Marie Curie

Care and support through terminal illness

Executive summary

Missing data in palliative and end of life care trials

Guidance on how to reduce, handle and report incomplete data

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Executive summary

Missing data are observations (i.e. information) that would be meaningful to help answer a research question and which were intended to be collected, but for whatever reason were not.

Large amounts of missing data are found in palliative and end of life care studies. These can reduce the ability of a study to detect whether a new treatment is helpful or not, and how applicable the findings are to different types of people. Crucially, missing data can also affect how truthful the findings of a study are, as they can introduce bias.

Who is this guidance for?

This document provides guidance on how to reduce, handle and report missing data in palliative and end of life care trials. It aims to inform interested patients and carers, patient and public involvement (PPI) partners, clinical teams, researchers, funders and policymakers about how missing data should be addressed throughout the course of a study and how to evaluate the risks missing data pose to research findings.

Although this guidance focuses on palliative care studies, many of the recommendations will be relevant to other areas of healthcare research.

How were the guidelines developed?

The guidelines are based on research evidence, other guidelines and practice both within and outside of palliative and end of life care research. This information was synthesised and shared with participants at a missing data workshop hosted by Marie Curie. Participants included PPI partners, clinicians, researchers, statisticians and methodologists, who helped refine and develop the guidance presented[1].

Summary of the guidance

The guidance is structured as follows:

- Part A: how to **reduce** missing data in palliative and end of life care trials
- Part B: how to **handle** missing data in palliative and end of life care trials
- Part C: how to **report** missing data in palliative and end of life care trials.

The full report is available on **www.mariecurie.org.uk/missing-data**

[1] Hussain JA, White IR, Johnson MJ, et al. Development of guidelines to reduce, handle and report missing data in palliative care trials: A multi-stakeholder modified nominal group technique. *Palliat Med*; 2022, Vol. 36(1) 59–70. *journals.sagepub.com/doi/full/10.1177/02692163211065597*

A. How to reduce missing data in palliative and end of life care trials

All statistical methods to analyse datasets with missing data have limitations – therefore, reducing missing data is essential. This is because statistical techniques are often based on assumptions that cannot be verified, as the true values of the data that are missing are not known. The box below summarises the recommendations for reducing missing data in palliative and end of life care trials.

A summary of recommendations for reducing missing data in palliative and end of life care trials

1) Prepare and plan for how to reduce missing data at the trial design and protocol development stage.
This includes developing a flexible and inclusive study design, consulting members of the multidisciplinary team involved in conducting a trial on how to reduce missing data, reducing the trial burden and evaluating strategies to reduce missing data.

2) Resource the trial adequately to minimise missing data.
This includes funding for data collection across settings and the use of different modalities of data collection, incentives for sites to provide complete data and reasons for missing data, and recruitment of staff with a good track record for data collection.

3) Train all research staff to understand the risks posed by missing data and how to minimise missing data.

4) Discuss the value of complete data and how to reduce missing data with participants before they consent to enter the trial.
This includes exploring their concerns about the data collection process and informing them why each outcome is being collected, the importance of complete data and why collecting the reasons for missing data is important. Also gain consent for the use of proxies and/or access to their medical records if they are unable to provide data.

5) Collect the reasons for missing data.

6) Distinguish participants who want to withdraw from providing any further data from participants who wish to withdraw from part of the study protocol but consent to ongoing data collection or access.

7) Monitor and address missing data during the trial.

B. How to handle missing data in palliative and end of life care trials

Even with careful consideration of how to reduce missing data, some data will be missing in a large proportion of studies. It is crucial that such data are handled with a principled statistical approach that reduces bias as much as possible. The box below summarises the recommendations for handling missing data in palliative and end of life care trials.

A summary of recommendations for handling missing data in palliative and end of life care trials

1) Include a statistician in the trial team during the design, conduct and analysis stages of the study.

2) Decide how missing data will be handled in the design and conduct of the study and in its analysis, and report these decisions in the protocol and statistical analysis plan.

3) Prepare for missing data analyses at the trial design stage.
This includes collecting the reasons for missing data and considering whether any auxiliary variables should be collected.

4) Inflate the sample size to account for expected missing data in order to achieve the number of participants necessary to power the study adequately.

5) Consider how to handle data truncated due to death.

6) Explore the nature of the missing data in order to inform the missing data analyses.

7) Decide which assumptions about the missing data mechanism are plausible for primary and secondary outcome analyses in light of recommendation 6 (above).

8) Choose and conduct primary analyses that provide valid inferences under the missing data assumptions chosen in recommendation 7 (above), taking into account any auxiliary variables in the model(s).

9) Conduct missing data sensitivity analyses that assess the sensitivity of the results to plausible departures from the primary missing data assumption. These should include an exploration of missing not at random (MNAR) assumptions if plausible.

C. How to report missing data in palliative care trials

To enable users of research to evaluate the risks that missing data pose, clear and complete reporting of data is required. Poor reporting of trials is a persistent source of research waste and considered to be unethical. The box below summarises the recommendations for reporting missing data in palliative and end of life care trials.

A summary of recommendations for reporting missing data in palliative and end of life care trials

In the Methods section:

1) Report strategies used to reduce missing data throughout the trial process.

2) Report if and/or how the original sample size calculation accounted for expected missing data and the justification for these decisions. Report if and/or how the sample size was reassessed during the course of the trial.

3) Report the assumption about the missing data mechanism for the primary analysis and the justification for this choice for all outcomes with missing data.

4) Report the method used to handle missing data for the primary analysis and the justification for the methods chosen, for all outcomes with missing data. Include whether/which auxiliary variables were collected and used.

5) Report the assumptions about the missing data mechanism and methods used to conduct the missing data sensitivity analyses for all outcomes with missing data, and the justification for the assumptions and methods chosen.

6) Report how data that were truncated due to death were handled with a justification for the method(s) (if relevant).

In the Results section:

7) Report the numbers and proportions of missing data in each trial arm.

8) Report the reasons for missing data in each trial arm.

9) Report a comparison of the characteristics of those with observed and missing data.

10) Report the primary analysis based on the primary assumption about the missing data mechanism for all outcomes with missing data.

11) Report results of the missing data sensitivity analyses for all outcomes with missing data. As a minimum, a summary of the missing data sensitivity analyses for the primary outcome(s) should be reported in the main paper with the full results in the supplementary material.

In the Discussion section:

12) Discuss the impact of missing data on the interpretation of findings, considering both internal and external validity.

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