Palliative Care and the Ethics of Research: Medicare, Hospice, and Phase I Trials

Ira Byock, MD

People living with advanced, incurable cancer comprise a highly vulnerable population. As a group, they are burdened with pain, fatigue, and other physical symptoms that erode their quality of life. They are often anxious and justifiably worried about the future—both for themselves and their families'.

It is well recognized that, despite being formally informed that research is not intended or likely to help them, patients with far-advanced illness frequently enter clinical trials in the hope that the experimental treatments will extend their lives. The understandable tendency to grasp at any chance for survival, however tenuous, renders such patients at risk of being influenced by a health system and research culture that are wholly focused on fighting disease and extending life. Attention to people's quality of life, family experience, and family support can easily get lost in the process–not intentionally, but because our protocols don't include them, and customary measurement tools do not encompass these domains of illness. Basic issues of patients' personal values, individual choice, and informed consent need to be revisited in light of current end-of-life research and recent advances in the delivery of health services and clinical palliative care.

Recently, a number of authors have called attention to ethical issues of research involving terminally ill people [1, 2], and a conference was convened in September 2002, jointly sponsored by the National Institutes of Health and the Greenwall Foundation, a private healthcare philanthropy, to address the subject. In a recent issue of the *Annals of Internal Medicine,* Dr. Steve Miles and I addressed one of these issues—the exclusion by payers of coverage for hospice care of patients who are eligible for services but who decide to enter clinical trials [3]. For the sake of brevity, the article focused on Medicare beneficiaries with advanced cancer who meet criteria for hospice care but, because of their decision to enter a phase I cancer clinical trial, effectively lose access to hospice services. We pointed out that there is no clinical or ethical justification for this situation. Hospice care comprises an array of services that many patients with advanced cancer and families value highly. Although Medicare requires patients who accept hospice care to forgo Part A benefits along with most life-prolonging care, phase I trials that test toxicity and safe dosing of new treatments are not intended to be therapeutic. We pointed out that despite the potential benefits of hospice to patients and their families, routine consent processes for phase I research and the forms people are asked to sign do not disclose that participants will forfeit access to hospice services.

Who Is to Blame?

Although this prevailing situation is untenable, it is important to emphasize that no one is to blame. Rather, this situation has arisen from developments in therapeutics, research, and ethics. It represents a need to update research protocols and consent processes to bring them in line with current standards of clinical care concerning patient comfort, quality of life, and family support.

Early response to our article has been mixed but instructive about the receptivity of the disciplines involved in this change. To this point, the response from providers and payers has been muted and defensive. The Center for Medicare and Medicaid Services (CMS) told health journalists that it is technically permissible for a dying patient to enter a phase I trial and receive hospice care. They implied that if patients and hospice providers read the fine print of regulations, they will discover no problem exists. A letter of clarification from CMS to cancer researchers and hospice providers pointing out this

Dr. Byock is Director of Promoting Excellence in End-of-Life Care, a national program of The Robert Wood Johnson Foundation.

Correspondence to: Ira Byock, MD, Director, Promoting Excellence in End-of-Life Care, a national program of The Robert Wood Johnson Foundation Practical Ethics Center, University of Montana, 1000 E. Beckwith Avenue, Missoula, MT 59812; telephone (406) 243-6601; fax (406) 243-6633; e-mail: ibyock@aol.com

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capacity would be helpful but as of this writing has not been forthcoming.

Not surprisingly, the most ardent support for our concerns has come from hospice and palliative care clinicians. Official voices of national hospice associations, who might be expected to champion the rights of terminally ill Americans, have so far been publicly silent. Privately, we have been informed that a few progressive hospice programs will accept patients on phase I trials. Yet, in this circumstance, don't these rare exceptions prove the rule?

It is undeniable that in the vast majority of American communities and medical centers, discharge planners, researchers, and clinicians do not routinely mention hospice to an individual who enters a cancer clinical trial. Hospice and cancer research are considered mutually exclusive options.

Most Oncologists Agree

To this point, most feedback from the oncology community has been notably positive. Several senior researchers have pointed out that the concerns we raise are not restricted to phase I trials but apply more broadly to any research involving patients who otherwise meet hospice eligibility criteria.

Negative responses from clinicians and researchers have generally taken two forms. Some have written to say that few, if any, hospice patients are interested in phase I research trials. Others have asserted that cancer research subjects are not interested in or ready for hospice care. "In their life perspective, these are sequential—phase I, then hospice when the drugs fail," wrote one academic colleague who explicitly spoke of "psychological types." Dismissing our concerns, he concluded, "I think your issue is more a theoretical than real issue."

Both categories of comments reflect an apparently common assumption that two distinct types of people with advanced cancer exist–those who are willing to enter research and those who are willing to accept hospice care. The notion of inherent characterologic traits that somehow firmly dispose people with advanced illness one way or the other is not supported by empiric data. Since in the world of mainstream American healthcare and research, the choices that exist are often discrete–you can *either* participate in research *or* have hospice care, but not both–any such evidence is at best tautological. We must be wary to avoid a tendency on the part of people in authority to defend the status quo by "blaming the victim." It's worth repeating: No one intentionally caused this problem. No one is at fault. Therefore, no defensiveness is necessary.

The Truth

The truth is that people who are living with advanced, incurable cancer may well benefit from hospice services for themselves and their family *and* simultaneously value the opportunity to participate in clinical research. These two things are not incompatible. In actuality, the sequential model of life-prolonging *and then* palliative care was imposed–and is maintained–to a great extent by rules of reimbursement. Concerns of both ethics and clinical quality strongly mandate a new standard of concurrent disease-modifying *and* palliative care.

During the past 5 years, the Promoting Excellence in End-of-Life Care program of The Robert Wood Johnson Foundation sponsored four cancer programs that included access to phase I and II cancer clinical trials, integrated with concurrent palliative care [4]. The demonstration projects were well received and consistently valued by patients, families, and clinicians. There were no apparent detrimental effects on the concurrent cancer research. Anecdotally, investigators have said that, indeed, the addition of team-based palliative care may have enabled patients to remain on experimental protocols longer and improved the quality of data collected.

It is important to note that these studies are small, involving only several hundred patients, and clinical findings are preliminary, because the projects were designed to build new models of care and to primarily assess their programmatic feasibility and acceptability. Still, the early results, including high levels of satisfaction with concurrent care, counter assumptions about discrete "personality types." Presently, there is simply no reason to assume that a person with cancer who is enrolled in a phase I trial would not want the array of services for self or family that is provided by team-based palliative care.

The Need to Speak Up

Who will protect the rights of this vulnerable population?

Obviously, we all have a stake in and share responsibility for correcting this situation. By social

construction, Institutional Review Boards (IRBs), sometimes called Human Research Committees, are charged with reviewing proposed research for ethical soundness and protection of subjects from unacceptable burden and risk. Without IRB approval, clinical research cannot proceed; even if a study went forward, peer-reviewed journals would almost surely refuse to publish its results.

The situation outlined in our paper and discussed here presents a pressing challenge to IRBs. Most narrowly, the question is: Should an IRB approve a phase I study under circumstances that effectively exclude from hospice services those patients who elect to participate? It would seem, at an absolute minimum, that IRBs must insist that the loss of access to hospice services while participating in these trials be fully disclosed.

The more general question posed to IRBs is: Given the local clinical context in which proposed research will take place, should any study that effectively diminishes participants' access to palliative services be approved?

The IRB's answer to these questions may well turn on the issue of whether or not palliative care for patients with advanced, incurable illness–people who in all likelihood are dying–is a standard of care.

Is Palliative Care a Quality Standard?

I imagine that around conference tables at IRB meetings in medical centers throughout the country, some committee members will argue that palliative care is not yet a community standard and, therefore, that researchers (and those who fund research) should not be required to ensure access to hospice or similar palliative care programs. However, as new standards of care emerge, there is always a lag in implementation. Even with the most seemingly simple, straightforward advances in practice–think of the use of beta blockers in patients with myocardial infarction–it takes time for community practice to catch up to established new standards. It is unlikely any IRB would approve a clinical trial that obviated a patient's access to a new and valuable treatment during a period of concerted efforts to improve this same aspect of quality.

Reports over the past decade by the Institute of Medicine and its National Cancer Policy Board [5, 6] and an abundance of formal statements by relevant professional associations [7–10] have recognized palliative care as a core component of care for patients with advanced, incurable conditions. This perception is supported by a wide variety of recent curricula, educational initiatives, and quality improvement efforts within American healthcare. Collectively, these reports, position statements, and initiatives to improve the comfort and quality of life of dying patients and their families can be seen to establish a new clinical standard. The burden of proof currently lies with those who would assert they do not.

The purpose of research is to advance treatment and improve future care. Therefore, research protocols can reasonably be expected to build from existing best practices. Given the official calls for expansion of hospice and other interdisciplinary team-based palliative care during the past decades, it no longer seems acceptable for research protocols to exclude such core clinical services.

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