PRO), was created. It is hoped that the establishment and implementation of CONSORT-PRO will improve the completeness of reporting of RCTs that have PROs listed as outcomes. Therefore, our primary objective was to evaluate the completeness of PRO reporting of RCTs investigating the management of CTS.

Methods

Study design

Our design is a meta-epidemiological study analyzing data extracted from published RCTs concerning CTS. Our study was not subject to Institutional Review Board oversight because it did not meet the regulatory definition of a human participant study. We followed reporting guidelines for meta-epidemiological studies established by Murad and Wang [12].

Search strategy

One investigator (B.H.), in consultation with a medical research librarian, utilized the Ovid interface to search the Cochrane Central Register of Controlled Trials (CENTRAL), Embase, and MEDLINE for published RCTs about CTS. The Cochrane highly sensitive search strategy was utilized to maximize sensitivity for identifying RCTs, which is a validated filter for OVID interfaces [13]. Our protocol, including our search string, is available on Open Science Framework (OSF) [14].

Eligibility

Included RCTs were published between 2006 and 2020 and address CTS with at least one PRO measure as a primary or secondary outcome. Only studies published in the English language were included. Observational studies, animal studies, case reports, meta-analyses, systematic reviews, clinical trial protocols, cost-effective studies, secondary analysis, letters to the editor, and trials without a PRO measure were excluded.

Selection process

Following the literature search, collected data was combined and uploaded into Rayyan (https://rayyan.qcri.org/), a systematic review screening platform. Duplicates were removed, and two investigators independently performed title and abstract screening in a duplicated, masked fashion. Following the initial screening, investigators then resolved disagreements by discussion and, when necessary, through collaboration with a third investigator.

Data collection process

Investigators were trained to extract data with the CONSORT-PRO adaptation utilizing work published by the guideline authors [11, 15]. As a calibration exercise, we performed masked, duplicate extraction from three RCTs not included in our sample until consensus was achieved. The data extraction was performed utilizing a pilot-tested Google Forms form by two investigators, also in a masked, duplicate fashion. Investigators were trained to assess risk of bias (RoB) utilizing material provided by Cochrane [16]. The RoB evaluation was performed by two investigators in the same fashion. Following data extraction and the RoB evaluation, the investigators resolved all discrepancies; a third investigator (B.H.) was available to resolve disagreements.

Data items

We assessed completion of the CONSORT-PRO checklist adaptation developed by Mercieca-Bebber et al. [15], for all RCTs as our primary objective reported as the mean percent completion (see scoring of CONSORT-PRO adaptation). Our secondary objective assessed relationships between the mean completeness of PRO reporting and trial characteristics. The trial characteristics analyzed were: (1) year of publication (before or after 2014, a year following the publication of the CONSORT reporting guidelines); (2) intervention of RCT (e.g., drug or surgical technique); (3) conflict of interest statement; (4) journal endorsement of CONSORT-PRO; (5) citation of CONSORT-PRO within the publication; (6) whether an RCT utilized a PRO as a primary or secondary outcome; (7) RoB assessed by the Cochrane RoB 2.0 tool (see Evaluating RoB); (8) the length of PRO follow-up time; and (9) sample size of the trial.

The publishing journal's endorsement of the CONSORT guidelines were coded as either *not mentioned, recommended*, or *required*. This data item was evaluated by screening the instructions to the authors' pages for mention of EQUATOR, CONSORT, or CONSORT-PRO guidelines.

RoB was assessed by evaluating the following bias domains: (1) bias arising from the randomization process; (2) bias due to deviations from

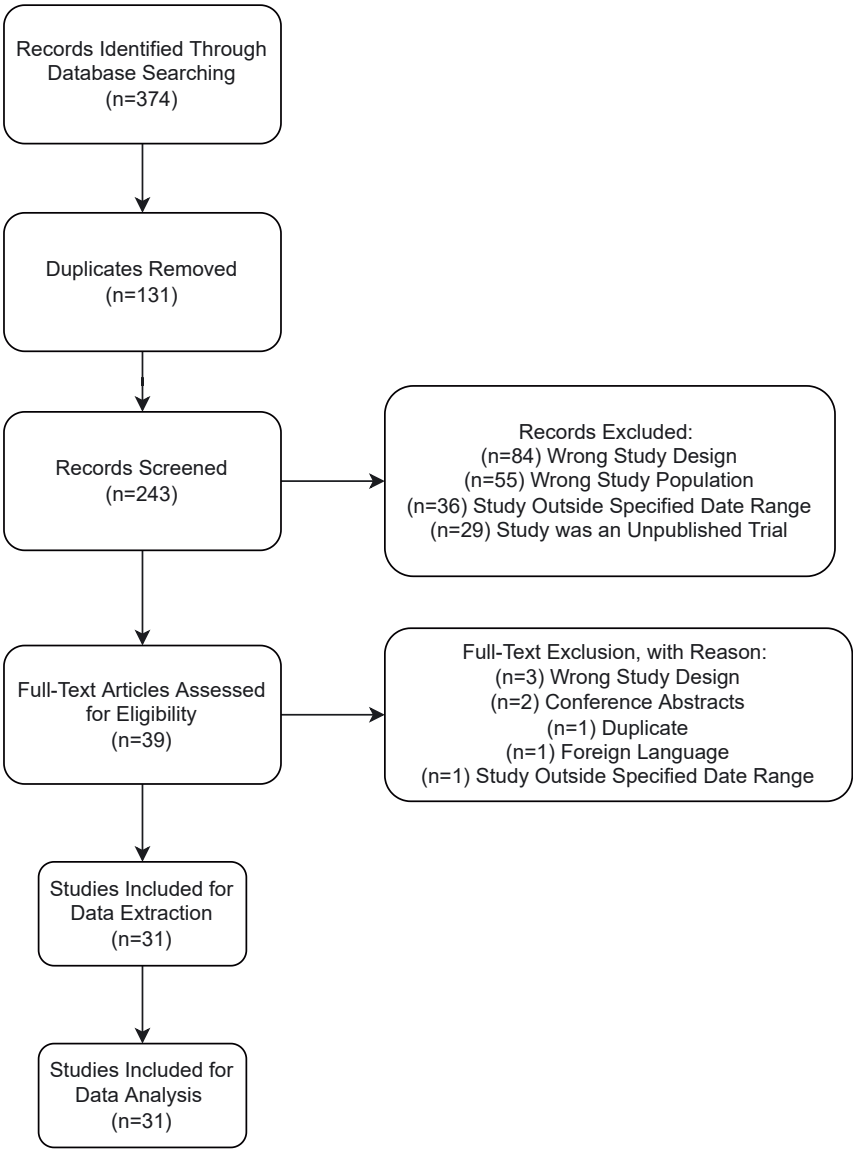

Figure 1: Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

the intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; (5) bias in selection of the reported result; and (6) overall RoB appraisal for each RCT.

Scoring CONSORT-PRO

Scoring methodology has been adapted from Mercieca-Bebber et al. [15]. We omitted Item 4a of CONSORT-PRO (the use of PROs in eligibility or stratification) because there is difficulty in the verification of this criterion. Instead, we recorded whether a study described adherence to this item as a 'yes' or 'no.' We allocated a maximum value of 0.5 or 1 when information for an item was present. Items that received the maximum value (1 or 0.5 if the item was double-barreled) were considered 'complete,' whereas items that failed to reach the maximum value are reported as 'not complete.' Item P1b was scored as partially complete if an RCT reported the PRO measure utilized in the study but failed to identify whether the PRO was a primary or secondary outcome. Therefore, Item P1b could be scored as 0, 0.5, or 1 based on the information available. Item 7a was dependent on the PRO measure being reported as a primary outcome. Because of this dependency, RCTs with a primary PRO outcome had a maximum score of 15, whereas RCTs with a secondary outcome had a maximum score of 14. A percent completeness of the checklist per RCT was calculated by adding the items and dividing by the total of possible items.

Evaluating risk of bias

We utilized a decision algorithm developed by the Cochrane Collaboration to evaluate RoB. If investigators had partially divergent assessments on bias domains (e.g., one investigator answered 'yes' and another investigator answered 'partial yes'), the overall RoB judgment

for the trial outcome was not altered. We evaluated the overall RoB domain per the Microsoft Excel tool provided by Cochrane as 'high,' 'some concerns,' or 'low' risk [17–19]

Data analysis

To address our primary outcome, we calculated the mean completion percentage of the CONSORT-PRO adaptation across all RCTs in our sample and by PROs as a primary or secondary outcome. Next, we reported frequencies and percentages for the trial characteristics listed in the Data Items section. To address our secondary outcome, we utilized bivariate regression models to determine the association between mean completion percentage of the CONSORT-PRO adaptation and the trial characteristics listed in the Data Items section. Finally, we reported on the frequency and percentage of individual items on the CONSORT-PRO adaptation for all RCTs, and by PROs as a primary or secondary outcome within the RCT. All analyses were performed utilizing STATA 16.1 (StataCorp, LLC, College Station, TX).

Reproducibility

Our study protocol, data sheets, analysis scripts, data dictionaries, and extraction forms are publicly available on OSF as a means to promote the transparency and reproducibility of our study. This investigation was conducted in tandem with other studies addressing completeness of reporting in other fields of medicine utilizing similar methodology.

Results

Systematic search and screening

Our systematic search returned 374 records, 243 of which remained after removing duplicates. Following title and abstract review, 39 studies were included for full-text review. After full-text evaluation, 31 published RCTs were included for data extraction. Rationales for the excluded studies are provided in Figure 1.

RCT characteristics

Among the included RCTs, 61.3% (19/31; Table 1) were published prior to 2014. The most common intervention type was a combination of interventions (12/31, 38.7%). There were no conflicts of interest reported in 54.8% (17/31) of the RCTs, while 45.2% (14/31) did not include conflict of interest statements. Twenty (of 31, 60.6%) studies were published in journals that recommended or required CONSORT guidelines, and 20 (of 31, 64.5%) endorsed CONSORT guidelines within the article. A total of 26 RCTs included a PRO as a primary outcome, and five RCTs included PROs as secondary outcomes. The percentage of RCTs in each overall RoB categories are as follows: 35.5% (11/31) were 'high' risk, 58.1% (18/31) were evaluated as 'some concerns,' and 6.5% (2/31) were 'low' risk. Nineteen (of 31, 61.3%) RCTs had PRO follow-up

Table 1: Bivariate regression analyses between study characteristics and completeness of PRO reporting.

Characteristic	Total n=31	Coef. (SE)	t	p-Value
Year of publication, no., %				
<2014	19 (61.29)	1 (ref)	–	–
≥2014	12 (38.71)	8.8, (6.82)	1.29	0.207
Intervention of RCT, no., %				
Combination	12 (38.71)	1 (ref)	–	–
Device	1 (3.23)	−1.31, (19.42)	−0.07	0.947
Drug	2 (6.45)	−2.98, (14.25)	−0.21	0.836
Surgical technique	8 (25.81)	−8.45, (8.52)	−0.99	0.33
Therapy	8 (25.81)	10.3, (8.52)	1.21	0.237
Includes COI statement, no., %				
No statement	14 (45.16)	1 (ref)	–	–
Reports COI	0 (0)	2.18, (8.78)	0.25	0.807
Reports no COI	17 (54.84)	13.5, (6.39)	2.11	0.043
Journal requirement of reporting guidelines, no., %				
Not mentioned	11 (35.48)	1 (ref)	–	–
Recommended	11 (35.48)	−4.33, (6.34)	−0.68	0.5
Required	9 (29.03)	23.46, (6.68)	3.51	0.002
Mention of CONSORT or CONSORT-PRO within RCT, no., %				
No	29 (93.55)	1 (ref)	–	–
Yes	2 (6.45)	19.72, (13.41)	1.47	0.152
PRO as a primary or secondary outcome, no., %				
Primary	26 (83.87)	1 (ref)	–	–
Secondary	5 (16.13)	−0.71, (9.28)	−0.08	0.939
Overall ROB, no., %				
High	11 (35.48)	1 (ref)	–	–
Some concern	18 (58.06)	21.04, (6.22)	3.38	0.002
Low	2 (6.45)	18.53, (12.5)	1.48	0.15
Length of PRO follow-up				
3 months or less	19 (61.29)	1 (ref)	–	–
3+ to 6 months	6 (19.35)	−3.32, (9.04)	−0.37	0.716
6+ months to 1 year	6 (19.35)	0.72, (9.04)	0.08	0.937
1+ years	0	–	–	–
Sample size				
Mean (SD)	83.65 (47.58)	0.11, (0.07)	1.61	0.118

COI, conflict of interest; CONSORT, Consolidated Standards of Reporting Trials; CONSORT-PRO, Consolidated Standards of Reporting Trials Patient-Reported Outcomes; PRO, patient-reported outcomes; RCT, randomized controlled trial; ROB, risk of bias; SD, standard deviation; SE, standard error.

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

CONSORT-PRO item	Primary (n=26)		Secondary (n=5)		Overall (n=31)	
	Complete n, %	Not complete n, %	Complete n, %	Not complete n, %	Complete n, %	Not complete n, %
Introduction						
P1b. Abstract—PRO as primary/secondary outcome	11 (42.31)	15 (57.69)	1 (20)	4 (80)	12 (38.71)	19 (61.29)
2a. Rationale for including PRO outcome	12 (46.15)	14 (53.85)	0 (0)	5 (100)	12 (38.71)	19 (61.29)
P2bi. PRO hypothesis present	2 (7.69)	24 (92.31)	0 (0)	5 (100)	2 (6.45)	29 (93.55)
P2bii. PRO domains in hypothesis	1 (3.85)	25 (96.15)	0 (0)	5 (100)	1 (3.23)	30 (96.77)
Methods						
P6ai. Evidence of PRO instrument validity	17 (65.38)	9 (34.62)	4 (80)	1 (20)	21 (67.74)	10 (32.26)
P6aii. Statement of the person completing the PRO questionnaire	17 (65.38)	9 (34.62)	2 (40)	3 (60)	19 (61.29)	12 (38.71)
P6aiii. Mode of administration (paper, e-PRO)	5 (19.23)	21 (80.77)	1 (20)	4 (80)	6 (19.35)	25 (80.65)
P7a. How sample size was determined (not required unless PRO is a primary outcome)[a]	12 (46.15)	14 (53.85)	–	–	12 (46.15)	14 (53.85)
P12a. Statistical approach for dealing with missing data (imputation, exclusion, other)	5 (19.23)	21 (80.77)	1 (20)	4 (80)	6 (19.35)	25 (80.65)
Results						
13ai. Report number of questionnaires submitted/available for analysis at baseline	17 (65.38)	9 (34.62)	3 (60)	2 (40)	20 (64.52)	11 (35.48)
13aii. Report number of questionnaires submitted/available for analysis principle time point for analysis	14 (53.85)	12 (46.15)	3 (60)	2 (40)	17 (54.84)	14 (45.16)
15. Demographics table includes baseline PRO	10 (38.46)	16 (61.54)	1 (20)	4 (80)	11 (35.48)	20 (64.52)
16. Number of pts (denominator) included in each PRO analysis	4 (15.38)	22 (84.62)	2 (40)	3 (60)	6 (19.35)	25 (80.65)
17ai. PRO results reported for the hypothesized domains and time point specified in the hypothesis—OR—reported for each domain of the PRO questionnaire if no PRO hypothesis provided	14 (53.85)	12 (46.15)	2 (40)	3 (60)	16 (51.61)	15 (48.39)
17aii. Results include confidence interval, effect size or some other estimate of precision	23 (88.46)	3 (11.54)	5 (100)	0 (0)	28 (90.32)	3 (9.68)
18. Results of any subgroup/adjusted/exploratory analyses	4 (15.38)	22 (84.62)	1 (20)	4 (80)	5 (16.13)	26 (83.87)
Discussion						
P20. PRO study limitations	14 (53.85)	12 (46.15)	5 (100)	0 (0)	19 (61.29)	12 (38.71)
P21. Implications of PRO results for generalizability, clinical practice	20 (76.92)	6 (23.08)	5 (100)	0 (0)	25 (80.65)	6 (19.35)
22. PROs interpreted in relation to clinical outcomes	13 (50)	13 (50)	2 (40)	3 (60)	15 (48.39)	16 (51.61)

[a]Item P7a only applies to PROs identified as a primary outcomes. CONSORT-PRO, Consolidated Standards of Reporting Trials Patient-Reported Outcomes; PRO, patient-reported outcome.

times of 3 months or less. There were no RCTs that performed follow-up appraisals later than 12 months. The mean sample size of the RCTs in our sample was 83.7 (SD=47.6).

Completeness of reporting according to CONSORT-PRO adaptation

The overall mean completion percent for the CONSORT-PRO checklist adaptation among our sample was 40.9% (SD=13.5). RCTs that listed PRO as a primary outcome had a mean completeness of 38.3% (SD=7.07) and was not significantly different from RCTs with a PRO as a secondary outcome (41.2%; SD=14.1) (t_1=−0.28, p=0.79).

Among all RCTs in our sample, item 17aii *results include an estimate of precision*––was the most consistently reported item overall (28/31; 90.3%; Table 2). Conversely, item P2bii––*PRO domains specified in the hypothesis*—was reported least often (1/31; 3.2%), which was also the lowest reported item among primary studies

(1/31; 3.9%). For RCTs with PROs as a primary outcome, item 17aii was also the most consistently reported item (23/26, 88.5%).

RCTs that included a PRO as a secondary outcome consistently reported the following: *results include an estimate of precision* (17aii), *study limitations* (P20), and *implications of PRO results for generalizability, clinical practice* (P21). No RCTs with a secondary PRO outcome reported the following items: *rationale for PRO outcome* (2a), and *PRO hypothesis is present and domains specified in the hypothesis* (P2bi and P2bii).

Associations between PRO outcomes, completion, and study characteristics

Lastly, our bivariate regression analyses revealed that RCTs reporting no conflicts of interest among authors were 13.5% (SE=6.39) more complete than RCTs that did not include a conflict of interest statement (t_1=2.11; p=0.043). Furthermore, RCTs that were published in a journal that endorsed CONSORT reporting guidelines were 23.5% (SE=6.68) more complete compared to RCTs published in journals that did not mention reporting guidelines (t_1=3.51; p=0.002). Additional relationships are demonstrated in Table 1.

Discussion

RCTs examining PROs have the potential to play an important role in driving clinical decision making [20]. Therefore, it is essential that the reporting of PROs within trials be robust. The 2013 CONSORT-PRO checklist serves as a guideline for trialists to follow. The primary outcome of this study was to examine CONSORT-PRO adherence within CTS trials. Our results indicated a poor overall completion rate on the CONSORT-PRO checklist with a high suspicion of bias—93% of the included RCTs had an overall evaluation of 'some concerns' or 'high' risk for bias. Results of our study also show low completion rates to select items on the CONSORT-PRO checklist. Less than 10% of the included RCTs adequately reported information regarding the PRO hypothesis or domains within the hypothesis. In addition, less than 20% accounted for missing trial data. Finally, our results indicate that journals requiring the CONSORT statement showed statistically significant greater completeness of reporting. Here, we address the underreported CONSORT-PRO items and the implications of these elements, and we offer recommendations to increase the frequency and accuracy of PRO reporting within CTS trials.

The results of our study indicated that a PRO hypothesis was reported in only 6.5% of included RCTs. Our finding of low adherence to CONSORT-PRO among CTS trials is consistent with the medical literature. A trial examining 557 RCTs within the field of oncology found that only 17% of trials accurately reported a PRO-related hypothesis in accordance with the CONSORT-PRO guidelines [21]. Another trial analyzing cancer therapies in 2019 had a PRO hypothesis completion rate of 28%. When deviation from the guidelines occur, specifically the requirement of reporting PRO hypotheses, there is a risk of reporting bias due to selective outcome reporting [11]. Reporting bias occurs when only a portion of the original data are fully reported due to the magnitude of effect or the statistical significance of selected outcomes [22], which can affect a study's validity [23]. This potential for bias illustrates the need for preemptively formulating a PRO hypothesis to ensure high-quality evidence collection and increase the confidence of clinicians and readers alike when reviewing the latest CTS studies.

Despite the importance of PROs, the majority of included RCTs within our study failed to appropriately account for missing data, specifically PRO data. For this data to be meaningful—and to ensure that treatment outcomes are not overshadowing true patient experiences—the missing data must be handled correctly [24]. Calvert et al. [11] notes that missing data can reduce the validity of the study, serve as a source of bias, and produce misleading results. Further, they suggest that missing PRO data is not a coincidence but often occurs in relation to the outcome of interest [11]. For example, a trial included within our RCT sample assessing PROs involving manual dexterity (i.e., writing, cooking, utilizing eating utensils, etc.) after treatment of tendon- and nerve-gliding exercises for CTS, failed to include patients lost to follow-up within their statistical analysis [25]. Similarly, in another trial from our sample, Hefny et al. [26] contrasted the benefits of shock-wave therapy vs steroid injections among CTS patients and measured their effect on daily activities such as household chores, bathing, dressing, and grasping small objects. Nearly 20% of the participants were excluded from the final analysis. These findings may weaken the validity of each study's recommendations and render their conclusions less convincing [27]. Missing PRO data among CTS trials at a minimum alters confidence intervals and reduces statistical power to accurately detect treatment effect. At its worst, missing data distort treatment outcomes and can be detrimental to the patient [28].

To improve CONSORT-PRO adherence, we provide the following recommendations. First, medical journals should require the use of CONSORT and extensions (when applicable) for RCTs. Currently, CONSORT is "endorsed" by over 50% of medical journals worldwide [29], with varying

instructions to authors from recommended to required. However, CONSORT extensions are referred to by less than 3% of journals [30]. Our results showed a significantly higher completion rate of CONSORT-PRO when the publishing journal required the CONSORT statement. Therefore, the journals should require CONSORT adherence prior to publication, and this requirement may increase the transparency and accuracy of reporting within CTS trials. Second, wherever possible, missing data sources must be uncovered and appropriately handled to allow for accurate and precise analyses [28]. When perfect compliance to the protocol is unfeasible, and missing data are unavoidable—which is more common than rare—the proper methodological practices need to be implemented to mitigate bias and misinterpretation [28, 31].

Study limitations

Our study has several strengths. First, to facilitate reproducibility and transparency, we uploaded our protocol, data sheets, and data extraction forms to OSF, a free and open source archive. In addition, investigators completed a training course for either CONSORT-PRO and the Cochrane Collaboration RoB 2.0 tool to standardize data extraction. Lastly, data were extracted in duplicate by two independent, masked researchers. This practice is in accordance with Cochrane Collaboration guidelines and is considered the gold standard for data extraction [32], further heightening the validity of this study.

Our study is not without limitations, however. We extracted all CTS trials examining PROs as either a primary or secondary outcome between a specified date range, which led to a reduced sample size. Additionally, our study is cross-sectional by design, and thus, these findings are not generalizable to other neurological or orthopedic topics. Finally, we utilized three bibliographic databases, MEDLINE, Embase, and CENTRAL to locate RCTs containing PROs. However, these are not all-encompassing of available trials.

Conclusions

Adherence to the CONSORT-PRO guideline is poor across RCTs examining PROs in CTS. Our results indicate specific areas where reporting could be improved. The failure to report a PRO hypothesis and the accountability of missing data are not exclusive to RCTs investigating CTS. Explicit endorsement of the CONSORT-PRO guidelines may improve reporting completeness of PROs within RCTs.

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