Special Article

Clinical Trials Focusing on Cancer Pain Educational Interventions: Core Components to Include During Planning and Reporting

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Abstract

Context. Robust recommendations on the reporting of methods and results of clinical trials such as *therapeutic* intervention trials are widely used, such as the Consolidated Standards of Reporting Trials (CONSORT) recommendation. There has not been agreement on analogous publication standards for *educational* intervention trials, making interpretation of educational intervention studies difficult.

Objectives. The purpose of this report is to describe common deficiencies in reporting of educational intervention trials for cancer pain control, and to offer suggestions for authors to consider as they plan their studies, and report and publish research findings for educational interventions that use randomized controlled trials and other educational trial methodologies.

Methods. A systematic review of published knowledge translation intervention trials intended to improve cancer pain was undertaken, of which most were educational interventions.

Results. Many educational intervention clinical trials designed to improve management of cancer pain appeared methodologically weak, and their results were more difficult to interpret because of reporting deficiencies. In the course of the review, patterns of deficiencies in reporting of methods and trial results were documented. Deficiencies in reporting were compared with the CONSORT recommendations for reporting clinical trials, and parallel recommendations were drafted for educational intervention trials. Patterns of deficiency in reporting cancer pain educational intervention trials were synthesized into seven domains, generically applicable to a range of study designs. Draft recommendations intended to address these deficiencies were constructed to improve communication of educational research results.

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Conclusion. Development of a standardized reporting template for clinical trials in cancer pain educational interventions could advance knowledge transfer research and thereby increase effectiveness of national and international cancer control policy designed to support cancer pain control. J Pain Symptom Manage 2010;40:301–308. © *2010 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

Key Words
Educational interventions, reporting requirements

Introduction

Evaluation of the peer-reviewed clinical trials literature reveals a wide range of approaches to reporting the design and results of clinical trials. The tendency to not fully or systematically report trials methods has been addressed for randomized controlled trials (RCTs) by the Consolidated Standards of Reporting Trials (CONSORT) statement and related publications.[1–3] The authors of the CONSORT statement have developed a succinct list of items, which has been very recently updated, that should be referred to when publishing RCTs results.[4]

Uptake of CONSORT recommendations has supported comparison of results among clinical trials. For example, greater standardization of the reporting of the design and analysis of individual clinical trials has allowed the results from various clinical trials to be combined and synthesized, through rigorous methodology such as systematic reviews and meta-analyses.

Systematic reviews and meta-analyses involve extensive searching of the literature to locate and select published clinical trials; completing a formal quality assessment of each selected study; extraction of relevant study data; and analysis, synthesis, and presentation of the collective results. Systematic reviews may be conducted with the intent of review and acceptance by international networks such as The Cochrane Collaboration or as a means to collate and summarize literature findings independently. Some Cochrane Review Groups, such as the Effective Practice and Organization of Care (EPOC) group, have developed materials, including handbooks,[5] quality assurance tools, and data collection checklists, to guide researchers through the process of conducting a systematic review. The outcome of these efforts has been remarkable: whole fields of biomedical research have greatly advanced the standards of care, leading to improved clinical outcomes, and less effective, ineffective, or outright dangerous treatments have been eliminated as a result of standardized, rigorous reporting of the design and results of clinical trials.

Quality assessment is necessary to obtain a measure of the validity of each study, limit bias in conducting the systematic review, and guide the interpretation of findings.[5] Poor research designs, methods, or reporting may skew study results (they tend to inflate the intervention effect), which may lead to less than optimal care when synthesized results or meta-analysis results are offered to the target patient population.[1]

Unfortunately, studies often have been conducted in a manner compliant with recommended approaches but have not been reported in a manner that demonstrates this compliance. Referring to reporting guidelines during the planning stages of the study may assist in addressing possible gaps. The phenomenon of inadequate reporting is not isolated to randomized interventions, and several groups are attempting to offer sound guidelines for reporting.[6,7] In addition, a number of resources that guide reporting on various types of research have been developed.[8] A high prevalence of underreporting of specific aspects of the design and results of clinical trials has been described.[9,10] Possible explanations for these reporting deficiencies may lie, in part, with journal limitations relating to length, word count, or editor preferences.

We recently performed a Cochrane Collaboration systematic review on Best Practice Guidelines for Oncology Pain Management.[11] As our team reviewed literature on *educational*

intervention trials designed to improve cancer pain control, we discovered a pattern of deficiencies in reporting results within published articles that was remarkably similar to deficiencies that led to the CONSORT recommendations. Because of these deficiencies in reporting, many otherwise informative educational intervention trials were excluded from our formal review. A standardized framework for reporting has not, to our knowledge, been widely applied to educational intervention trials within the health care setting.

The purpose of this report was to describe common deficiencies in reporting of educational intervention trials for cancer pain control. We then offer suggestions for authors to consider as they plan their studies, and report and publish research findings, for educational interventions that use RCTs and other educational trial methodologies. We hope to foster discussion within the knowledge transfer community to promote standardized approaches to reporting educational intervention clinical trials in cancer pain, thereby supporting processes as rigorous as Cochrane Systematic Reviews.

Initiatives to improve the impact of national cancer control strategies for cancer pain routinely refer to the use of educational approaches to support improved pain control.[12] Development of a standardized reporting template for clinical trials in cancer pain educational interventions can be anticipated to advance knowledge transfer research and thereby support application of more effective national and international cancer pain control policy. Furthermore, we hope lessons learned within these approaches to report cancer pain educational intervention studies more systematically can be considered by the broader knowledge transfer research community.

Methods

A systematic review of randomized knowledge translation intervention trials designed to improve cancer pain control was undertaken. Trials were included if they reported an intervention, including education, that was targeted to physicians, nurses, patients, or their families and evaluated outcomes including uptake of knowledge, skills, attitudes, and behavior change related to pain control or pain control outcomes of patients. The protocol has been published in the Cochrane Database of Systematic Reviews.[11] After the review of 14,000 titles (2300 abstracts, 308 full articles, and the final 26 articles included in the study), we evaluated our field notes characterizing deficiencies in reporting within these trials.

Field notes were developed based on two individuals' independent review of each article. Reviewers scrutinized specific issues based on two different quality assessment tools. The first tool used was the *Effective Public Health Practice Project Quality Assessment Tool 2003—Quality Assessment Tool for Quantitative Studies* (http://www.hamilton.ca/HealthandSocialServices/Research/EPHPP/) developed by the Effective Public Health Practice Project, Canada.[13] As the project evolved, we pursued collaboration with the EPOC Cochrane group, at which time the *Cochrane Collaboration Risk of Bias Tool* was introduced.[14] Based on scrutiny of each article using both tools, reporting deficiencies were identified and discussed. If discrepancies were found during quality assessment of each article, the article was reviewed again and consensus was reached.

Results

Twenty-six articles reporting on randomized trials of knowledge translation interventions designed to improve cancer pain control were assessed for study quality as part of our systematic review. The following deficiencies were identified: 96% of trials did not report on patient blinding, 81% did not report on personnel blinding, 88% did not report whether incomplete data were addressed, 69% did not report on concealment of allocation, 50% did not report sequence generation methods, 85% did not report fidelity, and 96% of trials were deemed to be at risk of other bias. A more detailed account of these specifics has been addressed elsewhere.[11]

Consistent with other literature,[10] deficiencies in reporting rather than poor methodology appear to be the issue. In another systematic review examining educational interventions targeted toward patients only (with some differences in analytic procedures and outcome measures), several of the same publications were scrutinized.[15] That publication echoed our findings of reporting deficiencies: In the 21 articles included for analysis in their

review, Bennett et al.[15] found that 62% did not report the method of randomization, 62% of articles failed to report how group differences at baseline were accounted for, and 86% of articles did not report blind outcome assessment.

Similarly, authors of other systematic reviews evaluating cancer pain education trials, or other cancer-related education trials, supported shortcomings in the quality of reporting of these types of studies. Many articles lack detailed descriptions of the format and content of their education programs,[16,17] details surrounding randomization methods are often missing,[16,17] the nature of blinding is not always clear,[18] sample characteristics are commonly omitted,[18] and the psychometric properties of assessment instruments are rarely reported adequately.[16] In a systematic review including 71 trials of educational interventions for symptom management in patients with chronic diseases (including some patients with chronic cancer pain), 24% of the included articles did not describe a formal syllabus for their education programs, 11% reported using intention-to-treat analysis, and only rarely were important patient attributes (e.g., education level, disease duration, disease severity, and social supports) reported.[19] These authors encouraged the development of CONSORT-like recommendations for trials of education programs.

Based on our own findings regarding quality of reporting, as well as those described in the literature, we mapped out common themes of these deficiencies based on the CONSORT recommendations,[4] and synthesized them within seven domains generically applicable to a range of study designs (Table 1). We also developed recommendations pertinent to three specific types of educational clinical trials.

Table 1
Seven Domains for Improving Reporting of Methods and Results in Educational Clinical Trials

Domain
Introduction and background
Outcome measures
Sample selection
Interventions
Statistical plan
Adverse events
Results

Reporting Recommendations Applicable to a Range of Study Designs of Cancer Pain Educational Interventions

Introduction and Background. All study reports should include some background for the reader to understand the clinical significance, prevalence of issue, and previous research undertaken, if any, to foster understanding of why the study was conducted.

Outcome Measures. All study designs should report precisely on the prospectively selected primary outcome and the tools and tests that facilitated data collection. Ideally, this should be an objective measurement, as opposed to self-reported data, or subjective information. Information that outlines methods by which the outcomes were measured (e.g., repeat sampling) should be included. In addition, relevant and interpretable data should be presented in a comprehensive, easy-to-read format. Educational interventions for cancer pain control are hypothesized to positively influence knowledge, attitudes, skills, and behaviors in pain control rather than clinical pain outcomes; the latter are at greater risk to be missed within the complex clinical picture of multisystem illness. Failure to see a significant improvement in pain control does not mean the intervention was ineffective. For this reason, we recommend that cancer pain educational interventions include primary end-points focusing on process outcomes such as uptake of knowledge, attitudes, skills, and behaviors of health care practitioners and patients and evaluate clinical outcomes as secondary end-points. Extensive information has been published on recommended core clinical outcomes for chronic pain trials, and these can be applied to clinical outcomes within pain educational interventions.[20–22]

Sample Selection. Eligibility criteria should be clearly described. It is helpful to include a schematic of how participants moved through the trial. Again, the CONSORT team has developed a template that is relatively easy to fill out and easy to understand.[4] This includes details regarding the number of individuals approached to participate, the number of individuals who actually entered the study, and the number of individuals who completed

data collection. If professionals were part of the study, a description of profession, level of training, and clinical specialty should be included. The clinical problem being tested should be clearly stated. The setting in which the study took place should be described (e.g., academic setting, rural vs. urban, outpatient vs. inpatient, and country), as well as the time period during which recruitment took place. A statement that ethical approval was granted should be added.

Interventions. A core principle of educational interventions is the educational dose intensity. Ideally, the trial's actual educational material will be posted on the Web or in a similarly accessible public repository so that the study readership can directly evaluate the material in detail. The duration of the educational intervention, the circumstances of the intervention (the learning environment, the extent, and intensity of direct interactions with the educators and other environmental parameters), the medium used, the kind and extent of institutional or other support for the learners, and any other relevant information to characterize the educational dose should be included. Details regarding the intervention instruments should be clearly described for each group and how they were administered or initiated. If an educational placebo was used, the article should characterize the placebo and how it compares with active treatment. The explanation of the interventions should allow readers to fully understand the process (what was done, to whom, and when) in such a way that the study could be fully replicated if desired and comprehensive comparisons between interventions can be made. *Fidelity*, defined as the delivery of the intervention as intended,[6] should be reported. Melde et al.[23] argue that failure to implement interventions as they were intended has a negative impact on evaluatory outcomes. As program providers tend to overestimate the fidelity of the intervention,[24] it is advisable that strategies to capture fidelity be determined *a priori* during protocol development. This would include all quality assurance activities, checklists, pretest/post-test, and random audits during the study period. Any protocol deviations should be explained, as well as their impact on outcomes, and if those subjects were included in the analysis.[1] Intention-to-treat analyses should be delineated as compared with on-treatment analyses. An indication of timelines should be reported (i.e., time from start of enrollment to end of follow-up), including when the study took place, to allow for historical context.

Statistical Plan. A power calculation (*a priori* estimate of required sample size to detect a significant effect and avoid a Type 2 error) should be reported, as well as statistical methods of analysis. If an interim analysis was incorporated, this should be explained in detail, as well as rationale for why it was done at a specific time in the trial. Measures and the unit of analysis should be reported, including names of all measures, instruments, subscales, and items used, along with variable derivations, formulas, units of analysis (facility, unit, and individual), aggregation, and analytic procedures.

Adverse Events. Adverse events of educational interventions are uncommon, but when they arise, they need to be documented. These can include the burden of undertaking the educational intervention on the health care providers, patients, or families; burden on the health care organization because of additional tests, treatments, or other health care activities that appeared to be linked to the trial; professional tension related to the uptake of innovations by the early adopters within the health care community; and others. A table format is often the easiest way to display this data. With common events, length of duration of the adverse event and severity can be collapsed and collated for ease of reporting. Although rare, serious adverse events should be reported, including whether the event was possibly, probably, or definitely related to the intervention.

Results. Results should include whether a significant difference was found between groups. The direction of effect should be reported as being positive (favorable) or negative. Clear representation of findings must be included in the results section of the manuscript. This includes *P*-values, confidence values, means, and standard deviations. In this way, research may be included for meta-analysis, which adds to the overall information available to clinicians. Unusual findings should be reported, along with the authors' interpretation of

findings. Results should address the hypothesis and objectives that were stated in the study design. Generalizability of the study results, or homogeneity of the study population, should be discussed. Problems encountered during the conduct of the study, and strategies developed to address these problems, should be discussed. As the authors reflect on the research experience, typically they are able to identify weaknesses in study design or can make recommendations on other ways to conceptualize this area of research. In this way, readers will learn not only about the results of the study being described but also practical applications that can be incorporated within their own research.

Reporting Suggestions Applicable to Specific Study Designs

Most Cochrane reviews consider only RCTs or quasi-RCTs.[5] However, some review groups (e.g., EPOC group) allow for the inclusion of other study designs, such as controlled before and after (CBA) studies or interrupted time series (ITS) studies, when few randomized trials are available. There are specific reporting requirements for each study design that should be included in the manuscript.

Educational Interventions Involving RCTs and Controlled Clinical Trials. In a randomized controlled trial, participants are assigned to groups within the study by means of random allocation (e.g., coin toss and random number generation). In a controlled clinical trial (CCT), participants are assigned to groups by means of a quasi-random allocation method (e.g., alternation). Reporting for both designs is similar. The manner in which randomization or allocation was achieved should be stated. Whether allocation was concealed, how it was generated and implemented, the percentage of participants for which outcome measures were obtained, and whether assessment of outcome measures was blinded should be stated. Reporting for blinding should explicitly indicate if subjects, team members, or those administering the interventions were blinded, and the risk for contamination should be stated. Reporting of concealment of allocation of participants is a commonly excluded but critical component in clinical trials.[9]

A comprehensive summary of participants' baseline characteristics (outcomes) should be included, along with an analysis of whether any differences existed between groups at baseline, to ensure that groups were comparable. Differences should be identified, and a statement of how these differences were handled during analysis is necessary. If a control group was used, a brief description regarding what the control group entailed is essential. Reliability of the primary outcome measures should be stated by means of interrater agreement, kappa scores, or standardized tests or tools used. Consideration of the possibility of contamination between groups should be described.

CBA Studies. A CBA study involves both an intervention and a control group. Outcome measures are collected during a baseline period and again after the intervention is initiated. In order for a CBA study to be included in a Cochrane review, data collection should have occurred at the same time for both control and intervention groups and include at least two post-intervention data collection points. Periods of study should be explicitly stated. In addition, both sites should be comparable with respect to level of care, setting, and academic status. These details should be included in the manuscript.

A comprehensive summary of baseline characteristics (outcomes) for *participants* should be included, along with an analysis of whether any differences existed between the groups at baseline to ensure that groups were comparable. Differences should be identified, and a statement of how these differences were handled during analysis is necessary. In addition, if a *second site* was used as a control group, differences should be explored and reported in a similar fashion. All other recommendations for reporting RCTs and CCTs as previously listed should be followed (contamination, reliability, whether the control and intervention groups were similar in size and function but were geographically distinct, and so forth).

ITS Studies. In an ITS study, outcome measures are collected at multiple time points where a change in trend may be attributable to the intervention. The publication must clearly identify when the intervention occurred relative to the data collection points,

with at least three data points collected before and three after the intervention.

The manuscript must explain if other changes happened simultaneously (or if the intervention was independent from other changes), type of data analysis used, rationale for the number of data point sets, completeness of data, shape of intervention effect, protection against detection bias, whether the assessment of the primary outcome was blinded or not, and reliability of measures for the primary outcome (agreement scores, kappa, and others).

Discussion

Recent literature[6,10,11,15] identifies common deficiencies in planning and reporting of educational intervention clinical trials. If these deficiencies were broadly addressed by the research community, individual study results would be easier to evaluate, and comparison between trials would be more informative.

Much work remains to be done by the academic knowledge transfer community. The CONSORT recommendations represent many years of collaborative work by clinical trials investigators around the world. These recommendations are captured within a 22-item checklist.[25] The elegance of the checklist does not capture the extensive collaboration and commitment required to develop such a powerful tool. A comprehensive expression of recommendations for educational intervention clinical trials in cancer pain is well beyond the scope of our current work. However, such a list of recommendations is urgently needed. Furthermore, a great strength of broad recommendations regarding clinical trials methodology lies in the collaborative discussions and endorsement that are required to develop them. Until such time as the knowledge transfer community has developed a checklist to guide intervention trials in cancer pain, the CONSORT 22-item checklist may potentially serve as a guide, seen through the lens of observations included within this present study. We strongly recommend that full reporting of fidelity be added to this list.

Conclusions

As the acumen in educational research methodology is growing within the health care community, there are increasing numbers of well-conducted studies using a randomized controlled trial design. Many such educational publications in cancer pain appear methodologically weaker, and their results are more difficult to interpret because of reporting deficiencies. Development of a standardized reporting template for clinical trials in cancer pain educational interventions holds the promise to greatly advance knowledge transfer research and thereby support more effective national and international cancer pain control policy. Further evaluation and development of this reporting framework is needed to assess whether it could be more broadly applied to health care educational intervention research.

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