

## Specifying interventions in a clinical trial

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THE CONSORT STATEMENT is a checklist and flow diagram developed by an international group of clinical trialists, statisticians, epidemiologists and biomedical editors for reporting randomised controlled trials.<sup>1</sup> Item 4 in the checklist relates to interventions (Box 1).

The interventions used in a randomised clinical trial should be clearly defined in the protocol and reported in enough detail to be replicated. The control or placebo treatment arms should be described with the same degree of detail as the treatment arms. If the control group receives standard care rather than an intervention, this care must be described in detail, as it may differ between institutions or countries. The characteristics of any placebo (eg, tablet or capsule form, taste) and the way it is administered should be documented. If the study interventions are delivered in a blinded (masked) fashion, details of how the blinding was achieved should be described, including any procedures for unblinding subjects during the study.

The use of blinding is desirable to reduce reporting and measurement bias.<sup>1</sup> A study is classified as single-blind when only the study subject is unaware of which treatment has been assigned, and double-blind when the responsible clinician is also unaware of the assigned treatment. Double-blind studies, in which data are presented to the data-monitoring committee in a blinded fashion (ie, as treatments A and B), are sometimes referred to as triple blind.<sup>2</sup> If blinded interventions are not feasible or ethical, blinded assessment of outcomes should be attempted. For example, in a study comparing psychological outcomes after coronary surgery or percutaneous angioplasty for coronary heart disease, the assessor can still be blinded to treatment if patients are carefully gownned to obscure the presence or absence of a surgical scar and trained not to disclose the type of treatment received (assessments can even be videotaped to check that the blinding is preserved).

### Pharmaceutical interventions

Generally, the dose of a drug intervention used in a comparative trial would be the maximum effective tolerated dose determined from earlier-phase trials. The dose may be the same for all patients or modified according to criteria such as body weight or surface area. Alternatively, dose escalation or reduction may be appropriate to achieve a

### 1: CONSORT checklist of items to include when reporting a trial<sup>1</sup>

Section and topic	Item no.	Descriptor
Methods Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered

particular degree of response (eg, lowering of cholesterol or raising of haemoglobin levels) or where known side-effects have been reported. In addition to the usual monitoring of patients' details, any special safety investigations required as part of the trial should be reported. For instance, if a medication has been known to cause liver toxicity in some patients, the schedule used for monitoring liver enzymes should be included in the protocol and study report.

The description of pharmaceutical interventions should include the generic name, proprietary name (where brand substitution is not allowed), dosage formulation, route of administration, frequency of dosage, duration of therapy and any criteria for dosage modifications or cessation of the intervention during the course of the trial.<sup>3</sup> Any special handling procedures and storage conditions should be noted.

### Non-pharmaceutical interventions

Interventions that do not use drugs, such as surgical procedures and behavioural therapies, are more likely to vary in the way they are administered. It is therefore important to document the aspects of such interventions that were controlled closely by the protocol to enable readers to best ascertain how the intervention differed from their own practice. Similarly, multimodality treatments may follow specific schedules of delivery, and should be detailed in reports.<sup>4</sup>

### How was the intervention received?

Some indication of the proportion of patients receiving the interventions and how well these were tolerated should be reported. Poor compliance generally results in an underestimation of the actual benefits of treatment and may even produce a false negative result. Pilot studies can be useful in identifying problems with the delivery of treatments before a major study is initiated.

### Ancillary care

Details relating to ancillary care and the criteria for providing it should be reported. Some studies stipulate that, except for the intervention under investigation, all other

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**2: Checklist for specifying interventions in a clinical trial**

- Is enough detail provided so that the intervention could be replicated by others?
- Is the control group intervention described in enough detail?
- If blinding was used, has this been described and was it maintained?
- Is background and evidence for choice of dose included?
- Have criteria for dose modification or cessation of therapy been included?
- Were additional investigations or non-standard monitoring schedules required to ensure patient safety?
- Is any evaluation of compliance or tolerance included?
- Was ancillary care described or specified?

patient care is left to the discretion of the attending clinician. As ancillary care varies depending on the study centre, clinician preferences and patient comorbidities, key details should be documented. Ancillary care may also be specified in the protocol. For example, antiemetics may be used routinely in an oncology trial to allow for a planned fixed dose of a chemotherapy regimen for all patients. Many interventions are used with specified "rescue or salvage options" in the event of treatment failure.


**Other aspects**

Study sponsors and suppliers of any intervention should be acknowledged and any potential conflicts of interest declared. Documentation that appropriate ethical and regulatory approval has been obtained to conduct the trial is essential. All drugs and devices not listed on the Australian Register of Therapeutic Goods require Therapeutics Goods Administration (TGA) approval for use in a trial under the Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX) schemes. This also applies to trials evaluating new doses of drugs or indications for approved products.

In conclusion, a checklist for specifying interventions is shown in Box 2.

**References**

1. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *Ann Intern Med* 2001; 134: 657-662.
2. Friedman LM, Furberg CD, DeMets DL. Fundamentals of clinical trials. 3rd ed. New York: Springer, 1998.
3. Pocock SJ. Clinical trials: a practical approach. Chichester: Wiley, 1983.
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