Original Article

How Accurately Do Consecutive Cohort Audits Predict Phase III Multisite Clinical Trial Recruitment in Palliative Care?

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Abstract

Context. Audits have been proposed for estimating possible recruitment rates to randomized controlled trials (RCTs), but few studies have compared audit data with subsequent recruitment rates.

Objectives. To compare the accuracy of estimates of potential recruitment from a retrospective consecutive cohort audit of actual participating sites and recruitment to four Phase III multisite clinical RCTs.

Methods. The proportion of potentially eligible study participants estimated from an inpatient chart review of people with life-limiting illnesses referred to six Australian specialist palliative care services was compared with recruitment data extracted from study prescreening information from three sites that participated fully in four Palliative Care Clinical Studies Collaborative RCTs. The predominant reasons for ineligibility in the audit and RCTs were analyzed.

Results. The audit overestimated the proportion of people referred to the palliative care services who could participate in the RCTs (pain 17.7% vs. 1.2%, delirium 5.8% vs. 0.6%, anorexia 5.1% vs. 0.8%, and bowel obstruction 2.8% vs. 0.5%). Approximately 2% of the referral base was potentially eligible for these effectiveness studies. Ineligibility for general criteria (language, cognition, and geographic proximity) varied between studies, whereas the reasons for exclusion were similar between the audit and pain and anorexia studies but not for delirium or bowel obstruction.

Conclusion. The retrospective consecutive case note audit in participating sites did not predict realistic recruitment rates, mostly underestimating the impact of study-specific inclusion criteria. These findings have implications for the applicability of the results of RCTs. Prospective pilot studies are more likely to predict actual recruitment. J Pain Symptom Manage 2016;51:748–755.

Key Words

Randomized controlled trial, audit, recruitment, palliative care, prediction, screening

Introduction

Robust and high-quality palliative care and end-of-life clinical research is vital for improving quality of care and the quality of life of individuals with a limited life expectancy.[1] However, successfully recruiting to multisite randomized controlled trials (RCTs), the gold standard design for health care intervention evaluation studies, is often a commonly reported problem in these types of studies, and recruitment and retention rates are frequently overestimated.[2–4] If the sample size is too small, studies may lack the necessary power to detect statistically significant and clinically important differences in treatment, undermining study findings.[2,5] Furthermore, conducting palliative care research involves unique challenges such as ethical and logistical barriers, and recruitment is often more difficult than originally anticipated.[1,6–10]

Feasibility (pilot) studies can support successful completion of high-quality research in a timely manner by identifying difficulties with research methods and

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protocols before undertaking a larger clinical trial, particularly if there are any concerns about burden or feasibility.[11,12] Furthermore, such studies can refine eligibility criteria to optimize selection and accrual, thus minimizing selection bias,[11,13] and highlight key issues in trial design in the planning stages.

Audit methodology has been previously used to estimate potential recruitment.[11,14–16] This approach reviews eligibility criteria from the planned studies against a consecutive cohort of patients' case notes in sites that intend to participate in the study.

In 2006, the Australian Palliative Care Clinical Studies Collaborative (PaCCSC) was established to conduct adequately powered multisite RCTs investigating the effectiveness and cost-effectiveness of treatments for pain, bowel obstruction, delirium, and anorexia.[17,18] The PaCCSC is a national network with more than 20 recruiting sites, funded under the National Palliative Care Strategy by the Australian Government. Before commencement of the PaCCSC studies, a retrospective consecutive cohort audit was conducted to determine the frequency of pain, delirium, anorexia, bowel obstruction, and cholestatic itch symptoms in inpatient clinical settings across Australia in sites that had agreed to participate. The findings were used to estimate the likely proportion of patients meeting the eligibility criteria for the proposed studies.[14] Few, if any, studies in the palliative setting have validated recruitment estimates in feasibility studies or audits. Consequently, the aim of this study was to determine how accurately a retrospective consecutive cohort audit predicted Phase III multisite RCT recruitment, using completed studies.

Methods

Recruitment data from multiple sites in Australia were collected during the planning phase (retrospective cohort audit) and conduct of four large, completed, multisite RCTs of palliative medicines for pain,[18,19] delirium,[20] bowel obstruction,[21] and anorexia,[17] and compared.

Retrospective Consecutive Cohort Audit

The audit was conducted across six Australian specialist palliative care services in the second half of 2007. Full details of the audit are reported elsewhere.[14] Briefly, a retrospective chart review of clinical care data for a consecutive cohort of people who died within a three-month period and had at least one inpatient admission between referral and death with formal involvement of the supportive and palliative care service was conducted.[14] Retrospective data collected included patient demographics, primary diagnosis, reasons for referral to specialized palliative care services, reason for inpatient admission, functional status, prevalence of symptoms on admission, and medication use. Recruitment potential was estimated based on the presence of the symptom under consideration, the selection criteria common to all studies (language, cognition, and geographical proximity to the service), and study-specific eligibility criteria.

Actual Recruitment

Patients were referred from inpatient, outpatient, and community settings across the four studies. Before study screening, potential participants were prescreened to determine whether individuals met the broad inclusion characteristics for the study under consideration. These characteristics could be determined through discussion with the referring clinician, examination of the referral letter or case note review, either by the referring clinical team or the research staff subsequent to permission from the referred patient. If potentially eligible for the study, informed consent was obtained, and individuals were screened against the eligibility criteria.

The PaCCSC sites that were involved in the original audit and were recruiting at the time of the analysis were invited to participate in the study. The total numbers of referrals to each participating palliative care service between January 1, 2009 and December 31, 2012 were collected retrospectively using hospital activity data for each site, and an average monthly referral rate was multiplied by the duration of each study to estimate the total potential referral base. The total number of patients referred to each PaCCSC study, prescreening data (referral date, name and clinical area of the referring person, name and speciality of the treating consultant and knowledge of the referral, admission details, eligibility criteria, and reason for no further action), and the number of patients screened and excluded were collected prospectively throughout the recruitment periods for all four RCTs.

Analysis

To assess whether the audit predicted actual recruitment, the proportion of potentially eligible study participants estimated from the consecutive cohort of 468 people with life-limiting illnesses and actual recruitment data extracted from study *prescreening* information from participating sites were compared. Study selection criteria were recategorized into general (common to all PaCCSC RCTs) and study-specific (unique to an individual study), and the predominant reasons for exclusion were analyzed (Table 1).