

ORIGINAL RESEARCH

Metaresearch on patient-reported outcomes in trial protocols and results publications suggested large outcome reporting bias

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Abstract

Objectives: Patient-reported outcomes (PROs) provide crucial information for evaluating health-care interventions, but previous research in specific disease areas suggested infrequent use and incomplete reporting of PROs. We examined the prevalence and characteristics of PROs in randomized clinical trial (RCT) protocols across medical fields, their reporting quality, and the consistency between PROs specified in trial protocols and subsequent reporting in trial publications.

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Study Design and Setting: We included 237 RCT protocols approved in 2012 and 251 approved in 2016, by ethics committees in Switzerland, Germany, and Canada. We systematically searched for corresponding peer-reviewed results publications and results on trial registries. Pairs of reviewers independently extracted characteristics of RCT protocols, PROs specified in protocols and reported in corresponding results publications, and assessed the reporting quality of RCTs with a PRO as the primary outcome using the Consolidated Standards of Reporting Trials—patient-reported outcome (CONSORTs-PRO) extension.

Results: Out of 488 included RCT protocols, 147 (30%) did not report use of a PRO; 97 (20%) specified a PRO as the primary outcome and an additional 244 (50%) as a secondary outcome. The prevalence of PROs varied substantially across medical fields, ranging from 100% in rheumatology and psychiatry to about one-third in cardiology and anesthesiology. At 8–10 years after RCT approval, results were available for 264 of the 341 (77%) trial protocols that prespecified PROs. Forty-four percent of the published trials (115/264) reported all PROs as defined in the protocol, 21% (55/264) did not report any prespecified PROs, and 36% (94/264) reported more, fewer, or different PROs than those prespecified. These findings were consistent between trial protocols approved in 2012 and 2016. Among 63 peer-reviewed RCT publications that reported a PRO as their primary outcome, reporting quality was often inadequate, with seven of 13 CONSORT-PRO items.

Conclusion: Less than half of RCT protocols with planned PROs reported them as specified in corresponding published results, suggesting outcome reporting bias, and PRO reporting quality was often deficient. These limitations complicate informed decision-making between patients and health-care providers, as well as the development of evidence-based clinical practice guidelines. © 2025 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Keywords: Patient-reported outcomes; Randomized clinical trials; Trial protocols; Trial publications; Outcome reporting bias; Reporting guidelines

1. Introduction

Patient-reported outcomes (PROs) are reported directly by patients and not interpreted by an observer [1]. PROs may include patient assessments of disease symptoms or treatment side effects, such as pain, fatigue, or anxiety; functional outcomes such as physical, sexual, social, emotional, or cognitive functioning; or multidimensional outcomes such as quality of life (QoL) or health utility [2]. PROs play an essential role in capturing patients' experiences and perspectives and informing evidence-based clinical practice and shared decision-making [3–5]. Routine use of PROs can minimize nondetection of symptoms and physical impairments in clinical care, so that opportunities to intervene and alleviate suffering are timely taken [6,7]. There is evidence from cancer care that routine use of PROs can improve patients' QoL, enhance patient–clinician communication, reduce emergency department visits, and prolong survival [8,9]. The importance of PROs has been recognized by regulatory authorities, international policymakers, and patients [1,10–12].

Metaresearch studies have found that randomized clinical trial (RCT) protocols often fail to include PROs and that the reporting quality of PROs in results publications is low [13–15]. Furthermore, PROs may be modified when reported, potentially reflecting outcome reporting bias [16–21]. Recognition of suboptimal reporting has led to the development of reporting guidelines for PROs in RCT protocols and RCT publications [22–25]. Failure to specify important PRO characteristics in the protocol may result in insufficient data gathering for these outcomes during the trial [26]. Previous metaresearch studies on PROs have largely focused on specific diseases (eg, cancer) or on a specific type of PRO (eg, QoL) [15,27–33]. A current analysis of the planning and reporting of PROs in RCTs across

medical fields is lacking. In a previous study we evaluated the completeness of RCT protocols before and after publication of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRITs) statement in 2013 using a sample of RCT protocols approved by research ethics committees in Switzerland, Germany, and Canada in 2012 (before SPIRIT) and in 2016 (after SPIRIT) [34,35]. Using the same RCT protocols, we aimed to investigate in the present study: (i) the prevalence and characteristics of PROs (eg, content, use of validated instruments) specified in RCT protocols without restrictions to specific disease areas or types of PROs; (ii) the reporting quality of PROs when specified as the primary outcome; and (iii) concordance between prespecified PROs in protocols and reported PROs in published trials.

2. Methods

2.1. Study sample

The present study is a prespecified subproject of the Adherence to Spirit Recommendations Study (ASPIRE) [34–36], which evaluated the completeness of RCT protocols before and after the SPIRIT statement. In the present study we analyzed 549 RCT protocols from ASPIRE that were approved by nine research ethics committees in 2012 ($n = 257$) and 2016 ($n = 292$), in Switzerland (Basel, Belinzona, Bern, Geneva, Lausanne, St. Gallen, and Zurich), Canada (Hamilton), and Germany (Freiburg). All trial protocols randomly assigned participants to different interventions to evaluate effects on health outcomes. Methodologic details, including eligibility criteria, protocol selection process, data extraction, and additional objectives addressed in add-on studies, have previously been published [34]. We report

What is new?**Key findings**

- The prevalence of patient-reported outcomes (PROs) in clinical trials varied substantially across medical fields.
- Among corresponding result publications, only 44% reported PROs as defined in their protocols, 21% failed to report any prespecified PROs, and 36% reported more, less, or different PROs than prespecified in the protocol.
- Reporting quality of PROs in result publications of trials was often deficient.

What this adds to what was known?

- PRO reporting needs to become more reliable across medical fields.

What is the implication and what should change now?

- Investigators should improve PRO reporting, and ethics committees, funding agencies, and journal editors should enforce the use of reporting guidelines for PROs.

our cross-sectional study according to the Strengthening the Reporting of Observational Studies in Epidemiology statement [37] ([Supplement](#)).

2.2. Search for results publications

We systematically searched for full text results publications corresponding to trial protocols in PubMed, Google Scholar, Scopus, and Google [38]. In addition, we searched trial registries for posted trial results. For the RCTs approved in 2012, we searched for results up to February 2022; for RCTs approved in 2016, we searched for results up to May 2024. We excluded trial protocols that were never initiated (ie, no participants recruited) or still ongoing at the time of analysis (for search details see Supplementary Material) [38].

2.3. Data collection

Using a web-based, password protected data extraction tool (<https://aspire-pro.squiek.io>), investigators trained in trial methodology worked in pairs of two and abstracted each study protocol and corresponding trial publication independently and in duplicate.

From all included RCT protocols, we extracted trial characteristics such as sponsorship, intervention type, country, whether the trial was multicenter or single-center, and planned sample size [34]. We checked if the primary

outcome was a PRO. If the primary outcome was not a PRO, we assessed whether PROs were considered as secondary outcomes. We extracted information captured by PROs (eg, physical functioning, disease-specific QoL), the instrument used to capture each PRO, evidence provided for its validity (defined as a reference to a validation study), the presence of a PRO hypothesis, and whether a method for PRO data collection was described (eg, use of diaries, survey, forms to be filled on-site at follow-up visits). We selected data extraction items based on previous metaresearch and through discussions with experts. We extracted the same information from all identified RCT results publications. In addition, for all trials with a PRO as the primary outcome and results published in a peer-reviewed journal, we assessed the quality of reporting using the Consolidated Standards of Reporting Trials—patient-reported outcomes (CONSORT-PROs) extension checklist [22]. Any disagreements between investigators with respect to extracted data or reporting quality assessments were resolved through discussion and consensus; in a few cases, A.A. or M.B. were approached for advice or arbitration.

2.4. Analyses

The characteristics of RCT protocols, corresponding trial publications, and PROs were summarized as frequencies and proportions for categorical variables and as medians and interquartile ranges for continuous variables. In the analysis, we treated composite outcomes—which included both PRO and clinician-reported outcome components (eg, the American College of Rheumatology 20/50/70 Response Criteria [ACR20/50/70])—as PROs and conducted a sensitivity analysis treating such composite outcomes as non-PROs. We used R (version 4.0.2) for all analyses. The analysis code is provided in the supplemental material.

3. Results

Of 549 approved RCT protocols (257 approved in 2012, and 292 in 2016), 61 were excluded because they were either ongoing, duplicates, or never initiated, leaving a total of 488 protocols (237 approved in 2012 and 251 approved in 2016) for inclusion in the present study ([Supplementary Fig](#)). Fifty-three percent of the trials were sponsored by industry (258/488), and 79% (384/488) were multicenter trials ([Table 1](#)).

While 30% of trial protocols did not include a PRO (147/488), 20% used a PRO as the primary outcome (16%, 39/237 in 2012; 23%, 58/251 in 2016) ([Table 1](#)). The other 50% of RCTs included PROs as secondary outcomes (52%, 123/237 in 2012; 48%, 121/251 in 2016). However, the prevalence varied substantially across medical fields, from 100% in rheumatology (21/21) and psychiatry (23/23), to 38% in cardiology, (22/58) and 33% in

Table 1. General characteristics of included RCT protocols

Characteristics	Protocols approved in 2012 <i>n</i> = 237			Protocols approved in 2016 <i>n</i> = 251			Protocols approved in total <i>n</i> = 488		
	PRO as primary outcome (<i>n</i> = 39; 16%)	PRO as secondary outcome (<i>n</i> = 123; 52%)	No PRO (<i>n</i> = 75; 32%)	PRO as primary outcome (<i>n</i> = 58; 23%)	PRO as secondary outcome (<i>n</i> = 121; 48%)	No PRO (<i>n</i> = 72; 29%)	PRO as primary outcome (<i>n</i> = 97; 20%)	PRO as secondary outcome (<i>n</i> = 244; 50%)	No PRO (<i>n</i> = 147; 30%)
Country of research ethics committee, <i>n</i> (%)									
Switzerland	24 (61.5%)	92 (74.8%)	49 (65.3%)	42 (72.4%)	97 (80.2%)	48 (66.7%)	66 (68.0%)	189 (77.5%)	97 (66.0%)
Germany	10 (25.6%)	16 (13.0%)	11 (14.7%)	10 (17.2%)	15 (12.4%)	9 (12.5%)	20 (20.6%)	31 (12.7%)	20 (13.6%)
Canada	5 (12.8%)	15 (12.2%)	15 (20.0%)	6 (10.3%)	9 (7.4%)	15 (20.8%)	11 (11.3%)	24 (9.8%)	30 (20.4%)
Medical field, <i>n</i> (%)									
Surgery	7 (17.9%)	13 (10.6%)	10 (13.3%)	6 (10.3%)	13 (10.7%)	5 (6.9%)	13 (13.4%)	26 (10.7%)	15 (10.2%)
Psychiatry	2 (5.1%)	2 (1.6%)	0 (0%)	13 (22.4%)	6 (5.0%)	0	15 (15.5%)	8 (3.3%)	0
Neurology	6 (15.4%)	8 (6.5%)	5 (6.7%)	4 (6.9%)	10 (8.2%)	6 (8.3%)	10 (10.3%)	18 (7.4%)	11 (7.5%)
Oncology	0	32 (26.0%)	10 (13.3%)	2 (3.4%)	32 (26.4%)	7 (9.7%)	2 (2.1%)	64 (26.2%)	17 (11.6%)
Rheumatology	4 (10.3%)	6 (4.9%)	0	8 (13.8%)	3 (2.5%)	0	12 (12.4%)	9 (3.7%)	0
Cardiology	1 (2.6%)	8 (6.5%)	16 (21.3%)	1 (1.7%)	12 (9.9%)	20 (27.8%)	2 (2.1%)	20 (8.2%)	36 (24.5%)
Other ^a	19 (48.7%)	54 (43.9%)	34 (45.3%)	24 (41.4%)	45 (37.2%)	34 (47.2%)	43 (44.3%)	99 (40.6%)	68 (46.3%)
Type of intervention, <i>n</i> (%)									
Drug	24 (61.5%)	80 (65.0%)	50 (66.7%)	29 (50.0%)	72 (59.5%)	50 (69.4%)	53 (54.6%)	152 (62.3%)	100 (68.0%)
Behavioral	3 (7.7%)	5 (4.1%)	0	15 (25.9%)	5 (4.1%)	1 (1.4%)	18 (18.6%)	10 (4.1%)	1 (0.7%)
Medical device	9 (23.1%)	22 (17.9%)	14 (18.7%)	4 (6.9%)	19 (15.7%)	13 (18.1%)	13 (13.4%)	41 (16.8%)	27 (18.4%)
Surgical procedure	1 (2.6%)	4 (3.3%)	3 (4.0%)	4 (6.9%)	8 (6.6%)	2 (2.8%)	5 (5.2%)	12 (4.9%)	5 (3.4%)
Other ^b	2 (5.1%)	12 (9.8%)	8 (10.7%)	6 (10.3%)	17 (14.0%)	6 (8.3%)	8 (8.2%)	29 (11.9%)	14 (9.5%)
Planned sample size									
Median [IQR]	240 [109, 600]	302 [100, 775]	300 [118, 600]	198 [100, 446]	240 [120, 560]	210 [102, 378]	200 [100, 496]	293 [112, 629]	250 [110, 558]
Sponsorship, <i>n</i> (%)									
Investigator	15 (38.5%)	45 (36.6%)	43 (57.3%)	33 (56.9%)	51 (42.1%)	43 (59.7%)	48 (49.5%)	96 (39.3%)	86 (58.5%)
Industry	24 (61.5%)	78 (63.4%)	32 (42.7%)	25 (43.1%)	70 (57.9%)	29 (40.3%)	49 (50.5%)	148 (60.7%)	61 (41.5%)
Center status, <i>n</i> (%)									
Single center	10 (25.6%)	20 (16.3%)	11 (14.7%)	23 (39.7%)	22 (18.2%)	18 (25.0%)	33 (34.0%)	42 (17.2%)	29 (19.7%)
Multicenter- international	25 (64.1%)	88 (71.5%)	46 (61.3%)	25 (43.1%)	87 (71.9%)	37 (51.4%)	50 (51.5%)	175 (71.7%)	83 (56.5%)
Multicenter- national	4 (10.3%)	15 (12.2%)	18 (24.0%)	10 (17.2%)	12 (9.9%)	17 (23.6%)	14 (14.4%)	27 (11.1%)	35 (23.8%)

PRO, patient-reported outcome; RCT, randomized clinical trial; IQR, interquartile range.

^a Dermatology, Gastro/intestinal, Pediatrics, Respiratory Medicine, Anesthesiology, Endocrinology, Nephrology, Hematology, Intensive care, Infectious diseases, Ophthalmology, Obstetrics and Gynecology, Geriatrics, Hepatology, Public health, Primary care.

^b Dietary Supplement, Rehabilitation, Process optimization in health care, Diagnostic, Creams, and cosmetics.

Table 2. Planning and reporting of PROs in RCTs

PRO reporting	PRO prespecified in 2012 (<i>n</i> = 162)	PRO prespecified in 2016 (<i>n</i> = 179)	Total (<i>n</i> = 341)
PRO as primary outcome	<i>n</i> = 39	<i>n</i> = 58	<i>n</i> = 97
No results available, <i>N</i> (%)	10 (26%)	16 (27%)	26 (27%)
Results available, <i>N</i> (%) ^a	29 (74%)	42 (73%)	71 (73%)
PRO reported as specified	23 (79%)	35 (83%)	58 (82%)
PRO reported differently as specified ^b	6 (21%)	7 (17%)	13 (18%)
PRO as secondary outcome	<i>n</i> = 123	<i>n</i> = 121	<i>n</i> = 244
No results publication, <i>N</i> (%)	22 (18%)	29 (24%)	51 (21%)
Results publication available, <i>N</i> (%) ^c	101 (82%)	92 (76%)	193 (79%)
PROs reported as specified	28 (28%) ^d	29 (31%)	57 (29%)
Specified PROs not reported at all	31 (31%)	24 (26%)	55 (28%)
Some specified PROs not reported	18 (18%)	18 (19%)	36 (18%)
Unspecified PROs reported	8 (7%)	7 (8%)	15 (10%)
Reported unspecified & not-reported all prespecified PROs	16 (16%)	14 (16%)	30 (15%)

PRO, patient-reported outcome; RCTs, randomized clinical trials.

^a 2012: We identified 26 RCTs in peer-reviewed articles and three RCTs in the results section of trial registries. 2016 We identified 37 RCTs in peer-reviewed articles and five RCTs in the results section of trial registries.

^b Differences with respect to employed instruments, secondary outcomes switched to primary outcomes, captured domains, and time points of interest.

^c 2012 We identified more information on trial registry for 12 RCTs. 2016: We identified more information on trial registry for 19 RCTs.

^d 1 RCT vaguely mentioned results of the PROs, did not publish data elsewhere.

anesthesiology (6/18) ([Supplementary Table S1](#)). Furthermore, almost all trials testing behavioral interventions (97%, 28/29) included a PRO. Results were consistent across different countries and the year of protocol approval.

Of the 97 trial protocols that specified a PRO as their primary outcome, 27% (26/97) had not published their trial results at 8–10 years follow-up ([Table 2](#)). Of the 71 protocols that had corresponding trial results published, 82% (58/71) reported PROs as specified in their protocol, and 18% (13/71) reported PROs differently as specified (eg, primary and secondary outcomes were switched, time points of interest or employed instruments changed). Of the 244 RCT protocols that specified a PRO as a secondary outcome, 21% (51/244) had not published their trial results at 8–10 years follow-up. Of the 193 protocols with corresponding trial results published, 30% (57/193) reported PROs as specified in their protocol and 70% (136/193) either did not report some or all of their PROs, or reported PROs not specified in their protocol. Results were consistent across medical fields and the year of protocol approval, with the exception that most published psychiatry trials with a PRO as primary outcome (55%, 6/11) reported PROs differently than specified ([Table 2](#), [Supplementary Table S1](#)).

Most PROs captured either symptoms or disease-specific outcome measures, lacked supporting information regarding validity of the instrument used, but did provide details on how data collection was conducted ([Table 3](#)). This was consistent across medical fields ([Supplementary Table S5](#) and [S6](#)).

The reporting quality of PROs was often low, with seven of 13 CONSORT-PRO items met by less than half of the 63 published trials that reported a PRO as the primary outcome ([Table 4](#)). However, there was improvement in trials associated with more recently approved protocols on two items. Twenty-three percent (6/26) of trial results based on protocols approved in 2012 reported a supporting hypothesis for their PRO primary outcome vs 57% (21/37) for trials based on protocols approved in 2016. Furthermore, 69% (18/26) trial results associated with a protocol approved in 2012 adequately reported a sample size calculation for their PRO primary outcome vs 92% (34/37) of trials associated with protocols approved in 2016. Sensitivity analyses treating composite outcomes including PRO components as non-PROs revealed similar results ([Supplementary Tables S2–S4,S7](#)).

4. Discussion

4.1. Main findings

This metaresearch study of 488 RCT protocols found that 30% did not capture PROs. Of those that did, 72% defined PROs as a secondary outcome and 28% as a primary outcome; however, the prevalence of PROs varied substantially across medical fields. Among corresponding RCTs results (considering peer-reviewed publications and results on trial registries), only 44% reported PROs as defined in their protocols, 21% failed to report any

Table 3. Detailed characteristics of PROs reported in protocols and in publications

PRO characteristics	2012				2016			
	PROs in protocols		PROs in publications		PROs in protocols		PROs in publications	
	PROs as primary outcome (n = 42)	PROs as secondary outcome (n = 349)	PROs as primary outcome (n = 30)	PROs as secondary outcome (n = 184)	PROs as primary outcome (n = 63)	PROs as secondary outcome (n = 352)	PROs as primary outcome (n = 44)	PROs as secondary outcome (n = 177)
What is captured by specified PROs?								
Symptoms ^d	15 (36%)	85 (24%)	11 (38%)	43 (23%)	24 (38%)	75 (21%)	14 (32%)	26 (15%)
Physical functioning ^d	3 (7%)	24 (7%)	1 (3%)	12 (6%)	4 (6%)	15 (4%)	3 (6%)	9 (5%)
Mental/emotional functioning ^d	2 (5%)	23 (6%)	0	15 (8%)	5 (8%)	37 (10%)	1 (2%)	15 (9%)
Social functioning ^d	1 (2%)	3 (1%)	0	0	1 (1%)	1 (1%)	0	1 (1%)
Disease-specific outcome measure	19 (46%)	83 (24%)	17 (56%)	65 (36%)	19 (30%)	77 (22%)	20 (45%)	48 (27%)
Multidimensional quality of life	1 (2%)	68 (19%)	1 (3%)	29 (16%)	0	60 (17%)	0	49 (28%)
Overall sense of well-being ^d	0	6 (2%)	0	2 (1%)	0	3 (1%)	0	9 (5%)
Satisfaction with treatment	1 (2%)	19 (5%)	0	1 (0.5%)	2 (3%)	29 (8%)	1 (2%)	5 (2%)
Utility	0	6 (2%)	0	1 (0.5%)	0	14 (4%)	0	6 (3%)
Other	0	32 (10%)	0	16 (9%)	8 (12%)	41 (12%)	5 (13%)	9 (5%)
Is any hypothesis specified for PROs?	18 (43%) ^a	38 (11%)	6 (20%)	9 (5%)	46 (73%) ^b	57 (16%)	21 (47%)	11 (8%)
Is there any evidence for validation of used instrument?	15 (35%) ^{a,c}	143 (41%) ^c	15 (52%) ^c	61 (33%) ^c	25 (39%) ^{b,c}	141 (40%) ^c	22 (50%) ^c	68 (51%) ^c
Data collection method for PRO reported?	27 (64%) ^a	233 (66%)	7 (24%) ^c	11 (6%)	35 (55%) ^b	223 (63%)	16 (36%)	21 (16%) ^d

PRO, patient-reported outcome; RCT, randomized clinical trial.

*Other: cannabis use, tolerance of treatment, abstinence, alcohol consumption.

^a 4 RCTs and five outcomes are missing.

^b 2 RCTs and two outcomes are missing.

^c Outcomes that use diaries as a tool to capture PRO are excluded: 2012 Protocols: primary 5, secondary 10; 2012 Publications: primary 2, secondary 7. 2016 Protocols: primary 5, secondary 9; 2016 Publications: primary 7, secondary 4.

^d In the absence of a disease-specific outcome measure or a multidimensional quality of life instrument.

Table 4. Quality of PRO reporting among published trials according to the Consolidated Standards of Reporting Trials–patient-reported outcomes extension checklist

CONSORT-PRO items ^a	2012 (<i>n</i> = 26)	2016 (<i>n</i> = 37)	Total (<i>n</i> = 63)
Identifying PRO in abstract	22 (85%)	31 (84%)	53 (84%)
Rationale of choosing a PRO	9 (35%)	16 (43%)	25 (40%)
PRO hypothesis mentioned	6 (23%)	21 (57%)	27 (43%)
Evidence for validation of instrument used to capture PRO ^{b,c}	15 (63%)	21 (70%)	36 (67%)
Method of PRO collection described ^c	7 (27%)	15 (41%)	22 (35%)
Mention of a minimal clinically important difference for the PRO ^c	12 (46%)	13 (35%)	25 (40%)
Sample size calculation adequately described (statistical test & alpha value & statistical power)	18 (69%)	34 (92%)	52 (83%)
Handling of missing PRO data described	15 (58%)	23 (62%)	38 (60%)
Reporting of a participant flow diagram	23 (88%)	35 (94%)	58 (92%)
Reporting of baseline data for PROs	17 (65%)	29 (78%)	46 (73%)
Results provided for each domain and time point ^d	3 (3%)	2 (25%)	5 (33%)
PRO-specific limitations/implications for generalizability reported	1 (4%)	3 (8%)	4 (6%)
Interpretation in relation to clinical outcome provided ^e	2 (10%)	2 (14%)	4 (11%)

PRO, patient-reported outcome.

^a We did not consider CONSORT PRO items 4a (participants), 16 (numbers analyzed), 18 (ancillary analyses), because these appeared equally relevant for PROs and non-PROs.

^b Outcomes that used diaries as a tool to capture PROs were excluded: two from 2012 to seven from 2016.

^c These items are all components of CONSORT PRO item 6a (outcomes) which we assessed separately, because each component appeared specifically relevant for PROs.

^d Nonmultidimensional PROs were excluded: 19 from 2012 to 29 from 2016.

^e Trials not planning further clinical outcomes were excluded: five from 2012, 23 from 2016.

prespecified PROs, and 36% reported more, less, or different PROs than prespecified in their protocol. Among published trials that reported a PRO as their primary outcome, reporting quality was often inadequate with seven of 13 items on the CONSORT-PRO met by less than half of trials. These findings were similar between trial protocols approved in 2012 and 2016.

4.2. Strengths and limitations

Strengths of our study include full access to a large sample of approved RCT protocols from three countries, a comprehensive search for corresponding results publications eight to 10 years after trial approval, and engagement of reviewers with methodologic training who performed all data abstraction independently and in duplicate. Furthermore, our results proved robust in sensitivity analyses with a more conservative definition of primary PROs.

Our study has several limitations. First, our study sample was limited to RCT protocols approved by research ethics committees in Switzerland, Germany, and Canada in 2012 and 2016, and may not be generalizable to other

settings. Second, we focused on the comparison of PROs planned in approved protocols with published PROs and did not consider PRO reporting in protocol amendments. Third, we did not assess whether research questions in RCTs were suitable for PROs or not. Fourth, we used only three criteria (predefined hypothesis mentioned for PRO, validated instrument for PRO measurement, method for PRO data collection specified) to assess the quality of PRO reporting in protocols, because our protocol sample predated the publication of the SPIRIT-PRO in 2018 [23]. Fifth, to keep data extraction from trial protocols manageable, we had to simplify our data extraction forms once during the course of the ASPIRE project. Therefore, we did not collect all data that we had planned to collect from trial protocols as specified in our study outline [34]; eg, whether a PRO was considered in the power/sample size calculation or whether a validated minimal important difference was reported, was only assessed for PROs defined as primary outcomes in results publications. Sixth, we did not consider statistical analyses of PROs in RCTs; this was comprehensively investigated by the Setting International Standards in Analyzing Patient-Reported

Outcomes and Quality of Life Endpoints Data Consortium (SISAQOL) in trials with locally advanced and metastatic breast cancer [39]. Seventh, this is a prespecified subproject of the ASPIRE study with a protocol outline only [34] and not a full protocol. The sample size was determined through ASPIRE limiting the representativeness of the results across all medical fields. Eighth, because CONSORT-PRO was not developed with the intent to be used as an assessment tool, we adapted the original 14-item checklist of CONSORT-PRO (see legend Table 4) before using it for assessment of reporting quality in an attempt to better reflect PRO-specific challenges [40]. Lastly, we did not assess the reporting of important secondary outcomes in RCT publications as recommended by CONSORT-PRO, because it proved challenging to clarify the importance of secondary outcomes.

4.3. Comparison with other studies

To our knowledge, this is the first study focusing on the prevalence of PROs in trial protocols and the consistency of reporting in corresponding published results across medical fields. There are, however, several studies on the planning and reporting of QoL outcomes in oncology trials. Previous meta-research on 173 protocols of cancer trials approved between 2000 and 2003 and corresponding results publications up to 2013 found that only 20% of approved trials reported QoL outcomes, with cancer trials either not specifying QoL outcomes in their protocol (48%), not publishing trial results (21%), or failing to report prespecified QoL outcomes in their published results (10%) [14]. Results were similar in our sample of RCT protocols approved in 2012 and 2016. Specifically, of the 83 oncology trials, 22% reported PRO results as planned in their protocol, 20% did not specify a PRO in their protocol, 10% not publishing any trial results, 24% failing to report prespecified PROs in their published results, and 24% publishing results of more, less, or modified PROs when compared to those specified in the protocol (Supplementary Table S2).

A separate meta-research study examined 172 RCTs testing new drugs in metastatic nonsmall cell lung cancer published between 2010 and 2021 and found, similar to our study, that only 1% of trials specified QoL as a primary outcome, 23% of RCTs did not consider QoL at all, and RCTs reporting effects on QoL as a primary outcome showed modest quality of reporting with respect to CONSORT-PRO items [32]. Another analysis of QoL assessments and reporting in 106 solid cancer trials published between 2013 and 2021, found none of the trials considered QoL as primary outcome [15].

Reasons for nonreporting of prespecified PROs in published trial results may include outcome reporting bias. For example, industry trials may include agreements that allow the sponsor to remove unfavorable results from draft manuscripts prior to submission [41]. Moreover, PRO data are often cumbersome to collect, and may not be

considered a “hard measurement” because they are inherently subjective [26]. Trialists should carefully plan the collection of PRO data and restrict themselves to not overburden trial participants and staff; developers of clinical practice guidelines and systematic reviewers should be cautious when considering PRO results and carefully check for potential outcome reporting bias.

Our findings suggest that, despite the publication of CONSORT-PRO guidance in 2013, the planning and reporting of PROs in trial reports remains suboptimal [15,20,40,42,43]. The Patient-Reported Outcomes Tools: Engaging Users and Stakeholders (PROTEUS) Consortium [43] aims for more patient-centered research and promotes tools such as the SPIRIT-PRO recommendations for protocol writing [23], the International Society for Quality of Life Research Minimum Standards for selecting a PRO measure [44], the SISAQOL recommendations for PRO data analysis [45], the CONSORT-PRO statement [22], recommendations for the graphic display of PRO data [46], and a Clinician’s Checklist for reading and using an article about PROs [47]. Further implementation of these tools in clinical trial research and involvement of patient partners in trial planning, conduct, and reporting may facilitate improved consideration and reporting of PROs in clinical trials. Another promising development is the increasing collection and use of PRO measures in routine clinical practice, which may also improve reporting of PROs in clinical trials [48,49].

5. Conclusion

Approximately, one in three trial protocols do not capture PROs, and of those that do, the majority specify them as secondary outcomes; however, large variability exists across medical fields. Less than half of RCT protocols with planned PROs reported them as specified in corresponding results publications, suggesting potential outcome reporting bias, and PRO reporting quality was often deficient. These limitations hamper informed decision-making of patients and health-care providers, as well as the development of evidence-based clinical practice guidelines. Investigators should routinely consider the specification of PROs when designing clinical trials, and ethics committees and journal editors should make the use of SPIRIT-PRO and CONSORT-PRO mandatory for RCT protocols and results publications with PROs as primary or prominent secondary outcomes.

CRediT authorship contribution statement

Ala Taji Heravi: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Dmitry Gryaznov:** Writing – review & editing, Data curation. **Jason W. Busse:** Writing – original draft. **Christof Manuel Schönenberger:** Writing – review

& editing, Data curation. **Belinda von Niederhäusern:** Writing – review & editing, Data curation. **Lena Hausheer:** Writing – review & editing, Data curation. **Manuela Covino:** Writing – review & editing, Data curation. **Johannes M. Schwenke:** Writing – review & editing, Data curation. **Selina Epp:** Writing – review & editing, Data curation. **Alexandra Griessbach:** Writing – review & editing, Data curation. **Malena Chiaborelli:** Writing – review & editing, Data curation. **Arnav Agarwal:** Writing – review & editing, Data curation. **Szimonetta Lohner:** Writing – review & editing, Data curation. **Julian Hirt:** Writing – review & editing, Data curation. **Stefan Schandelmaier:** Writing – review & editing, Data curation. **Simon B. Egli:** Writing – review & editing, Data curation. **Moshao Amos Makhele:** Writing – review & editing, Data curation. **Alain Amstutz:** Writing – review & editing, Data curation. **Dominik Mertz:** Writing – review & editing, Data curation. **Anette Blümle:** Writing – review & editing, Data curation. **Erik von Elm:** Writing – review & editing, Data curation, Conceptualization. **Ramon Saccilotto:** Software. **Ayodele Odutayo:** Data curation, Conceptualization. **Sally Hopewell:** Writing – review & editing, Data curation, Conceptualization. **Benjamin Speich:** Writing – review & editing, Data curation. **Matthias Briel:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Data curation, Conceptualization.

Ethics statement

All participating ethics committees were project partners.

Declaration of competing interest

B.v.N. is currently employed by Roche Pharma AG, Grenzach-Wyhlen, Germany. A.T.H. is currently employed by Novartis, Switzerland, and D.G. is currently employed by Viartis Innovation GmbH, Switzerland. There are no competing interests for any other author.

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Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jclinepi.2025.111822>.

Data availability

Data will be made available on request.

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