Methodologic Issues in Collecting Data From Debilitated Patients With Cancer Near the End of Life

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Purpose/Objectives: To report the experience of a group of researchers who have had a year of experience in a clinical trial with homecare hospice patients.

Sample: 150 hospice patients with cancer and their primary caregivers who were accrued to a National Cancer Institute-funded clinical trial focusing on quality of life.

Methods: The investigative team kept careful records of the numbers of patient/caregiver dyads accrued to the study and the reasons for nonaccrual as well as reasons for attrition. Data were analyzed using descriptive statistics.

Findings: During a nine-month period, the hospice admitted 2,517 patients; 75% had cancer and 95% had caregivers, making them eligible for the study. However, after further screening, only 19% were eligible for contact and only 5% finally were accrued to the study. For the 125 patient/caregiver dyads actually accrued to the study, baseline data were obtained on only 50% and evaluable follow-up data on only 50%.

Conclusions: Accruing patients to clinical trials and retaining them when they are critically ill and near death are extraordinarily difficult tasks. The inability to recruit and retain subjects for clinical trials has implications for integrity of data, data analysis, success of the project, and the cost of conducting such projects in the future.

Key Points . . .

- Randomized clinical trials are needed to generate knowledge about the most appropriate ways to deliver care to people with cancer at the end of life.
- Entering patients into clinical trials near the end of life can be difficult, slow, and costly because of the deterioration in the health of patients and because of the burden of caregiving on the families.
- Declining physical and functional abilities of patients near the end of life and increasing burden on caregivers can result in high attrition rates from studies, thereby threatening study integrity.

Research involving people with cancer at the end of life is fairly new, and very few large clinical trials have been attempted with this population. Although the healthcare industry has accepted that randomized clinical trials are needed to address the problems of people at the end of life, researchers are just learning about the complex issues involved in such studies (Barnett, 2001; Ling, Rees, & Hardy, 2000; Mazzocato, Sweeney, & Bruera, 2001a). The number of patients who are able to participate may be very small, requiring longer data collection periods; patients may be too ill and debilitated to provide self-reported data; or they may experience a decline during the course of the study, leaving large amounts of missing data. If studies do not result in adequate data of high quality, the results of these long and expensive clinical trials would be uninterpretable. Not only is this wasteful of resources, but it also poses the potential risk of losing knowledge about hospice care, where precious little is available about evidence-based interventions.

Data collection for a project designed to support the quality of life of patients and caregivers by teaching caregivers a method of coping with symptom management was begun in early 2000. The subjects were randomized to one of three arms of the study: standard care, standard care plus supportive visits, and standard care plus teaching of a method of coping with patient symptoms (Grant number RO1 CA77307 McMillan, 1999–2003). Although one goal of hospice care is to positively affect the lives of patients with cancer, the research team was very aware that interventions could not be aimed at patients near the end of life who were incredibly debilitated. Instead, the intervention was directed at the caregivers in the hope that both patients and caregivers would benefit.

Researchers who study symptom management and quality of life in hospice patients with cancer are painfully aware of the problems that are encountered in this population (McMillan & Mahon, 1994). A number of problems exist in these studies that do not occur in healthier groups. The purpose of this article is to report the researchers' experience accruing patients after the first year of a clinical trial with homecare hospice patients and their caregivers.

Literature Review

Adequate management of physical and psychosocial distress is the main purpose of palliative care, and the need for research

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in palliative care has been well documented (Ling et al., 2000; Mazzocato et al., 2001b; Twycross, 1993). Currently, palliative cancer care is a complex, individually tailored, comprehensive healthcare arrangement. Very few clinical studies have examined this patient population because of the severity of illness, the presence of several coexisting symptoms, polypharmacy, and other clinical and logistic factors (Bruera, 1998; Bruera & Pereira, 1999; Mazzocato et al., 2001b). Recruitment to trials and research projects often is slow and further complicated by high attrition rates. The patient population is very unwell and nearing the end of life. Consequently, the problems experienced are complex physical, emotional, and ethical ones. Recognition of the difficulties in undertaking research in palliative care does not exclude the specialty from the rigors of scientific research. On the contrary, palliative care needs a more scientific foundation on which to base its practice (Mazzocato et al., 2001a, 2001b; McQuay & Moore, 1994).

Clinical research in this setting presents investigators with a series of obstacles (Bruera, 1998). The credibility of research findings depends on the design chosen by the investigators. Prospective, controlled, randomized trials, the gold standard for research, provide the highest level of evidence because they reduce various biases to a minimum (Grande & Todd, 2000; Mazzocato et al., 2001b). A distinction should be made between explanatory trials and pragmatic trials. An explanatory trial seeks to determine whether a treatment is efficacious (i.e., whether it works under ideal conditions). Such trials usually investigate a single causal factor, very often a drug. Pragmatic trials investigate effectiveness (i.e., whether something works in real practice conditions) and often examine more than one variable at a time. Trials of palliative care services are almost entirely pragmatic trials, and they should be distinguished from trials of drugs in palliative medicine, which usually are not pragmatic (Grande & Todd).

Effectiveness research in comprehensive palliative cancer care is scarce (McQuay & Moore, 1994). The need for randomized trials in effectiveness research in palliative cancer care has been debated (McQuay & Moore; Rinck et al., 1995). The difficulties in conducting effectiveness research in the palliative care setting have been described (Porzsolt, 1993; Rinck et al., 1997). First, the course of disseminated cancer is diverse (Porzsolt). Second, patients with advanced cancer experience deterioration of physical health over time and have acute complications such as fatal bleeding, sepsis, paralytic ileus, and thromboembolic processes, irrespective of their primary tumor. This helps to explain why patients with the same primary tumor have different symptomatology and why patients with different primary tumors may have a common clinical pathway in the advanced phase of their diseases. Therefore, individual needs of patients with advanced cancer in day-to-day clinical practice may vary a great deal (Rinck et al., 1997).

A review of palliative care studies is useful to appreciate the difficulties inherent in conducting this type of research. A recent review of palliative care studies revealed that all had methodologic flaws, including study recruitment, homogeneity of the study population, patient attrition, defining and maintaining the contrast between treatment strategies, and selection of outcome variables (Rinck et al., 1995). The investigators concluded that successful effectiveness research in palliative care must stress the importance of careful case finding, strict eligibility criteria, precise documentation of the process of care, and comprehensive outcome measurement.

Subject recruitment certainly is a major problem for palliative care studies. This was highlighted in a recent study focusing on factors that influence patients to accept or reject entry into a study (Ling et al., 2000). Information about all patients treated at a cancer center who were considered for entry into any of the 23 open clinical trials in palliative care was collected prospectively over four years. Of the 1,206 patients referred, only 46% met entry criteria. Of that number, only 30% agreed to enter; 21% of all those referred completed the study. The most common reasons cited for unwillingness to participate were a wish to defer to a later date, a deterioration in condition, distance from home to the hospital, a lack of interest, transfer to another unit, inability to give consent, and family objection. Potential solutions proposed by the investigators were to use trial designs that reflect clinical practice, have wide inclusion and exclusion criteria, require few extra hospital visits, are of short duration, take place at multiple centers, and use brief, simple assessments (Ling et al.). In an attempt to overcome some recruitment problems, various research methodologies have been used, with qualitative research becoming a popular option (Clark, 1997).

Another recent study used a cluster randomized design, with two rural communities and six urban health districts identified as the units for randomization, to compare organized palliative care to conventional care (Jordhoy et al., 1999). Of the 707 referrals made to the study, 61% were included. The reasons for ineligibility included refusal to participate, death after referral but before inclusion procedure was completed, inability to complete questionnaires because of physical or cognitive impairment, and life expectancy less than two months or more than nine months. The investigators documented a total compliance rate for completion of questionnaires of 66%. This study was able to meet recruitment goals. Success was ensured by the research procedures, which included continuous monitoring of relevant services, engaging leading nurses, and informing potential referral sources. An important key was the research assistants' regular screening visits at all relevant hospital departments. A majority of the patients were identified during these meetings or in cooperation with the appointed nurse at each study site. Few direct referrals were received from physicians. This study, as others, emphasized the need for local coordinators for successful recruitment (Brown, Haining, & Hale, 1997).

Recruitment and retention of an adequate number of study participants are critical to the success of any clinical trial because power to detect a difference after intervention is based on sample size, effect size, and *a priori* alpha level. Poor recruitment to clinical trials is not a problem that is exclusive to palliative care. Similar problems in recruitment to clinical trials in oncology have been reported (Tannock, 1995). Recruitment is a problem in most clinical trials (Ashery & McAuliffe, 1992; Swanson & Ward, 1995). Gotay (1991) estimated that less than 3% of patients with cancer enter clinical trials of medical and surgical therapies. In a recent study focusing on recruitment of patients with breast cancer into clinical trials, only 39% of women were offered participation in clinical trials (Simon, Brown, Du, LoRusso, & Kellogg, 1999). An offer of enrollment was associated with younger patient age and earlier stage of disease. Whether women enrolled after an offer of participation also was associated with younger age. This suggests some inherent bias against enrolling older women or women with more advanced disease into

clinical trials. Comparable estimates of accrual rates in clinical trials of psychosocial interventions are not available. A recent study assessed the effectiveness of a home-based intervention program for child-rearing families experiencing nonmetastatic breast cancer in the mother (Motzer, Moseley, & Lewis, 1997). The therapeutic goal of the intervention was to facilitate the family's management of the impact of the mother's illness on the family. The intervention was delivered in the home to women with recently diagnosed (within eight months) early-stage (stage 0, 1, or 2) breast cancer and their husbands or male partners. A total of 313 referrals of women meeting eligibility criteria were made, with 217 families accrued (69%); 181 families (83%) completed participation. Those not completing the study withdrew because they did not have enough time to participate, the study did not meet the family's needs, the study created additional stress, subsequent visits were not scheduled in a timely fashion, the family moved out of the area, the survey was too long or complicated, or the family considered itself too private to participate.

Burden for study participants is another potential obstacle for palliative care research. The potential for causing distress among terminally ill patients with interview-based research, especially when no immediate benefit exists, was the focus of another project that assessed terminally ill patients' psychological morbidity and their doctor-patient relationships (Barnett, 1995). The original study had an interview design that included standardized questionnaires, a study-specific questionnaire, and semistructured and open-ended questions covering a wide range of topics, including illness history, breaking of bad news, and current worries. The interview averaged one hour but ranged from 30–215 minutes. To minimize potential distress, the study design included several safety factors. First, it was cross-sectional to allow the interviewer to act on participant concerns without jeopardizing the study outcome. Second, the interviewer had a clinical background to address informational concerns. Finally, participants were given a feedback questionnaire (Barnett, 1995). The present study focused on that feedback questionnaire (Barnett, 2001). A total of 195 patients with advanced cancer were approached to participate; 65% agreed to participate and 78% of those returned the questionnaire. Up to 85% of participants thought the length of the interview was all right. The vast majority of participants thought the questions were relevant but not probing enough. Overall, 66% of participants were glad they had participated, and the other 34% had no strong feelings either way.

As a result of the potential burden that completion of questionnaires or interviews may be to study participants, data collection also represents a major difficulty in palliative care research. Unfortunately, a substantial loss of data often occurs (McWhinney, Bass, & Donner, 1994; Rinck et al., 1997). Researchers often have no choice but to rely on assessment by proxy and retrospective accounts if a sufficient data set is to be collected.

Another problem in palliative care research is the choice of study population. Clinical trials should be performed in populations that resemble as much as possible the populations within which the interventions will be used. Patients with advanced cancer often present with a large variety of severe physical and psychological symptoms (Bruera, 1998). They frequently have several symptoms at the same time, such as severe pain, profound anorexia, asthenia, chronic nausea, confusion, and anxiety. In addition, the nature and intensity of symptoms and responses to treatment change continuously. Studies often are performed in patients at an earlier stage of disease or who are younger than most patients with advanced cancer in an effort to characterize the biologic effects of certain agents better and to simplify the trial design. The results of these studies then are extrapolated to the terminally ill population (Mazzocato et al., 2001b). The low number of successful palliative care trials bears witness to the particular difficulties associated with conducting randomized controlled trials in palliative care. One study had sought to evaluate, in a randomized, controlled fashion, immediate referral to a palliative care home support team as compared to referral after one month using a waiting list control group (McWhinney et al., 1994). The study failed as a result of some very common issues besetting palliative care studies: problems with recruitment, death before the comparison point, failure to complete questionnaires, and exposure of patients in the control group to specialized palliative care. Denial of a service or treatment to a control group was an ethical problem that affected referral to the study. Another concern was that the outcomes chosen for assessment might not have been sensitive to the benefits of the service. In addition, patients and caregivers had difficulty completing questionnaires.

Unfortunately, given the difficulty in recruiting and retaining subjects in palliative care studies, investigators find themselves needing allies in the recruitment process. Often, the allies must be healthcare professionals (i.e., physicians who care for the patients). In fact, many studies require healthcare professionals to identify patients to enter trials (Grande, Todd, Barclay, & Farquhar, 1999; Hughes et al., 1992). Ultimately, the difficulty in identifying, recruiting, and retaining patients has the effect that randomized, controlled trials in palliative care may be evaluations of interventions on those who are best able to cope and least ill. It also means that trials often lack statistical power because of diminishing patient numbers and incomplete data (Grande & Todd, 2000). Palliative care applies to a wide range of patients and phases of different illnesses. Although some studies may define patient samples in terms of a single diagnosis and stage of cancer, most have used prognosis as the key criterion for inclusion (Hughes et al.). Even when estimated prognosis is accurate, this approach yields a heterogeneous patient sample with different courses of illness.

Palliative care is, by nature, holistic and often tailored toward individual patients' needs. Thus, another potential obstacle in palliative care research is the definition and standardization of the intervention to be tested. This clearly differs from randomized, controlled trials of drugs, in which the intervention is standard. Palliative care also typically is multidisciplinary; other services with similar characteristics occur alongside the intervention. Defining how these services are different from the intervention may be difficult. In randomized controlled studies in palliative care, patients often fail to receive the intervention to which they were allocated, requiring an intention-to-treat analysis (McWhinney et al., 1994). This can result in a dilution of the experimental effect. This dilution, along with the heterogeneity of care provision and contamination, can make it difficult to detect any effect of an intervention (Grande & Todd, 2000).

Finally, palliative care research creates unique ethical challenges. Dying patients are an especially vulnerable population. Adequate informed consent may be difficult to obtain.

Balancing research and clinical roles may be very difficult. In addition, the risks and benefits of palliative care research are difficult to assess (Casarett & Karlawish, 2000; Janssens & Gordijn, 2000).

Methods

Setting

This article reports on the experience of the investigators during the first year of data collection for a four-year, funded clinical trial. The setting was a large not-for-profit hospice in Florida that provides mostly home care for patients who have primary caregivers at home. The average daily census for the hospice was about 850 patients per day at the time of the study.

Sample

The sample consisted of hospice patients with cancer and their primary caregivers, who were screened and approached prior to accrual to an institutional review board-approved, National Institutes of Health-funded clinical trial focusing on symptom management and quality of life. Patients had to be adults, have a cancer diagnosis, have a caregiver in the home, be alert and able to self-report, pass a screening with the Short Portable Mental Status Questionnaire, and have a problem with at least two of the following: pain, dyspnea, and constipation. Patients who were comatose, excessively debilitated, or actively dying were excluded. Caregivers also had to be adults, have no current cancer diagnosis, and pass a screening with the Short Portable Mental Status Questionnaire. Patient/caregiver dyads were assigned randomly to one of three groups using a computerized randomization scheme that was accessed by telephone from the patients' homes.

When the proposal was written and submitted for funding, the team had to demonstrate the feasibility of the study by showing that the hospice would admit sufficient patients to allow the study to be completed. At the time of the proposal, the hospice was caring for slightly more than 600 patients per day. The researchers estimated that 220 patients would be admitted per month, or 2,640 patients per year. Of those, 62% would have a cancer diagnosis, providing 1,636 patients with cancer per year for the study. They estimated that 95% would have caregivers, providing 1,555 per year. Of those, 77% were expected to be alert and able to consent, providing a potential sample of 1,197 patients per year. Because the estimates said that only 1,122 patients would have to be approached in 28 months to accrue a sample of 846 in 28 months, the study looked very promising.

Data Collection and Analysis

The investigative team kept careful records of the number of patient/caregiver dyads accrued to the study, reasons for nonaccrual, and reasons for attrition. These were entered into a computerized grid daily as the data were collected. Results are presented as frequencies and percentages.

Results

Admission Screening

By the time data collection began, the hospice was caring for 850 patients per day. It admitted 3,356 patients in the first year of the project. Of those, 2,500 (75%) had a cancer diagnosis and 95% had caregivers as predicted, providing a sample of 2,375 patients with cancer with caregivers (see Table 1). However, the in-office screening using the admission face sheet made 51% ineligible for contact by telephone, leaving 1,209 patients eligible.

Using data from the first nine months of data collection, the researchers identified specific reasons that patients were not eligible. During that specified period, the hospice admitted 2,517 patients; 75% of those had cancer and 95% of homecare patients had caregivers, making them eligible for the study. However, after further screening, only 19% were eligible for contact and only 5% finally were accrued to the study. The primary reasons that patients were ineligible were admission to an assisted-living facility or nursing home, therefore having no consistent family caregiver; low performance status as measured by the Karnofsky Performance Status Scale or low level of consciousness as assessed by the admission team; or being located out of the county in which the study was being conducted (see Table 2).

Telephone Screening

The researchers attempted to contact 467 (19%) apparently eligible patient/caregiver dyads; 156 agreed to a home visit and 311 refused. The most common reasons for refusals were related to the caregivers: They were not interested, were not available to the investigators, were ill, or felt overwhelmed (see Table 3). In addition, the caregivers believed that the patients were too ill, despite the objective data collected by the investigative team that indicated that the patients were capable of participation. Thus, the data collectors finally visited only 5% of patients who were thought to be eligible. Clearly, a very large hospice population is needed to support a clinical trial when only 5% of available patients can be enrolled.

Home Visits

Of the first 150 subjects visited in the home, 25 (17%) failed screening with either the mental status examination (i.e., Short Portable Mental Status Questionnaire), performance examination (Karnofsky Performance Status Scale), or both, leaving a total of 125 patient/caregiver dyads from whom baseline data could be collected.

However, some problems continued. The protocol required the team (i.e., data collectors and intervention nurses) to collect data at baseline, provide the intervention to two-thirds of the patient/caregiver dyads over a nine-day period, and continue data collection at day 16 and at day 30 (see Figure 1). The median survival time at the hospice had dropped to 25 days by the time the study started so that half of the patients were dead by day 25, making further data collection

Table 1. Proposed and Actual Numbers of Patients Admitted to the Hospice During the First Year of Data Collection

	Proposed		Actually Admitted	
Variable	n	%	n	%
Daily census	600	100	850	100
Admissions per year	2,640	100	3,356	100
Cancer diagnosis	1,636	62	2,500	75
Caregiver available	1,555	95	2,375	95

Table 2. Reasons for Study Ineligibility

Reason	n	%
No cancer diagnosis	642	26
Assisted-living facility or nursing home patient (no family caregiver)	609	24
Low Karnofsky or level of consciousness scores	327	13
Out of county	236	9
No family caregiver available	140	6
Actively dying on admission to hospice	51	2
Does not speak English	43	2
Younger than 18	2	< 1

N = 2,470

impossible. Some of the patients who were alive at day 30 were so debilitated that they could not provide self-report data. For the 125 patient/caregiver dyads actually accrued to the study, baseline data was obtained on only 50%. Evaluable follow-up data was obtained on 64 (51%) at day 16 and 47 (38%) at day 30. So, some follow-up data were obtained on slightly more than 50% of patient/caregiver dyads, but complete data were obtained on only 38%. Reasons for subject attrition (see Table 4) for the 48 who dropped out after baseline included patients' decline or death (24, 50%) and caregivers feeling too busy or overwhelmed (11, 23%).

Discussion

Methodologic Problems

Patient eligibility: Screening every patient to end up with a 5% sample is expensive. The data collectors read the face sheets of all 2,517 patients admitted to glean the 125 that finally were randomized and accrued to the study. So, instead of being paid to collect data 40 hours a week, data collectors were being paid, in part, to screen patients who never would enter the study.

Debilitated patients: Consistent with earlier studies in palliative care settings, the patients often were too ill and debilitated to participate (Jordhoy et al., 1999; Ling et al., 2000). If researchers go into an outpatient clinic to collect data, they can make some basic assumptions about the functional abilities of the patients. They know at the least that the patients were well enough to get up, get dressed, and get to the clinic. When researchers visit dying patients at home, they cannot make that assumption. And, of course, once in the homes, data collectors frequently find that patients are just too ill or debilitated to participate at all. Not only is this a costly and time-consuming problem, but it also leads to the problem of subject bias. In such a situation, results will not be generalizable to a majority of the patients in hospice care. How to overcome that problem is unclear.

Table 3. Reasons for Refusal of Investigator Home Visits

Reason	n	%
Caregiver believed patient was too ill	130	42
Not interested	94	30
No response to repeated telephone messages	35	11
Caregiver not available	20	6
Caregiver overwhelmed	16	5
Caregiver ill	9	3
Beyond study time frame when reached	5	2
Patient did not know he or she was in hospice care	2	< 1

N = 309

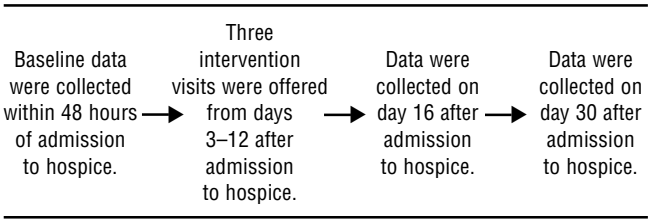

Figure 1. Protocol for Data Collection and Intervention Visits

Overwhelmed patients and caregivers: Clearly, patients and caregivers from this project and others are overwhelmed by the situation in which they find themselves (Barnett, 1995). In their first hospice study, the researchers attempted to admit patients and caregivers to a study at the time of admission to hospice (McMillan & Mahon, 1994) because they needed before and after data to evaluate the success of the hospice program. What they found was that being admitted to hospice is such an emotionally draining experience that, by the time patients have consented to hospice care and agreed not to call 911 and to give up lifesaving emergency procedures, they are just not able to think about whether they want to participate in a study. Thus, for all future studies, the researchers have collected the before data within 48 hours after admission to hospice.

Barriers to accruing patients: Patients often are willing to participate in research, but nurses and family caregivers feel very protective of the patients and try to keep researchers out. Studies can overcome the problem of nurses blocking access by having data collectors screen every patient themselves, thereby bypassing nurses. In the current project, the nurses never were asked whether the patients were appropriate for the study. However, caregivers cannot be bypassed, so being blocked on the phone or at the door by concerned family members of willing patients often was a problem.

Table 4. Reasons for Patient/Caregiver Attrition

Reason	n	%
Patient decline	14	29
Caregiver too busy or overwhelmed or unavailable	11	23
Patient died	10	21
Patient discharged from hospice or left city	3	6
Unable to determine	3	6
Miscellaneous reasons	7	15
• Caregiver did not want to talk about painful issues so stopped the support intervention	–	–
• Patient emotionally upset by questions—unable to continue	–	–
• Alcoholic caregiver—unable to participate	–	–
• Thought study was over after the intervention; did not want more data collection	–	–
• Caregiver would participate only if required	–	–
• Sent message by hospice nurse—no further contact from research team	–	–
• Just no interest in continuing	–	–

N = 48

Continued decline of patients: Patients continued to decline while in the study. One reality of this type of research is that hospice patients are where they are because they are nearing the end of their lives. The continuing decline of patients caused problems with missing data in this study and earlier ones (Jordhoy et al., 1999; McWhinney et al., 1994). This was seen in the final numbers that were collected on day 30 of the study; they were a dismal 38%, projecting a 62% attrition rate. Gathering such a small amount of data was very expensive. Some newer analytical techniques will have to be used to handle the problem of missing data.

The Plan for Addressing Problems

What can be done to save the study? It was funded for four years, 28 months of which was for data collection. As a first step, the team of investigators made some sacrifices to save some of the budgeted funds so that some excess would be left at the end of the project. For example, most funds were saved by decreasing the percent of salary reimbursement of each of the investigators. In addition, investigators did not use any of the allocated travel money to go to conferences to present results, and part of the indirect costs (overhead) were being used to actually conduct the study. If sufficient money was saved during the project, the researchers planned to approach the funding agency about a one-year, no-cost extension, during which the money that was saved could be used to pay the data collectors, the intervention nurses, and the data manager to continue with the project. Therefore, the researchers would be able to increase the sample size.

Conclusions and Implications

Accruing debilitated patients and their caregivers to a clinical trial and retaining them are extraordinarily difficult. The inability to do so has implications for integrity of the data, data analysis, success of the project, and the cost of conducting such projects in the future. Because of the myriad obstacles that palliative care researchers face in designing and conducting successful studies, investigators must focus on certain elements to ensure success, such as how the study population is accrued to the study, including such issues as identification of potential cases, relevance of eligibility criteria, and processes that will help to keep the refusal rate low. Another important factor is the homogeneity of patient characteristics. Health status, disease stage, and type of cancer must be included in eligibility criteria and baseline characteristics. Ensuring that the sample size is appropriate for the level of statistical power desired also is important. Procedures must be in place to keep the attrition rate low. For example, careful attention to study burden for patients and caregivers must be balanced with the need to measure all possible confounding variables. Although an attrition rate below 10% has been recommended for clinical trials, this goal may not be achieved with patients near the end of life. Documentation of the power analysis also is important. Procedures must be in place to prevent contamination of interventions, and interventions must be effective in a relatively short time so that patients with short lengths of stay can benefit. Outcome variables must be well chosen, relevant, and validated (Rinck et al., 1997). Researchers should continue to seek methods to overcome these barriers to research with patients near the end of life.

In addition, implications exist for others besides investigators. Clearly, hospice patients are admitted very near the end of life and thus are not able to take full advantage of services. Hospices need to make every effort to educate nurses, physicians, social workers, and the community about the value of hospice care and the advantages of getting patients admitted as soon as the terminal phase of care begins.

Implications exist for reviewers who make funding decisions, as well. They should allow investigators the funding needed for additional time and staff to account for the unusually low accrual rates and extremely high attrition that must be anticipated in studies of patients near the end of life.

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