Best-practice assessment of patient-reported outcomes in cancer clinical trials

A resource for clinical trial staff

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Introduction: Patient-reported outcome measures

Patient-reported outcome measures (PROMs) are questionnaires that ask patients about any aspect of their experiences with cancer and its treatment.

While PROMs measure patients' subjective experiences, they generate numerical scores that can be compared between individuals and groups.

However, comparisons will only be meaningful if PROM data have been collected in a consistent way across patients and timepoints.

To ensure the highest level of consistency, it will usually be necessary to develop a specific protocol for PROM data collection that goes into more detail than will be available from the larger trial protocol.

The PROM protocol should be developed through discussion between key members of the team, including investigators, the trial coordinator and at least some members of trials staff.

What value do PROMs add to cancer clinical trials?

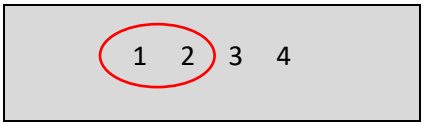
PROMs can:

- tell us whether benefits to survival from treatment outweigh side-effects and costs;
- tell us what supportive care should accompany treatments found to improve survival;
- screen for patient eligibility and provide prognostic information;
- assist regulatory authorities, clinicians and patients to make decisions between different treatments; and
- give patients a 'voice' appropriate to the current era of consumer-led, value-based healthcare.

The importance of high-quality data

Estimates suggest that 30% of clinical trials have over 20% of missing or invalid quality of life data.

An example of invalid data is:



Missing and invalid data reduce the statistical power of a trial and introduce 'bias'.

How can I ensure a high standard in PROM data?

The following guidance addresses issues raised by research trial staff and is based on guidelines to minimise missing PROM data.

1. Preparing to collect PROM data

Mode of administration

Familiarise yourself with the contents of each PROM and mode of administration. This includes whether the PROM will be administered via:

- self-completion or interviews (face-to-face or telephone), and
- pen-and-paper or electronic formats.

Timing of administration

Determine the timepoint(s) when PROMs need to be administered, for example, at baseline and two-week follow-up. Usually, there will be a 'window' allowed around each timepoint – for example, 1 or 2 days. Timepoints and windows should be defined according to when there are likely to be effects from treatment and disease – for example, at the end of each chemotherapy cycle.

Also determine any requirements for the timing of PROMs within the clinical visit or schedule of other assessments, for example, at the start or end.

If more than one PROM is being administered, determine if they are to be ordered in a specific way or in random order each time. Ordering is important because patients' responses on one PROM can sometimes influence their answers to those after.

Reminders for electronic PROMs

If PROMs will be administered electronically for patient self-report, set regular reminders, for example, via automated text messages.

2. Administering the PROM

Patient privacy

Where possible, make sure the patient is in a quiet space away from other people because:

- many PROMs include personal or sensitive questions that patients may want to keep private, and
- quiet environments help with concentration for patients facing cognitive challenges from cancer or treatment.

Patient motivation

Explain to patients that PROMs are important so they're more likely to complete them with care and attention.

Talk the patient through the CQUEST patient fact sheet, 'Understanding questionnaires in cancer clinical trials' to help them understand why PROMs are important and the dos/don'ts of completing them.

Should I provide any assistance to the patient in self-completing PROMs?

If the protocol for the trial asks for patients to self-complete PROMs, please offer as little help as possible.

At most, limit your assistance to reading the questions out loud and recording the responses for patients who are unable to do this for themselves.

If patients don't understand a question or ask for help with it:

- Never reword or try to explain it.
- Instead, ask the patient to answer as best they can. Reassure them that questions can mean different things to different people, and there are no right or wrong answers.
- If the patient remains unsure how to answer, leave the question blank, making a note of the reason why the data are missing.

3. Reviewing completed PROMs

Check for completeness

The Completion and Missing Data (CoMiDa) Form is recommended to assist with documenting PROM assessment at each timepoint.

Ensure the front cover of the PROM is completed with any details required, for example: the patient's study ID, the date and time of completion, and which staff member collected the PROM data via interview.

Wherever possible, check the PROM responses for completeness immediately after completion. Ask the patient to complete any questions they may have missed.

- Make notes for any reasons a patient has given for not completing a question.
- If answers appear inconsistent, invite the patient to read over and check their responses. If they choose to stick with the answers they provided, make a note that their responses were confirmed.

Sometimes PROMs are not received until after the timepoint window specified in the protocol – for example, if patients post them back via snail-mail. In these cases, it will not be possible for patients to change their responses, but you may still investigate reasons for missing data.

Responding to PROM data of concern

Some PROMs include questions that require clinical action if a patient answers in a certain way - for example, suicidal ideation or severe pain. These are commonly referred to as PRO alerts.

According to the Good Clinical Practice, the wellbeing of participants needs to be prioritised over the needs of the trial.

Familiarise yourself with any PRO alert protocols in place for the clinical trial in question. Seek clarification from the study coordinator/investigator team if you are unclear on any aspect. Formally, record any off-protocol interventions administered because of PRO alerts.

If you are unsure about any aspect of PROM data collection, please refer to the clinical trial protocol.

Further resources

For a checklist for clinical research professionals to support the systematic collection of PROM data, please see Wehrlen *et al.* (2016).

For guidelines to reduce, handle and report missing data, please see Hussain *et al.* (2022).

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