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Guidelines for Reporting Outcomes in Trial Reports The CONSORT-Outcomes 2022 Extension

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IMPORTANCE

- Clinicians, patients, and policy makers rely on published results from clinical trials to help make evidence-informed decisions.
- To critically evaluate and use trial results, readers require complete and transparent information regarding what was planned, done, and found.
- Specific and harmonized guidance as to what outcome-specific information should be reported in publications of clinical trials is needed to reduce deficient reporting practices that obscure issues with outcome selection, assessment, and analysis.

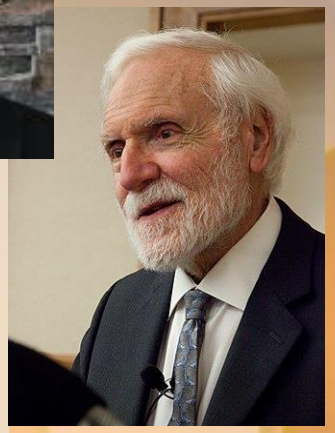
IMPORTANCE

- Insufficient outcome reporting remains common across academic journals and disciplines; key information about outcome selection, definition, assessment, analysis, and changes from the prespecified outcomes (ie, from the trial protocol or the trial registry) is often poorly reported.
- Such avoidable reporting issues have been shown to affect the conclusions drawn from systematic reviews and meta-analyses, contributing to ***research waste***.
- Although calls for improved reporting of trial outcomes have been made, what constitutes useful, complete reporting of trial outcomes to knowledge users such as trialists, systematic reviewers, journal editors, clinicians, patients, and the public is ***unclear***.

OBJECTIVE

- Question: What outcome-specific information should be included in a published clinical trial report?
- To develop harmonized, evidence- and consensus-based standards for reporting outcomes in clinical trial reports through integration with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement.

Background to CONSORT

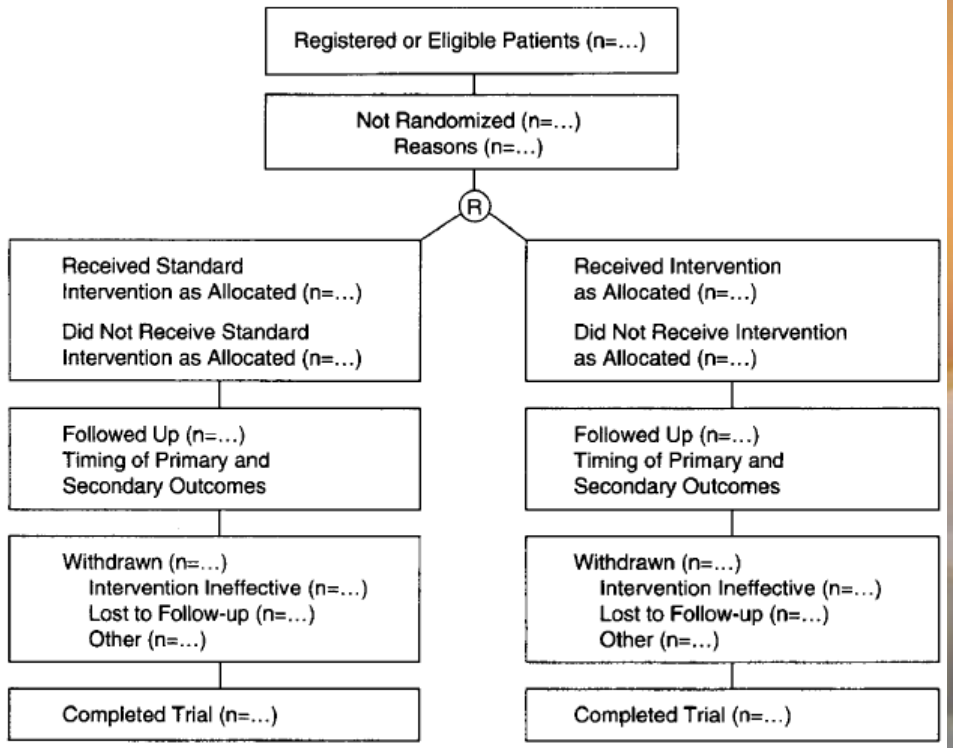


- RCT accelerated in the mid-1990s; authors reported such trials poorly, and empirical evidence began to accumulate that some poorly conducted or poorly reported aspects of trials were associated with bias.
- The development of the original CONSORT (Consolidated Standards of Reporting Trials) statement by 2 initiatives; David Moher and Drummond Rennie in 1996.
- The 1st revision in 2001 (22 items)
- The 2nd revision in 2010 (25 items: add *registration, protocol, fundings*) provides guidance for reporting all RCTs, but focuses on the most common design type-individually randomised, two group, parallel trials.

CONSORT version 1996

Consolidation of Standards for Reporting Trials—CONSORT[3,4]

Heading	Subheading	Descriptor	Was It Reported?	On What Page No.?
Title		Identify the study as a randomized trial.[7]		
Abstract		Use a structured format.[8,9]		
Introduction		State prospectively defined hypothesis, clinical objectives, and planned subgroup or covariate analyses.[10]		
Methods				
	Protocol	Describe Planned study population, together with inclusion/exclusion criteria. Planned interventions and their timing. Primary and secondary outcome measure(s) and the minimum important difference(s), and indicate how the target sample size was projected.[2,11] Rationale and methods for statistical analyses, detailing main comparative analyses and whether they were completed on an intention-to-treat basis.[12,13] Prospectively defined stopping rules (if warranted).[14]		
	Assignment	Describe Unit of randomization (eg, individual, cluster, geographic).[15] Method used to generate the allocation schedule.[16] Method of allocation concealment and timing of assignment.[17] Method to separate the generator from the executor of assignment.[17,18]		
	Masking (Blinding)	Describe mechanism (eg, capsules, tablets); similarity of treatment characteristics (eg, appearance, taste); allocation schedule control (location of code during trial and when broken); and evidence for successful blinding among participants, person doing intervention, outcome assessors, and data analysts.[19,20]		
Results				
	Participant Flow and Follow-up	Provide a trial profile (Figure) summarizing participant flow, numbers and timing of randomization assignment, interventions, and measurements for each randomized group.[3,21]		
	Analysis	State estimated effect of intervention on primary and secondary outcome measures, including a point estimate and measure of precision (confidence interval).[22,23] State results in absolute numbers when feasible (eg, 10/20, not 50%). Present summary data and appropriate descriptive and inferential statistics in sufficient detail to permit alternative analyses and replication.[24] Describe prognostic variables by treatment group and any attempt to adjust for them.[25] Describe protocol deviations from the study as planned, together with the reasons.		
Comment		State specific interpretation of study findings, including sources of bias and imprecision (internal validity) and discussion of external validity, including appropriate quantitative measures when possible. State general interpretation of the data in light of the totality of the available evidence.		



Progress through the various stages of a trial, including flow of participants, withdrawals, and timing of primary and secondary outcome measures. The "R" indicates randomization.

Background to CONSORT

- CONSORT 2010 does not include recommendations for designing, conducting, and analysing trials, but addresses the reporting of what was done and what was found.
- The explicit goal is to improve reporting.
- The Enhancing the Quality and Transparency of Health Research (EQUATOR) Network will facilitate development of reporting guidelines and help disseminate the guidelines: http://www.equator-network.org provides information on all reporting guidelines in health research.

CONSORT 2010 Checklist (25 items)

Section/Topic	Item No	Checklist item
Title and abstract		
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts [21, 31])
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
Sample size	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines

CONSORT 2010 Checklist (25 items)

Randomisation:		
Sequence generation	8a	Method used to generate the random allocation sequence
	8b	Type of randomisation; details of any restriction (such as blocking and block size)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
	13b	For each group, losses and exclusions after randomisation, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups

CONSORT 2010 Checklist (25 items)

Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms [28])	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration [13] for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials [11], non-inferiority and equivalence trials [12], non-pharmacological treatments [32], herbal interventions [33], and pragmatic trials [34]. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see http://www.consort-statement.org.

EVIDENCE REVIEW

equator network
Enhancing the QUAlity and Transparency Of health Research

- Using the Enhancing the Quality and Transparency of Health Research (EQUATOR) methodological framework, the CONSORT-Outcomes 2022 extension was developed by
  1) Generation & evaluation of outcome reporting items via consultation with experts and a scoping review of existing guidance for reporting trial outcomes (published within the 10 years prior to March 2018) identified through expert solicitation, electronic database searches of MEDLINE and the Cochrane Methodology Register, gray literature searches, and reference list searches
  2) A 3-round international Delphi voting process (Nov 2018-Feb 2019) completed by 124 panelists from 22 countries to rate and identify additional items
  3) An in-person consensus meeting (Apr 2019) attended by 25 panelists to identify essential items for the reporting of outcomes in clinical trial reports.

FINDINGS

- The scoping review and consultation with experts identified 128 recommendations relevant to reporting outcomes in trial reports
- The majority (83%) not included in the CONSORT 2010 statement.
- All recommendations were consolidated into 64 items for Delphi voting
- After the Delphi survey, 30 items met criteria for further evaluation at the consensus meeting and possible inclusion in the CONSORT-Outcomes 2022 extension.
- The discussions during and after the consensus meeting yielded 17 items that elaborate on the CONSORT 2010 statement checklist items and are related to completely defining and justifying the trial outcomes

FINDINGS

- How and when they were assessed (CONSORT 2010 item 6a)
- Defining and justifying the target difference between treatment groups during sample size calculations (CONSORT 2010 item 7a)
- Describing the statistical methods used to compare groups for the primary and secondary outcomes (CONSORT 2010 item 12a),
- Describing the prespecified analyses and any outcome analyses not prespecified (CONSORT 2010 item 18)

Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	6a.1	Provide a rationale for the selection of the domain for the trial's primary outcome
			6a.2	Describe the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, mean, proportion), and the time point for each outcome
			6a.3	If the analysis metric for the primary outcome represents within-participant change, define and justify the minimal important change in individuals
			6a.4	If the outcome data were continuous, but were analyzed as categorical (method of aggregation), specify the cutoff values used
			6a.5	If outcome assessments were performed at several time points after randomization, state the time points used for the analysis
			6a.6	If a composite outcome was used, define all individual components of the composite outcome
			6a.7	Identify any outcomes that were not prespecified in a trial registry or trial protocol
			6a.8	Provide a description of the study instruments used to assess the outcome (eg, questionnaires, laboratory tests) along with reliability, validity, and responsiveness in a population similar to the study sample
			6a.9	Describe who assessed the outcome (eg, nurse, parent) and any qualifications or trial-specific training necessary to administer the study instruments to assess the outcome
			6a.10	Describe any processes used to promote outcome data quality during data collection (eg, duplicate measurements) and after data collection (eg, range checks of outcome data values), or state where these details can be found (eg, an open access trial protocol)

The rationale may include (1) the importance of the outcome domain to the individuals (eg, patients, the public, clinicians, policy makers, funders, or health payers), (2) the expected effect of the intervention on the outcome domain, and (3) the ability to assess it accurately, safely and feasibly during the trial.

The minimal important change (MIC) for the relevant study instrument should be provided. If the MIC is unknown for the study instrument with respect to the trial's population and setting, this should be reported.

A composite outcome consists of 2 or more component outcomes that may be related. Participants who have experienced any 1 of the defined component outcomes comprising the composite outcome are considered to have experienced the composite outcome.

Among 67 trials published in 5 high-impact CONSORT endorsing journals, there were 365 outcomes added (a mean of 5 undeclared outcomes per trial). Less than 15% of the added outcomes were described as not being prespecified.

Sample size	7a	How sample size was determined	7a.1	Define and justify the target difference between treatment groups (eg, the minimal important difference)
	7b	When applicable, explanation of any interim analyses and stopping guidelines		

- The target difference is the value used in sample size calculations as the difference sought to be detected in the primary outcome between the intervention groups at the specific time point that should be considered realistic or important by 1 or more key stakeholder groups.
- The target difference may be the minimal important difference (MID; the smallest difference between patients perceived as important) or the smallest worthwhile effect (the smallest beneficial effect of an intervention that justifies the costs, harms, and inconvenience of the interventions as determined by patients).

Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	12a.1	Describe any methods used to account for multiplicity in the analysis or interpretation of the primary and secondary outcomes (eg, coprimary outcomes, same outcome assessed at multiple time points, or subgroup analyses of an outcome)
			12a.2	State and justify any criteria for excluding any outcome data from the analysis and reporting, or report that no outcome data were excluded
			12a.3	Describe the methods used to assess patterns of missingness (eg, missing not at random), and describe the methods used to handle missing outcome items or entire assessments
			12a.4	Provide a definition of the outcome analysis population relating to nonadherence of the trial protocol (eg, as a randomized analysis)

This is in reference to explicitly and intentionally excluded outcome data, such as too many missing items from a participant's completed questionnaire, or through other well-justified exclusion of outliers for a particular outcome.
This helps the reader to interpret the reported results, maybe presented in the CONSORT flow diagram where the reasons for outcome data exclusion are stated for each outcome by treatment group.

A lack of clarity about the magnitude of the missingness and how missing data were handled in the analysis makes it impossible for meta-analysists to accurately extract sample sizes needed to weight studies in their pooled estimates and prevents accurate assessment of any risk of bias arising from missing data in the reported results

Information on whether the investigators included all participants who were randomized to the group to which they were originally allocated (ITT) has been widely recognized to be particularly important to the critical appraisal and interpretation of trial findings.

Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% CI)	17a.1	Include the results for all prespecified outcome analyses or state where the results can be found if not in this report
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	18.1	If there were any analyses that were not prespecified, explain why they were performed

- The information available is often insufficient regarding prespecified analyses for the reader to determine whether there was selective nonreporting of any trial results.
- When it is not feasible to report on all prespecified analyses in a single trial report (eg, trials with a large number of prespecified secondary outcomes), authors should report where the results of any other prespecified outcome analyses can be found (eg, in linked publications or an online repository) or signal their intention to report later in the case of longer-term follow-up.

- These types of analyses can be called either exploratory analyses or analyses that were not prespecified.
- Communicating the rationale for any unprespecified analyses that, is important for trial transparency and for correct appraisal of the trial's credibility.
- State when such additional analyses were performed (eg, before or after seeing any results from comparative analyses for other outcomes).
- Multiple analyses of the same data create a risk for false-positive findings and selective reporting of analyses that were not prespecified could lead to bias.

DISCUSSION

- Similar to the CONSORT 2010, the CONSORT-Outcomes 2022 extension applies to the content of the trial report, including the tables and figures and supplementary material.
- Not prescriptive regarding the structure or location of reporting this information; authors should “address checklist items somewhere in the article, with ample detail and lucidity.”
- These additional items represent the minimum essential items for outcomes reporting and are being added to the CONSORT 2010 statement guidelines to maximize trial utility, transparency, replication, and limit selective non-reporting of results.
- The key users of the CONSORT-Outcomes 2022 extension: trial authors, journal editors, peer reviewers, systematic reviewers, meta-analysis researchers, academic institutions, patients and the broader public.

LIMITATIONS

- The included checklist items are appropriate for systematically collected outcomes, including most potential benefits and some harms, however, other items might be applicable for reporting harms not systematically assessed.
- Not yet integrated in the main CONSORT checklist, maybe considered burdensome by some authors and editors, which may affect uptake.
- The Delphi voting results could have been affected by a nonresponse bias because panelists were self-selecting.
- The consensus meeting panelists were purposively sampled based on their expertise and roles relevant to clinical trial conduct, oversight, and reporting.

CONCLUSIONS

- This CONSORT-Outcomes 2022 extension of the CONSORT 2010 statement provides 17 outcome-specific items that should be addressed in all published clinical trial reports and may help increase trial utility, replicability, and transparency and may minimize the risk of selective non-reporting of trial results.


Thank
you
so
much!