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**Article**

**Systematic evaluation of Patient-Reported Outcome protocol content and reporting in cancer trials**

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**ABSTRACT**

**Background**

Patient-Reported Outcomes (PROs) are captured within cancer trials to help future patients and their clinicians make more informed treatment decisions. However, variability in standards of PRO trial design and reporting threaten the validity of these endpoints for application in clinical practice.

## **Methods**

We systematically investigated a cohort of randomized controlled cancer trials which included a primary or secondary PRO. For each trial, an evaluation of protocol and reporting quality was undertaken using standard checklists. General patterns of reporting where also explored.

## **Results**

Protocols (101 sourced, 44.3%) included a mean of 10/33 (range = 2–19, SD = 4) PRO protocol checklist items. Recommended items frequently omitted included: the rationale and objectives underpinning PRO collection and approaches to minimise/address missing PRO data. Of 160 trials with published results, 61 (38.1%, 95% CI = 30.6% to 45.7%) failed to include their PRO findings in any publication (mean 6.43-year follow-up); these trials included 49,568 participants. Although two-thirds of included trials published PRO findings, reporting standards were often inadequate according to international guidelines (mean inclusion of 3/14 (range = 0–11, SD = 3) CONSORT PRO Extension checklist items). Over half of trials publishing PRO results in a secondary publication (12/22, 54.5%) took 4 or more years to do so following trial closure, with 8 (36.4%) taking 5-8 years and one trial publishing after 14 years.

## **Conclusions**

PRO protocol content is frequently inadequate, and non-reporting of PRO findings is widespread, meaning patient-important information may not be available to benefit patients, clinicians and regulators. Even where PRO data are published, there is oftenconsiderable delay and reporting quality is suboptimal. This study presents key recommendations to enhance the likelihood of successful delivery of PROs in the future.

Patient-Reported Outcomes (PROs) are increasingly captured within cancer trials to provide the patient perspective on the physical, functional, psychological and social consequences of disease and treatment.[1] This information is important in supporting patients to make more informed treatment decisions at the point of cancer diagnosis and beyond.[2, 3]

The utility of such data has been recognized by patients, clinicians, funders, regulators and policy-makers.[4-8] Despite this, emerging evidence suggests that important PRO information may be omitted from protocols[9, 10], potentially impairing data collection[11, 12], and PRO results are poorly reported in trial publications[5, 13-21], or may not be reported at all.[22] This represents a waste of limited healthcare and research resources, and may restrict the effective uptake of PRO trial findings in practice.

The American Society of Clinical Oncology (ASCO), United Kingdom (UK) National Institute for Health and Care Excellence (NICE) and European Medicines Agency (EMA) have all outlined the need to improve the quality of PRO trial results to better inform technology appraisals and licensing decisions.[8, 23, 24] Most importantly, patients with cancer have called for greater availability of high-quality PRO trial data to help them gain an insight into what their life will actually be like during and after a certain therapy, as well as how long they may survive.[25]

It has been hypothesised that omission of key PRO protocol components may be an important contributor to sub-optimal PRO reporting.[26] To our knowledge, however, only one study has examined this relationship in a small (n=26) sample of ovarian cancer trials.[27] Furthermore, a recent study has assessed the issue of availability of PRO trial data across Germany, Switzerland and Canada, but did not evaluate PRO protocol quality, so the relationship between the two could not be determined.[22] To investigate these issues, we conducted a systematic evaluation of PRO protocol content and reporting across a cohort of completed international cancer trials.

**Methods**

**Search strategy and extraction**

We identified randomized controlled cancer trials on the National Institute for Health Research (NIHR) Portfolio which included a PRO primary or secondary outcome (study protocol available[26]). The NIHR is the largest UK public funding stream, comparable to the National Institutes of Health in the US. Trials were eligible if they were listed as closed on the database by March 2014 (scheduled to allow time for reporting to occur) and/or had published results by the time of our final publication search in June 2017. We excluded trials lacking random allocation to one of 2 or more groups or a control arm and those that terminated early.

For each trial, we attempted to source the trial protocol (final ethically-approved version); published articles reporting final results; and secondary publications reporting PRO results. We defined a primary publication as the first/principal publication of the trial results regarding the primary outcome(s), and secondary publications as those published following/in support of the primary article. Abstracts and reports of preliminary results were excluded. Protocol retrieval was attempted via direct contact with research teams and by searching trial registries/databases/websites (see **Supplementary Box 1**). Publications were obtained via direct author contact, or by searching: MEDLINE; Embase; Cinahl+; PsycINFO; Cochrane Controlled Trials Register; or the Patient-Reported Outcome Measures Over Time In Oncology (PROMOTION) Registry.[28] Full search details are provided in the **Supplementary Methods**.

All searching, sourcing and extraction were conducted by two independent investigators (TK/KA), with a third researcher (DK/MC/AR) involved where required. Investigators extracted trial characteristics and determined the availability of PRO trial results. Unreported PROs were defined as those that were pre-specified in the NIHR portfolio database/trial registry/trial protocol, but that were not reported in either a primary or secondary publication. The University of Birmingham (Ref: ERN\_17-0085A) gave ethical approval for this study.

**Data analysis**

Investigators evaluated the completeness of general protocol sections using the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013 checklist.[29] Completeness of PRO-specific content was evaluated using a PRO protocol checklist.[9] For publications, general reporting standards were evaluated using the 2010 CONSORT (CONsolidated Standards of Reporting Trials) checklist.[30] PRO-specific aspects were reviewed using the 2013 CONSORT-PRO Extension.[31] For each trial protocol/publication assessed, individual checklist items were described as ‘present’ or ‘absent’, one point was assigned for each item ‘present’ giving a total score. Protocol and reporting standards did not make a distinction between study phases, however, investigators noted where a checklist item was deemed ‘not applicable’ according to the study design (e.g. SPIRIT item 17a on blinding, for a non-blinded study) and the denominator was adjusted accordingly during the analysis. Inter-rater agreement was calculated for each checklist based on the proportion of matching item-level decisions. A full breakdown of checklists is provided in **Supplementary** **Figures 1 and 2**. It should be noted that many included trials would have been developed prior to the existence of the SPIRIT/PRO protocol and CONSORT standards used in this study. Although developed recently, they present consolidated criteria drawn from many preceding years of published research outlining commonly considered good practice, thus, they remain a useful metric by which to assess the quality of PRO trial design and reporting.

**Statistical analysis**

Descriptive data are reported as numbers and percentages and where appropriate summarised using means and SDs or 95% CIs. We performed three pre-specified exploratory regression models including those trials for which a matching protocol and publication had been retrieved. Backwards elimination with a p-to-eliminate value of >0.05 was used to select variables to be included in all models. All tests were two-tailed. All analyses were conducted in STATA version 12 (StataCorp, College Station, Texas).

Model A investigated protocol inclusion of PRO protocol checklist items. The independent variable was the PRO Protocol Checklist score (adjusted for denominator variation) and the independent variables were: year of the protocol; whether the PRO was named as a primary or secondary outcome; cancer specialty; trial sample size; funding source; and the SPIRIT checklist score (adjusted for denominator variation).

Model B used logistic regression to determine factors associated with the reporting of PRO trial results. The dependent variable was ‘PRO trial results reported in the principal trial publication (yes/no)’. Covariates included year of the protocol; whether the PRO was named as a primary or secondary outcome; cancer specialty; trial sample size; funding source; the SPIRIT checklist score (adjusted for denominator variation); whether the primary outcome of the trial was statistically significant; and the PRO Protocol Checklist score (adjusted for denominator variation).

Model C explored factors associated with publication adherence to the CONSORT-PRO Extension. The dependent variable was the CONSORT-PRO Extension score (adjusted for denominator variation). Covariates included: the year of publication; whether the PRO was named as a primary or secondary outcome; whether there were single or multiple reports; trial sample size; funding source; journal impact factor; the CONSORT 2010 checklist score (adjusted for denominator variation); and the PRO protocol checklist score (adjusted for denominator variation). Full model details are provided in the **Supplementary** **Methods**.

**Results**

# Data screening and sourcing

# The NIHR Portfolio included 1,141 trials up to 1st March 2014, of which 913 were excluded as they were either not RCTs, did not include a PRO, or had not been completed by the cut-off date (Figure 1). The final sample included 228 trials, recruiting across 72 countries, which used 262 different measures to collect PRO data (see Table 1 for trial characteristics and Supplementary Tables 1-3 for full sample details and checklist scoring results).

# We were able to source 101/228 protocols (44.3%): 73 from the named trial contact; 13 as a supplementary journal file; 1 from the trial website; 5 from the sponsor/funder; and 9 using a Google search. Eighty percent of sourced protocols were associated with trials closing in 2008 or later, which was comparable to the overall sample. In addition, the demographics of trials where we were able to source the protocol, versus those where the protocol was unavailable, where broadly similar (Table 2). There were, however, some exceptions. Compared to the overall sample, studies for which we retrieved the protocol were less likely to be industry-funded, and included slightly fewer breast and prostate cancer trials, but slightly more lung, colorectal and ovarian cancer trials. Finally, inter-rater agreement for all checklists was high (≥75%).

**PRO protocol content**

Trial protocols (n=101) included a mean of 32/51 (range 11–43, SD 6) SPIRIT 2013 recommendations (66.2% adjusted for denominator variation) and 10/33 (range 2–19, SD 4) PRO protocol checklist items (31.9% adjusted). There were a number of PRO items deemed important in the literature[32] that were frequently omitted, for example: the rationale for PRO collection (missing in 68.2% of protocols); description of PRO-specific objectives (missing in 83.1%); justification of the choice of PRO instrument with regard to the study hypothesis (missing in 66.2%) and questionnaire measurement properties (missing in 48.5%); information regarding PRO data collection plans (missing in 40.7%); and methods to reduce avoidable missing PRO data (missing in 61.1%) (**Figure 2**). Where a PRO was the primary outcome, protocols included an adjusted mean of 62.4% SPIRIT recommendations and 38.3% PRO protocol checklist items. Where a PRO was the secondary outcome, protocols included an adjusted mean of 67.0% SPIRIT recommendations and 30.4% PRO protocol checklist items.

**Reporting of PRO trial results**

With a mean of 6.43 year's follow-up from trial closure, 160 trials had published their primary results by the time of our final publication search (**Figure 1**). Eighty-five trials included their PRO findings in the primary publication. Eight trials published their PRO data in both a primary and secondary publication and 14 solely in a secondary publication. More than one-third, 61/160 (38.1%, 95% CI = 30.6% to 45.7%), failed to include their PRO findings in any publication; these trials included 49,568 participants. Over half of trials publishing their PRO results in a secondary publication (12/22, 54.5%) took 4 or more years to do so following trial closure, with 8 (36.4%) taking 5 to 8 years and one trial publishing after 14 years.

Where a PRO was a primary outcome, 27/32 (84.4%) trials included PRO findings in the primary publication. Two trials (6.3%) published their PRO data in both a primary and secondary publication, 2 (6.3%) solely in a secondary publication and 3 (9.4%) failed to include their PRO findings in any publication. Mean time from trial closure to publication of PRO results in a primary publication was 3 years, versus 8 years for a secondary publication.

Where a PRO was a secondary outcome, 58/128 (45.3%) trials included PRO findings in the primary publication. Six trials (4.7%) published their PRO data in both a primary and secondary publication, 12 (9.4%) solely in a secondary publication and 58 (45.3%) failed to include their PRO findings in any publication. Mean time from trial closure to publication of PRO results in a primary publication was 4 years, versus 5 years for a secondary publication.

Publications included a mean of 23/37 (range = 13–32, SD = 4) CONSORT 2010 items (63.0% adjusted for denominator variation) and 3/14 (range = 0–11, SD = 3) CONSORT-PRO Extension checklist items (21.7% adjusted). Commonly omitted CONSORT-PRO Extension items included: description of the PRO hypothesis/objectives (missing in 71.8% of publications); evidence of the validity and reliability of the PRO instrument(s) (missing in 67.8%); detail regarding the number of PRO data collected at baseline and subsequent time points (missing in 72.8%); and description of the statistical approaches used to deal with missing PRO data (missing in 67.8%) (**Figure 3**). Where a PRO was the primary outcome, publications included an adjusted mean of 62.1% of CONSORT 2010 items and 41.1% CONSORT-PRO items. Where a PRO was the secondary outcome, protocols included an adjusted mean of 63.3% of CONSORT 2010 items and 16.9% CONSORT-PRO checklist items.

**Factors associated with PRO protocol content and reporting**

Eighty-four trials were included in the pre-specified exploratory regression analyses. Full details of each model are presented in **Supplementary Tables 4-6**.

For Model A, statistically significant predictors of the protocol inclusion of PRO protocol checklist items included: presence of the PRO as a primary outcome (Coef = 10.93; 95% CI = 4.46-17.41); later year of the protocol (Coef. = -0.82, 95% CI = -1.52 to -0.12); a higher adjusted SPIRIT 2013 checklist score (Coef. = 0.41, 95% CI = 0.20-0.62); and larger sample size (reference category <100; n=100-499, Coef. = 9.77, 95% CI = 1.84 to 17.71; n=500-999, Coef. = 14.14, 95% CI = 5.04 to 23.24; n>1000, coef. = 6.50, 95% CI = -2.70 to 15.70). Statistically non-significant covariates included cancer specialty and funding source.

For model B: increased odds of publishing PRO results was associated with inclusion of the PRO as a primary outcome (OR = 5.68, 95% CI = 1.09-29.5). With charity funding as a reference category, industry funding (OR = 0.24, 95% CI = 0.07-0.87) and mixed-funding (OR = 0.17, 95% CI = 0.04-0.66) were associated with decreased odds of publishing PRO results. Statistically non-significant covariates included: year of the protocol; cancer specialty; trial sample size; adjusted SPIRIT checklist score; whether the primary outcome of the trial was statistically significant; and the adjusted PRO Protocol Checklist score.

For model C: a higher adjusted PRO Protocol Checklist score was a statistically significant predictor of reporting quality, as measured by the CONSORT PRO Extension (Coef. = 0.44; 95% CI = 0.01-0.87). Statistically non-significant covariates included: year of publication; whether the PRO was named as a primary or secondary outcome; whether there were single or multiple reports; trial sample size; funding source; journal impact factor; and the adjusted CONSORT 2010 checklist score.

**Discussion**

In this study evaluating PRO protocol quality and reporting in cancer clinical trials, several key messages emerged. Non-reporting of PRO trial results was widespread, PRO protocol components were often inadequate, and where published PRO data were available, there was often considerable delay and standards of reporting were poor.

More than one-third of trials failed to include their PRO findings in either a primary or secondary publication. Thus, valuable information that may have an important impact on treatment decision-making and outcomes may not be available to patients and their clinicians, or to researchers undertaking meta-analyses. This represents a waste of limited healthcare research resources. Moreover, it devalues the considerable contribution of trial participants who spend time and effort providing PRO information in the belief that the data will be used for the benefit of future patients. Worryingly, we found almost 50,000 patients were involved in studies which failed to publish their PRO data. Non-reporting of these important patient data is unethical.

Our results concur with findings from a previous smaller study that reviewed 90 cancer trials collecting quality of life PROs, conducted in Switzerland, Germany, and Canada between 2000-2003 and a recent study evaluating PRO reporting across 11 major journals.[22, 33] Our methodology has the added value of being able to evaluate the quality of included PRO protocols and publications and the association between the PRO protocol quality and reporting, and to track the time from trial closure to publication of PRO results.

Our results identify a failure to include comprehensive PRO information in many trial protocols and publications. These findings concur with previous studies evaluating the quality of PRO protocols and publications, both in a cancer, and non-cancer settings.[9-11, 13-21, 34] Rudimentary design elements were consistently omitted from protocols reviewed in this study, including: a clear PRO rationale/objectives; justification for the choice of measure; guidance on data collection and, crucially: aspects around prevention/analysis of missing PRO data, which has been identified as a particular problem in trials collecting PROs.[35] These omissions may impair PRO-specific trial conduct, reduce data quality[11, 36, 37] and threaten the validity of these endpoints for application in clinical practice. Our exploratory regression analysis suggested an association between PRO-specific protocol completeness and reporting, which supports our *a priori* hypothesis.[26] We postulate that the inclusion of ‘good quality’ PRO protocol components facilitates more robust data collection, lower rates of avoidable missing data and more informative data with which to generate meaningful, publishable, PRO reports. The publication of the SPIRIT-PRO Extension in 2018 provides consensus recommendations regarding items that should be included in trial protocols in which PROs are a primary or key secondary outcome.[38] In addition, open access international reporting guidelines are available via the 2013 CONSORT PRO extension.[31] It is hoped the existence of these standards will help improve the completeness and homogeneity of PRO design and reporting in the future.

Alongside the current study, we conducted 44 follow-up qualitative interviews (unpublished data) with journal editors, funder representatives, international PRO methodology experts, people with lived experience of cancer and trialists, based in Austria, Canada, Belgium, the Netherlands, Spain, USA and the UK. The protocol is available[39] and results will be published elsewhere. The qualitative data suggest the reasons underpinning our concerning findings are multi-factorial, aligning with related research in this area.[11, 12, 36, 40]In summary, interviewees suggested that future trials collecting PROs should include more comprehensive PRO trial design and protocol development involving PRO expertise and patient input, with a focus on standardised administration; minimising burden; preventing/addressing missing data; development of *a priori* PRO analyses and dissemination plans; and training of all staff involved. We concur with these suggestions and propose several further methodological recommendations below (summarised in **Figure 4**).

Our study had limitations. We were unable to source all protocols in our sample, either due to out of date database/registry information, or because researchers refused to provide the document. The PRO Protocol Checklist we used was a precursor to the internationally endorsed SPIRIT-PRO extension, published after our study had taken place. However, SPIRIT-PRO represents minimum standards, whereas the PRO Protocol Checklist is more comprehensive and was developed by experts in the field following a large-scale systematic review.[32] Most included studies were developed prior to the publication of the PRO protocol and CONSORT-PRO checklists. However, as no other internationally endorsed PRO-specific consensus guidelines/checklists existed at the time of our study, we believe their use is justified. Moreover, they provide a useful benchmark with which may help leverage improvements in future trials collecting PROs. Whilst the criteria for publication and reporting of phase II and III trials can be different, the reporting standards we employed did not make a distinction between these study designs. To mitigate, investigators agreed where a checklist item was deemed ‘not applicable’ according to the study design and the denominator was adjusted accordingly during the analysis. NIHR portfolio trials are predominantly UK-led, thus, replication of our study results in other countries is needed to demonstrate generalisability. The confidence intervals for predictors in our exploratory regression models were quite wide; this should be taken into account when interpreting the results and reflect the spectrum of quality observed with regard to protocol content and reporting. It should be noted that the most recent trials included in our sample closed 3 years prior to our final literature search in June 2017. It may be that some studies went on to publish their PRO data after this cut-off, which should be taken into account when interpreting our results. We would, however, argue that even reporting delays of this magnitude may impair the uptake of PRO trial results in practice and contravene recent regulatory and funder requirements mandating publication of results within 12 months of trial completion.[41, 42]

Our findings suggest that non-reporting of PRO trial findings is widespread and concerns surrounding standards of PRO protocol content and reporting in cancer clinical trials appear valid. Thus, valuable patient-centred information may not be available to aid the decision-making of patients, clinicians and regulators. These deficiencies must be urgently addressed to ensure these data are made available to enhance clinical outcomes for the benefit of future patients.

We therefore recommend that researchers utilize the recently published SPIRIT-PRO Extension[38] alongside the original SPIRIT 2013 statement[29, 43] when developing protocols for trials including PROs. For reporting, we encourage the use of the CONSORT-PRO[31] extension alongside CONSORT.[44] Evidence suggests that the use of such checklists may be valuable in driving up standards of PRO research.[45] We urge funders and journals to endorse and enforce the use of SPIRIT-PRO and CONSORT-PRO; and to promote and facilitate prompt publication of PRO findings, preferably as part of the main trial report. Finally, we encourage all stakeholders to utilize the growing range of suitable open access PRO training resources/guidelines to support high quality PRO research and dissemination.

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**Notes**

The funders had no role in design of the study; the collection, analysis, and interpretation of the data; the writing of the manuscript; and the decision to submit the manuscript for publication. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Contributors:The study was initially conceived by members of the UK National Cancer Research Institute (NCRI) Psychosocial Oncology and Survivorship CSG subgroup: Understanding and measuring the consequences of cancer and its treatment (JA, LC (chair), AGa, AGl, DG, DK, AL and RT). DK, MC, JA, LC, Aga, AGl, DG, AL and RT acquired funding. DK and MC designed the study. KA, TK, AR and GT undertook data extraction and analysis with input from DK and MC. DK drafted the first manuscript, with all authors contributing to subsequent iterations. All authors provided critical input on the manuscript and approved the final version for publication. DK/MC is guarantor.

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**Table 1. Characteristics of included trials (n=228)**

|  |  |
| --- | --- |
| **Characteristic** | **No. of Trials (%)** |
| Trial phase |  |
| II | 32 (14.0) |
| II/III | 17 (7.5) |
| III | 151 (66.2) |
| Other | 28 (12.3) |
| Recruitment regions# |  |
| United Kingdom | 221 (96.9) |
| Spain | 65 (28.5) |
| Italy | 63 (27.6) |
| Canada | 62 (27.2) |
| France | 62 (27.2) |
| Germany | 58 (25.4) |
| United States | 55 (24.1) |
| Belgium | 54 (23.7) |
| Australia | 51 (22.4) |
| Poland | 47 (20.6) |
| Russian Federation | 43 (18.9) |
| Netherlands | 41 (18.0) |
| Korea, Republic of | 34 (14.9) |
| Brazil | 30 (13.2) |
| Austria | 29 (12.7) |
| Sweden | 29 (12.7) |
| Argentina | 28 (12.3) |
| Israel | 28 (12.3) |
| Czech Republic | 26 (11.4) |
| Hungary | 25 (11.0) |
| China | 24 (10.5) |
| Japan | 24 (10.5) |
| Taiwan | 24 (10.5) |
| Turkey | 24 (10.5) |
| Cancer type |  |
| Breast | 37 (16.2) |
| Lung | 28 (12.3) |
| Prostate | 21 (9.2) |
| Colorectal | 15 (6.6) |
| Ovarian | 14 (6.1) |
| Other | 115 (50.4) |
| Source of funding\* |  |
| Industry only | 79 (34.6) |
| Public only | 34 (14.9) |
| Charity only | 85 (37.3) |
| Mixed | 30 (13.2) |
| PRO |  |
| Primary outcome | 42 (18.4) |
| Secondary outcome only | 186 (81.6) |
| Both | 28 (12.3) |
| PROs measured |  |
| Quality of life | 163 (71.5) |
| Symptom burden | 128 (56.1) |
| Anxiety & depression | 24 (10.5) |
| Other | 12 (5.3) |
| PRO questionnaires used  |  |
| EORTC QLQ-C30 | 95 (41.7) |
| EQ-5D | 54 (23.7) |
| HADS | 21 (9.2) |
| Other | 92 (40.4) |
| Year of trial closure |   |
| 2001 | 2 (0.9) |
| 2002 | 5 (2.2) |
| 2003 | 4 (1.8) |
| 2004 | 3 (1.3) |
| 2005 | 12 (5.3) |
| 2006 | 9 (3.9) |
| 2007 | 8 (3.5) |
| 2008 | 20 (8.8) |
| 2009 | 23 (10.1) |
| 2010 | 32 (14.0) |
| 2011 | 34 (14.9) |
| 2012 | 34 (14.9) |
| 2013 | 38 (16.7) |
| 2014 | 4 (1.8) |

\*As listed on the NIHR Portfolio Database. #Additional recruitment regions included in < 10% of trials: Greece, Switzerland, New Zealand, Ireland, Mexico, Singapore, Hong Kong, India, Thailand, Denmark, Romania, Romania, Portugal, South Africa, Finland, Chile, Norway, Peru, Slovak Republic, Ukraine, Bulgaria, Colombia, Croatia, Czechia, Estonia, Puerto Rico, Philippines, Latvia, Egypt, Guatemala, Luxembourg, Panama, Serbia, Slovenia, Bosnia and Herzegovina, Costa Rica, Cyprus, Lebanon, Lithuania, Malaysia, Saudi Arabia, Bahamas, Belarus, Ecuador, Indonesia, Macedonia, Pakistan, Tunisia, Uruguay. See supplementary appendix for additional information.

**Table 2. Trial demographics stratified by availability of protocol**

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **Protocol sourced****No. (%)** | **No protocol available****No. (%)** |
| Total | 101 (100.0) | 127 (100.0) |
| Trial phase |  |  |
| II | 14 (13.9) | 18 (14.2) |
| II/III | 8 (7.9) | 9 (7.1) |
| III | 66 (65.3) | 85 (66.9) |
| Other | 13 (12.9) | 15 (11.8) |
| Cancer type |  |  |
| Breast | 12 (11.9) | 25 (19.7) |
| Lung | 16 (15.8) | 12 (9.4) |
| Prostate | 8 (7.9) | 13 (10.2) |
| Colorectal | 11 (10.9) | 4 (3.1) |
| Ovarian | 8 (7.9) | 6 (4.7) |
| Other | 46 (45.5) | 67 (52.8) |
| Source of funding\* |  |  |
| Industry only | 19 (18.8) | 60 (47.2) |
| Public only | 18 (17.8) | 16 (12.6) |
| Charity only | 45 (44.6) | 40 (31.5) |
| Mixed | 19 (18.8) | 11 (8.7) |
| PRO |  |  |
| Primary outcome | 19 (18.8) | 23 (18.1) |
| Secondary outcome only | 82 (81.2) | 104 (81.9) |
| Both | 15 (14.9) | 13 (10.2) |
| Year of trial closure |  |  |
| 2001 | 1 (1.0) | 1 (0.8) |
| 2002 | 1 (1.0) | 4 (3.1) |
| 2003 | 2 (2.0) | 2 (1.6) |
| 2004 | 1 (1.0) | 2 (1.6) |
| 2005 | 6 (5.9) | 6 (4.7) |
| 2006 | 5 (5.0) | 4 (3.1) |
| 2007 | 5 (5.0) | 3 (2.4) |
| 2008 | 10 (9.9) | 10 (7.9) |
| 2009 | 12 (11.9) | 11 (8.7) |
| 2010 | 13 (12.9) | 19 (15.0) |
| 2011 | 15 (14.9) | 19 (15.0) |
| 2012 | 15 (14.9) | 19 (15.0) |
| 2013 | 14 (13.9) | 24 (18.9) |
| 2014 | 1 (1.0) | 3 (2.4) |

\*As listed on the NIHR Portfolio Database.

**FIGURE LEGENDS**

**Figure 1. Study flow diagram.** NIHR: National Institute for Health Research; PRO: patient-reported outcome; RCT: randomised controlled trial; SPIRIT: Standard Protocol Items Recommendations for Interventional Trials; CONSORT: Consolidated Standards of Reporting Trials.

**Figure 2. Percentage of protocols (n=101) including each patient reported outcomes (PRO) Protocol Checklist item (adjusted for denominator variation).** PROM: Patient-reported outcome measure.

**Figure 3. Percentage of publications (n=101) including each CONSORT patient reported outcomes (PRO) Extension Checklist item (adjusted for denominator variation).** #1PRO elaboration to CONSORT checklist item 2a: “Scientific background and explanation of rationale”; #2PRO elaboration to CONSORT checklist item 4a: “Eligibility criteria for participants”; #3PRO elaboration to CONSORT checklist item 7a: “How sample size was determined”; #4PRO elaboration to CONSORT checklist item 13a: “For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome”; #5PRO elaboration to CONSORT checklist item 15: “A table showing baseline demographic and clinical characteristics for each group”; #6PRO elaboration to CONSORT checklist item 16: “For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups”; #7PRO elaboration to CONSORT checklist item 17a: “For each primary and secondary outcome, results for each group, the estimated effect size, and its precision (such as 95% confidence interval)”; #8PRO elaboration to CONSORT checklist item 18: “Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory”

**Figure 4. Summary of key recommendations and resources.** PRO: patient-reported outcome; SPIRIT: Standard Protocol Items Recommendations for Interventional Trials; CONSORT: Consolidated Standards of Reporting Trials; SISAQOL: Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints Data; FDA Food & Drug Administration; EMA: European Medicines Agency; ISOQOL: International Society for Quality of Life Research; CPROR: Centre for Patient-Reported Outcomes Research.