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Considerations in reporting palliative care clinical trials: Standardizing information reported and authorship practices

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Abstract

Purpose of Review—The nature of palliative care practice, especially the reliance on referrals and differing models of service delivery, poses unique challenges for the creation and interpretation of an evidence base, frequently limiting the applicability of data to patient care. Here we discuss two core aspects of clinical trials reporting in palliative medicine: 1) proposed standards governing the collection and reporting of data, and 2) rules governing authorship and publication.

Recent Findings—Existing literature often inadequately describes the characteristics of patients, caregivers, clinicians, systems, and interventions included in studies, thereby limiting the utility of results.

Summary—A generalizability framework is needed to ensure a robust evidence base that advances practice. Lessons learned through the development of research cooperative groups in palliative care reinforce the importance of an authorship protocol for large trials and working groups.

Keywords

palliative care; authorship; clinical trial; randomized controlled trials; generalizability

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INTRODUCTION

With the growth of palliative care comes the need for a more robust evidence base to guide clinical practice. As of 2005, articles on topics in hospice and palliative care accounted for only 0.38% of the published literature in the Medline database.[1] Recent trends hint at significant improvements therein, including the formation of research cooperative groups worldwide like the Palliative Care Research Cooperative Group in the United States and Palliative Care Clinical Studies Collaborative in Australia.[2–4] As further growth occurs in palliative care research, thoughtful governance of clinical trials reporting is warranted to maximize the impact of palliative care on improving patient outcomes.

Research in palliative care settings poses a number of unique challenges in the design, conduct, and reporting of trials.[5] This is due in part to the unique nature of the patient populations, their vulnerability, and their diversity of underlying disease states and care settings. Here we discuss two core aspects of clinical trials reporting in palliative care: 1) proposed standards governing the collection and reporting of data, and 2) rules governing authorship and publication.

PART 1: MAKING THE MOST OF THE DATA: STANDARDS FOR REPORTING AND MEASUREMENT

In order to advance clinical practice, published trials must be easily interpretable by clinicians practicing in a variety of settings. This generalizability is particularly problematic in palliative care research for several reasons: (1) definitional and terminological inconsistencies impair the effective reporting and description of study populations; (2) widely varying models of service delivery worldwide; and, (3) reliance on other clinical services to initiate the referral for palliative care in ways that are not standardized, leading to heterogeneity of the population served.

To date, most palliative care trials have accrued from a diverse pool of patients, diagnostically-speaking. This diversity was a positive factor in the early days of palliative care research. For example, a study enrolling “adult patients reporting pain who are receiving home hospice care” could yield important insights about general pain management across the spectrum of hospice care, regardless of disparate underlying etiologies like stroke and cancer. This inclusive philosophy also made it easier to accrue a larger sample, increasing the likelihood of completing adequately powered studies. As the palliative care evidence base grows, however, this inclusiveness can limit the likelihood of answering higher-level questions, such as those based on particular diagnoses or pathophysiologies. Findings cannot easily be generalized from research on diagnostically or otherwise physiologically diverse populations, especially if the population is not meticulously described. Using the pain example, a diverse palliative care population will likely include patients with a wide range of pathophysiologies generating their pain. Consequently, study results may be less useful if one is, for example, concerned with managing neuropathic pain in the setting of pancreatic cancer versus widespread musculoskeletal pain associated with advanced rheumatologic disease. While many authors of pain studies have become more astute in distinguishing between basic pain etiologies (such as neuropathic versus non-neuropathic), progressively more careful discrimination and characterization of subpopulations is important in all types of studies in palliative care, including interventions for other symptoms beyond pain. Even pain studies will need better discrimination to best target therapies to patients who will benefit. This higher level of evidence is needed to facilitate ongoing advancement of the care of persons with serious illness as well as palliative care as a specialty area of practice.

This difficulty is compounded by a lack of standardization of many common terms used to describe palliative care patients and practice settings,[6] which complicates interpretation and application of study findings. For example, “hospice” could describe a place where patients come for intensive management of refractory symptoms, usually in the last few days or weeks of life, or it could refer to the care of patients in the home setting who may have a life expectancy of upwards of 6 months. Thus, two studies that describe findings in a “hospice population” may actually be describing two very different types of patients and care delivered. Detailed description of the study population is essential.

These issues suggest the need for increased standardization of terminology in the design, conduct, and reporting of palliative care research along with more explicit descriptions of study populations and care settings. Just as the CONSORT diagram has become a standard language in clinical trials reporting, palliative care researchers must refine “Table 1” descriptions of patient populations and the service models in which that care is delivered to make results interpretable across studies.[7] These issues must be addressed in order for the palliative care evidence base to become more easily interpretable to practitioners, to speed the application of new evidence into clinical practice, and to allow the field to mature into answering higher-level questions.

Essential Data Elements

Currow, et al. have proposed a “generalizability framework” for studies in palliative care populations.[8] It includes five key “domains” that should determine data elements and study design prior to conducting a trial, and subsequent reporting thereof. These domains are: 1) patient/caregiver, 2) professional, 3) service, 4) health and social policy, and 5) research.

Patient/caregiver factors include the expected demographic information, but also a number other often-missing elements such as performance status, phase of illness, mean and median time between referral to the service and death, socioeconomic indices, and percentage of patients with a caregiver. Professional factors consist of the certification and training status of providers. Service data encompass details about the place and type of care (i.e. whether the intervention was community-based, consultative, inpatient, etc.). Health and social policy factors describe the general reimbursement modality (Medicare, self-pay, national coverage, etc.). The research domain focuses on details about the analysis, along with the nature of the intervention itself. These domains are outlined in Table 1.

Detailed information regarding these important factors tends to be absent from published studies in palliative care. A recent review of 189 research reports found that data elements regarding socioeconomic status, ethnicity, and presence of a caregiver were present in only 32%, 26%, and 11% of studies, respectively.[9] More detail and standardization of necessary information are important to ensure the applicability of palliative care research to practice whether or not this particular five-domain framework itself is used.

Defining the Intervention

In palliative care research, one particularly difficult problem is describing the intervention itself. With drug trials, it is quite easy to explicitly define the intervention in a way that lends itself to reproducibility and transparency, easily allowing for translation into practice (i.e. 300 milligrams of “substance x,” administered daily, with pill counts to assess adherence). Many palliative care interventions are much more difficult to define. The palliative care toolbox involves interdisciplinary teams, communication skills, inpatient consultations, and family meetings along with complex physical, psychosocial, and spiritual symptom assessment and treatment. These words describe very different things to different people or in different settings. A “consult,” for example, might have various meanings and

fundamental components across different countries, cultures, and hospitals or health systems. Similarly, a "family meeting" might involve different types of people who operate in very different ways at different institutions. Indeed, given the nature of research in hospice and palliative care, evaluation of anything but the most straightforward pharmaceutical intervention should be considered under the Medical Research Council's (MRC) framework for developing and evaluating complex interventions.[10] Originally proposed in 2000 and updated in 2008, this framework proposes processes akin to phase I, II and III studies that parallel the development of evidence of efficacy for a new medication, but allow for the sort of team interactions and multi-disciplinary processes that create many of the beneficial outcomes for palliative care.

Moving forward, we must design and report clinical trials that more explicitly describe the data elements, population factors, and the intervention itself. This is a significant, but important, challenge for palliative care to overcome as we expand the palliative care evidence base. First and foremost, authors should strive to carefully describe and define each aspect of their clinical service and the intervention. For example, authors must define key words such as "consult" using practical definitions that are intelligible outside of the local context; vetting such descriptions through international colleagues can be a useful litmus test. Whenever possible, interventions should also be standardized with clear operating procedures that can be provided to others on request.

When formally presenting a research report, authors may be confined to a specific number of words in the manuscript, limiting adequate detailed description. Supplementing these initial, more limited reports is essential. Options include publication of methodology manuscripts, descriptive sub-studies that define various elements of the clinical service, supplemental tables and data presented on the journal website, and presentation of detailed descriptions on the author's own website. The goal is transparency and reproducibility.

PART 2: AUTHORSHIP

It takes a village to design, carry out, analyze, and report research studies, especially in palliative care. Who then should receive credit for the work? Particularly in the academic world, attribution of such "credit" is generally inferred from authorship and the order in which authors are listed on a manuscript. This can seem unfair, or inadequate, as there are often many more people who contribute to a clinical trial than are listed as authors on the publication. This question is particularly complicated in cases of large, multi-site clinical trials as many journals strictly limit the number of authors allowed on a single manuscript. In these cases, if authorship is not carefully negotiated in advance, or governed by a policy, conflict can easily ensue.

This is certainly not a new problem. Disputes about authorship, and inconsistencies in applying it, are relatively commonplace in academia. For this reason, an increasing number of journals are following published standards governing the attribution of authorship. The "Vancouver protocol," for example, was an early example of such a rubric, which evolved into the current "uniform requirements for manuscripts" (URM), as formulated by the International Committee of Medical Journal Editors' (ICMJE).[11] An extensive list of journals following this guideline can be found on the ICMJE website (www.icmje.org). At a minimum, it stipulates that authorship must be based on all of the following:

1. substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data
2. drafting the article or revising it critically for important intellectual content, and
3. final approval of the version to be published.

In cases of group authorship for a large trial, the URM stipulates that authorship should be attributed to those individuals who, as identified by the group, also accept direct responsibility for the manuscript. Other contributors and participants should be mentioned in the acknowledgements section. The guideline further stipulates that authorship should not be granted on the sole basis of providing funding, participating in data collection, or supervising a research group. Historically, such contributions have often been the sole justification for authorship, which is sometimes "awarded" in thanks or honor; URM guidelines stipulate that this practice is no longer acceptable.

For cooperative research groups and/or large clinical trials networks, it is important to have an authorship protocol in place, *a priori*, to guide the timely and fair creation of manuscripts and other outputs, and attribution of credit via authorship (Table 2). This practice not only provides a framework for dispute resolution, but also ensures accountability for the timely reporting of results. Similarly, a protocol helps to ensure that authorship is granted on a basis that is concordant with individuals' efforts and involvement in the project. An effective authorship protocol should address four key areas:

1. Guidelines about the creation of manuscripts (who, when, how, etc.)
2. Dispute resolution
3. Generation and governance of working groups, to foster timelines
4. Accountability, including how to deal with collaborators not delivering on work as agreed.

The recently formed Palliative Care Research Cooperative Group in the United States recognized this challenge in its early development. The Steering Committee and founding members drafted and instituted a formal authorship protocol to govern research output. This protocol includes the basic authorship tenets of the ICMJE's URM, and adds provisions facilitating efficient publication timelines, governing the types of research output, and ensuring accountability. For each project one co-author is nominated as "executive author" for that area of research output. This individual is ultimately the "guarantor" of content, and is responsible for record keeping as well as keeping the team on track and accountable for the timely creation of manuscripts, posters, abstracts, etc. A signed authorship statement is also required for each author on each manuscript, attesting that each has met the URM requirements and Group requirements for authorship. A copy of the protocol is available to other researchers to use as a model, and can be obtained by contacting the authors of this manuscript.

Even with a detailed protocol in place, authorship order can become a contentious and murky topic. For example, there may be disagreement regarding the significance of various positions in authorship order, especially the "last author" and "corresponding author" designations. Rather than attempting to strictly define these variables, one approach to resolving this at the procedural level is to place attribution of authorship order under the jurisdiction of the "executive author," who is responsible for carrying out this negotiation equitably. The authorship protocol can then provide guidance about authorship order, what it signifies, and how it may be adjudicated fairly. This is consistent with the advice of the ICMJE.

In most cases, the "executive author" will be first author, having done the largest share of the work on a manuscript. Drawing from editorial guidelines at *JAMA* and *BMJ*, contributors are asked to quantify their relative percent effort of the final product, to guide the delineation of authorship order. As such, the list of authors between "first" and "last" would be ordered in terms of decreasing percent contribution to the published product. The

executive author must prepare a statement explaining and justifying the negotiated authorship order, to be kept on file.

The “last author” position is perhaps the most controversial, as it signifies different things in different academic circles. It might signify the most senior investigator, the laboratory head, or the individual who contributed least to the manuscript. An authorship protocol should provide guidance on this issue. For example, in the Palliative Care Research Cooperative Group the last author signifies the person making the second most sizeable contributions to the work and manuscript, or the senior most person on the project. In cases of disagreement among members of the working group, the “executive author” will be the arbiter and final decision-maker. Similarly, the executive author will assign the role of “corresponding author,” which involves administrative responsibilities including communications with journal editors, etc.; this will usually be either the first or last author. Recognizing the potential for conflicts of interest, the Palliative Care Research Cooperative Group’s Publications Committee reserves the right to arbitrate in cases of significant conflict.

CONCLUSION

As the palliative care evidence base grows, its research community must make calculated efforts to ensure the widest potential applicability of study findings. Achieving this goal will require careful scrutiny of current practices in clinical trials design and reporting, eliminating ambiguous terminology, especially with regards to the patient population in question, the intervention, and key data elements. Developing a standardized palliative care research “Table 1” would be an enormous step in the right direction. Similarly, palliative care researchers must standardize how we determine, interpret, and confer authorship in the reporting of multisite trials in the literature. The Palliative Care Research Cooperative Group’s authorship protocol provides an example of one approach to equitable assignment of authorship.

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KEY POINTS

- Palliative care practice poses unique challenges for the creation and interpretation of an evidence base, frequently limiting the applicability of data to patient care
- Existing palliative care literature often inadequately describes the characteristics of study populations and interventions, thereby limiting the utility of results
- A generalizability framework is needed to ensure a robust evidence base that advances practice.
- Lessons learned through the development of research cooperative groups in palliative care reinforce the importance of and need for an authorship protocol for large trials and working groups.

Table 1

Suggested Core Factors that May Affect Referral Patterns to Specialized Palliative Care Services, Referral to Their Studies, and Generalizability of Their Research Findings

Factors	Suggested Core Data Items	Example Data Fields	Example Output For People At The Time Of Referral
Domain 1: Patient and Caregiver	Patient factors	Age Gender Service socioeconomic indices (median income compared with national average, work force participation rates Locally relevant racial or ethnic issues compared with population served	Mean age, median age 54% female median income cover by the service/ median income of the country 9% of people refered had an Hispanic background compared with 13% of the region's population
	Patient's clinical issues	Primary life-limiting illnesses Performance status on referral Phase of illness Time from referral to death (days)	81% have cancer as their primary life-limiting illness Median performance status AKPS 60 Median phase 2 Mean 117; median 43
	Caregiver issues	Percentage of people with no identifiable caregiver	7% of people referred
Domain 2: Professional	Training in SHPC care as a specialty	Are nursing, medicine, and allied health professionals recognized as being in specialist SHPC clinical practice?	Subspecialty recognition – yes
Domain 3: Service	Local SHPC model of service delivery	Is the service mainly consultative (supporting primary health professionals and other specialists); a primary care service, or a hybrid? Is the service hospital-based or regional?	Consultative service Regional
	Admission and discharge policy	Is access to the SHPC service defined by diagnosis (cancer/noncancer), prognosis, or complexity of need?	Needs-based admission to the service
Domain 4: Health and Social Policy	Health system's funding mechanism	Is the health system predominantly user-pays or is there some form of universal health service?	Universal health coverage
Domain 5: Research	Outcome measures	Are the outcome measures used in reporting research validated for a palliative care population?	Yes/no (for each measure)

APKs=Australian-modified Karnofsky Performance Status; SHPC Specialist Hospice/Palliative Care.

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Table 2

	ICMJE Requirements for Authorship
1	Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data
2	Drafting the article or revising it critically for important intellectual content
3	Final approval of the version to be published
	Key elements of an authorship protocol
1	Guidelines regarding the creations of manuscripts (who, when, how)
2	Dispute resolution
3	Creation and governance of working groups, to foster timelines
4	Accountability