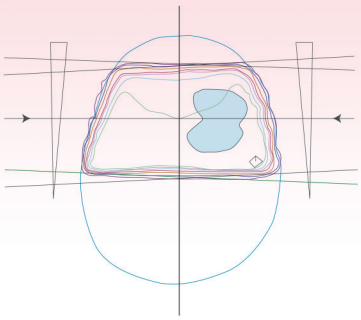
CHAPTER

12

Health Services Research in Radiation Oncology: Toward Achieving the Achievable for Patients with Cancer



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WHAT IS HEALTH SERVICES RESEARCH?

Medical research may be considered as a continuum of four overlapping domains: basic or biomedical research, clinical research, health services research (HSR), and population health research. HSR aims to create the knowledge required to improve population health by improving the delivery of health services. Although there is some overlap between the domains of clinical research and HSR, their purposes are distinct. *Clinical research* describes the natural history of diseases, it investigates their pathophysiology, and it seeks to discover more effective treatments. *HSR* describes how health systems work, it investigates how they go wrong, and it seeks to discover better ways to deliver health services. The results of clinical research are primarily intended to guide physicians' decisions about the care of individual patients, whereas the results of HSR are intended to guide the decisions of managers and policy makers about the design and implementation of healthcare programs.

Need for Health Services Research in Radiation Oncology

Clinical radiation oncology is a mature science. It has a sound theoretical basis, in both biology and physics. We have a universal language for describing the diseases treated, the treatments used, and the outcomes achieved. Much is now known about the factors that influence outcomes in the individual case. There is a well-established process for evaluating the efficacy of treatment, and a large body of empirical information now permits evidence-based decisions about the use of radiotherapy (RT) in the majority of cases.

In contrast, the science of HSR in radiation oncology is at a much earlier stage of development. There is no comparable universal language for describing the performance of RT programs. There is only limited information available about the factors that influence the performance of RT programs in the population at large. There is no well-established process for measuring the effectiveness of RT programs at the population level. In the absence of empirical evidence, most decisions about the design and management of RT services are guided only by theory and expert opinion, and their consequences are unpredictable. Given that we would no longer tolerate this unscientific approach to decision making in the care of individual patients, it is anomalous that it should still be used in making decisions about health systems that may affect tens of thousands of patients.

The challenges for the HSR community in radiation oncology are to create the knowledge required for evidence-based management of RT programs and to promote the use of evidence in the design and management of RT programs.

How Can Health Services Research Help to Improve the Outcomes of Cancer?

At any point in time, the state of scientific knowledge and technological development sets an upper limit on what is *achievable* for patients with cancer. What is achievable in any particular society is also limited by how much that society is able and willing to spend on cancer care. However, what is actually *achieved* depends not only on what would be achievable if we made optimal use of the available knowledge, technology, and resources, but also on how close we get to attaining the achievable, which is a quantity we have termed the *attainment factor*.

$$\text{Attainment Factor} = \text{Achieved outcome} / \text{Achievable outcome}$$

The achieved and the achievable outcomes are measured in units that correspond to the outcome of interest. Attainment can have any value between 0 and 1 or may be multiplied by 100 and expressed as a percentage. The equation may be rewritten as

$$\text{Achieved outcome} = \text{Achievable outcome} \times \text{Attainment factor}$$

Cancer outcomes can be improved by increasing the *achievable* or by increasing the *attainment factor*. Biomedical and clinical research aim to improve outcomes by increasing the *achievable*. HSR aims to improve outcomes by increasing the *attainment* of what is already potentially achievable within the limits of existing knowledge, technology, and resources.

What Is the Scope of Health Services Research?

Health system performance has three dimensions: accessibility, quality, and efficiency. Together these determine the extent to which we attain the achievable in health care. *Accessibility* describes the extent to which patients are able to get the care they need, when they need it. *Quality* describes the extent to which the right care is delivered in the right way. *Efficiency* describes the extent to which accessibility and effectiveness are optimized in relation to the resources expended. HSR is concerned with measuring these quantities, understanding the factors that influence them, and discovering and evaluating ways of enhancing them.

The scope of HSR in oncology covers the entire continuum of cancer care. In a systematic cross-sectional study of 1,113 HSR publications from 2009, the majority of HSR focused on active treatment (32%), with fewer studies addressing survivorship (19%) or screening (16%), and even fewer than that focused on diagnosis/assessment (10%), palliation (8%), or

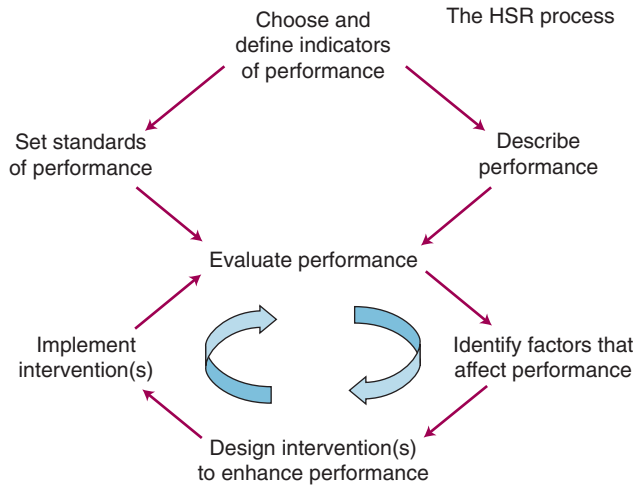

Figure 12-1 A general scheme for research on health system performance.

BOX 12-1 The Dimensions of Healthcare Accessibility

AVAILABILITY

Total system capacity in relation to total needs
Total resources, efficiency, and flexibility

SPATIAL ACCESSIBILITY

Distance, travel times, and costs of transportation

ACCOMMODATION

Hours of operation
Transportation services
Lodges/hostels

AFFORDABILITY

Prices in relation to patients' ability and willingness to pay
Indirect costs

AWARENESS

Physicians' awareness of patients' needs and of potentially useful services
Patients' awareness of needs and services

prevention (4%)[1] Across this continuum, the focus of HSR was most commonly on quality of care (56%), with fewer studies focused on accessibility (25%), efficiency (5%), or general well-being of subjects (14%).[1]

Figure 12-1 shows a general framework for a program of HSR aimed at improving some specific aspect of health system performance. The first step is to select, define, and validate appropriate indicators of the aspect of performance that has been targeted for investigation. The next two steps are to: (1) develop methods of measuring system performance in terms of the chosen indicator(s) and (2) prescribe standards or targets for system performance in terms of the chosen indicators. These two steps, which often involve the use of different methods, can sometimes be undertaken in parallel. Once standards have been set and methods for measuring performance have been established and validated, it becomes possible to evaluate the performance of the system against the standards. This in turn permits further explanatory studies aimed at identifying factors that are associated with better or worse performance. This information can be used to design interventions aimed at improving performance. The interventions may then be implemented and systematically evaluated. Interventions may be refined through further cycles of improvement before they are suitable for dissemination and incorporation into routine practice.

STUDIES OF THE ACCESSIBILITY OF RADIOTHERAPY

Concept of Healthcare Accessibility

The term *accessibility* was originally used narrowly to describe the ability of patients to obtain entry into the health system.[2] It is now used more broadly to represent the overall "degree of fit between the clients and the system."[2,3] Accessibility can be seen as having a number of dimensions that determine that overall degree of fit (Box 12-1). *Availability* describes the total volume of the service available in relation to the total number of clients that would benefit from it. Availability depends on the adequacy of supply of healthcare workers and on the adequacy of facilities and equipment. For any given level of resources, availability also depends on the degree of efficiency in production of services. *Spatial accessibility* describes the geographic relationships between the places where services are provided and the places where potential clients reside. The term *accommodation* describes the extent to which the system is designed and operated to facilitate clients' access to service, for example, by operating at convenient hours or by providing transportation for patients who may need it. *Affordability* describes the relationship between the cost of health services and clients' ability and willingness to pay. It depends not only on the direct cost of services, but also indirect costs, for example, loss of earnings during a protracted course of treatment. *Awareness* describes the extent to which those who need the service know that it is available and that they might benefit from it. In the context of a specialized service such as RT, patients' awareness of the potential benefits of RT depends largely on their attending physician's awareness of the indications for RT.

Need for Studies of Access to Radiotherapy

There are compelling reasons for doing research aimed at optimizing the accessibility of RT. In To achieve optimal cancer outcomes at the population level, it is necessary to make effective treatments accessible to every patient who needs them. RT is known to be effective in many clinical situations and the World Health Organization (WHO) recognizes RT as a key component of any overall program of cancer control. In its 2005 declaration on Cancer Control, the WHO states that "recognizing that the technology for treatment of cancer is mature and that many cases of cancer can be cured …, all nations should improve access to appropriate technologies."[4] Many nations aspire to providing adequate and equitable access to health care for all of their citizens, but there is remarkably little information available about how successful they are in achieving this laudable goal with respect to RT. In reality, the widespread reports of waiting lists for RT in the medical literature and news media and the limited supply of radiotherapy equipment and personnel in many developed and developing countries suggest that access to RT remains suboptimal in many parts of the world.

Waiting Lists for Radiotherapy

Long waiting times for RT were first identified as a cause for concern in the medical literature in a report from Norway more than 20 years ago.[5] Waiting lists for RT have since been

reported in many other countries including Australia,[6] the United Kingdom,[7] Canada,[8] New Zealand,[9] Denmark,[10] Germany,[11] Spain,[12] and Italy.[13] In countries affected by waiting lists of RT, they have been a major concern for both patients and the providers. The problem of waiting lists for RT is an ongoing challenge for health services researchers in radiation oncology; but the first step in dealing with the problem is to learn how to measure waiting times for RT.

Measuring Waiting Times for Radiotherapy

Different methods are available for quantifying waiting times and waiting lists for RT, including mail surveys, retrospective reviews of preexisting administrative data, and prospective collection of information about delays as patients pass through the system.

Mail and e-mail surveys can provide a lot of information about waiting times from multiple institutions and can also be used to compare waiting times between different centers within one country or compare waiting times between different countries. In the 1990s, a survey of heads of radiation oncology at comprehensive cancer centers in the United States and Canada showed that waiting lists for RT were widespread throughout Canada but revealed no evidence of similar problems anywhere in the United States. Median waiting times for a range of indications for RT were two to three times longer in Canada than in the United States.[14] Figure 12-2 shows, for example, that at almost every Canadian center, patients with laryngeal cancer waited longer for RT than they did at almost any U.S. center. However, the validity of such surveys may be questioned because they rely on the veracity of self-reports and because the primary information on which each report is based may differ from center to center.

Retrospective analysis of data that have been gathered for other purposes can provide more objective information about waiting times for RT. This may be an important first step in addressing this type of problem. At the beginning of the 1990s, reports of long waiting lists for RT in Ontario were frequently in Canadian news media. Health system managers felt that these reports were unduly alarmist and at first denied that there was any systemic problem.[8] To clarify the situation, we undertook an analysis of waiting times for RT based on computerized electronic records of all visits to the province's radiotherapy centers over the preceding decade. Once these administrative records had been linked to the province's cancer registry, we were able to describe waiting times for RT for various specific conditions.[8] For example, Figure 12-3, *A* shows that waiting times from diagnosis to start of radical RT

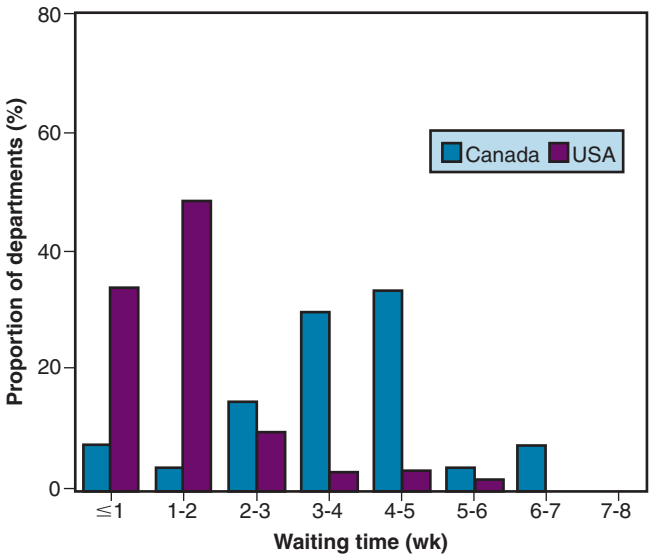

Figure 12-2 Waiting times for RT for carcinoma of the larynx in Canada and the United States. The frequency distributions illustrate the time from referral to initiation of RT for a T2N0M0 carcinoma of the larynx in Canada and the United States based on the results of a mail survey. *(Adapted from Mackillop WJ, Zhou Y, Quirt CF: A comparison of delays in the treatment of cancer with radiation in Canada and the United States. Int J Radiat Oncol Biol Phys 32:531–539, 1995.)*

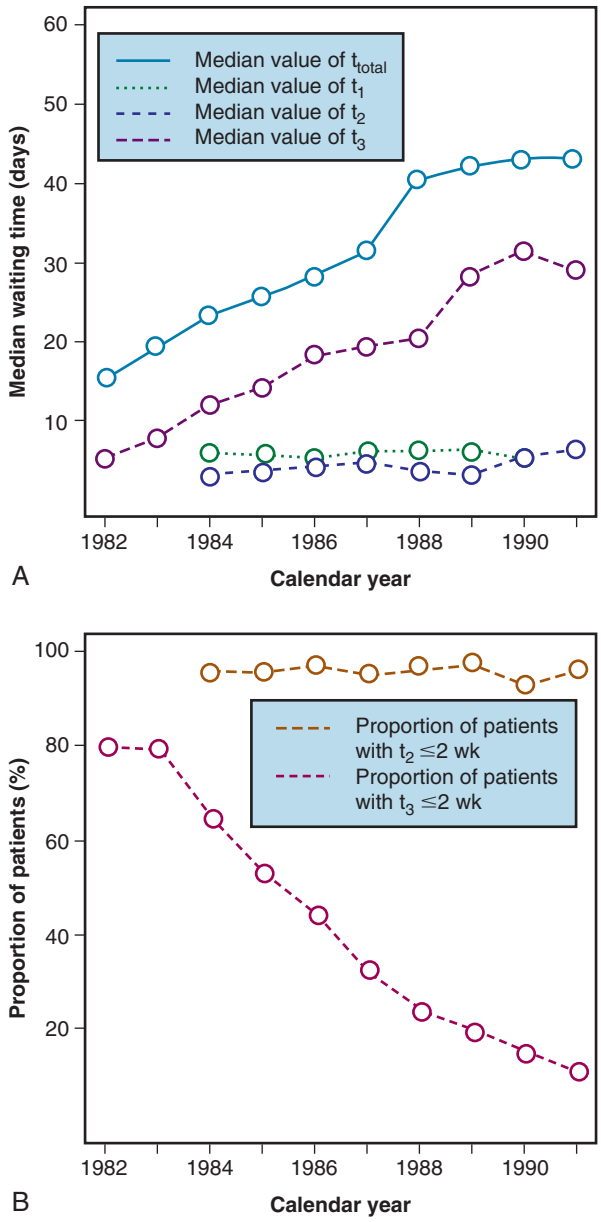

Figure 12-3 Waiting times for RT for carcinoma of the larynx in Ontario. **A,** Temporal trends in median waiting time for RT in Ontario, for which t_{total} is the interval between diagnosis and start of RT, t_1 is the interval between diagnosis and referral to RT, t_2 is the interval between referral and consultation, and t_3 is consultation and start of RT. Data needed to measure t_1 and t_2 were available only from 1984. **B,** The proportion of patients meeting the standards of the Canadian Association of Radiation Oncologists, which states that patients are to be seen in consultation within 2 weeks of referral (i.e., $t_2 < 2$ weeks) and started on RT within 2 weeks of consultation (i.e., $t_3 < 2$ weeks). *(Adapted from Mackillop WJ, Fu H, Quirt CF, et al: Waiting for radiotherapy in Ontario. Int J Radiat Oncol Biol Phys 30:221–228, 1994.)*

for laryngeal cancer increased dramatically through the late 1980s and early 1990s. Similar large increases in waiting times were found in many other clinical situations. Further, as shown in Figure 12-3, *A*, the observed increases in overall waiting time between diagnosis and treatment were entirely the result of increases in the waiting time between the first visit to a radiation oncologist and the start of RT. There was no increase in the interval between diagnosis and referral to radiation oncology or between referral and consultation. These findings pointed to rate-limiting problems in access to planning or treatment machines. It is useful, whenever possible, to report observed waiting times in relation to standards or guidelines. At the time of this first report, the Canadian Association of Radiation Oncology (CARO) had already set standards for acceptable waiting times for RT: the maximum acceptable delay between referral to, and consultation by, a radiation oncologist was deemed to be 2 weeks, and the maximum acceptable delay between consultation and the start of RT was deemed to be 2 weeks.[8] Although these standards were based only on expert opinion, they provided a useful framework for comparison. Figure 12-3, *B* shows trends in compliance with these standards over time. Most patients met the CARO standard for prompt consultation throughout the study period, but the proportion of patients meeting the CARO standard for prompt start of RT fell from 90% to 10%. This simple study, which merely quantified the magnitude of the problem in the community, was useful because it led to public recognition of the seriousness of the problem.[8] This proved to be an important first step in promoting the reinvestment in the infrastructure of the provincial RT system.

There are limitations to the retrospective analysis of waiting times. First, this approach is blind to patients who dropped off the waiting list before they were treated because it starts by identifying patients treated with RT and then follows them backward to measure waiting times from date of diagnosis or some other milestone. Secondly, it is unlikely that any database created for other purposes will provide all the information necessary to identify the rate-limiting step in the RT process. The date of the decision to treat with RT, for example, is an important milestone that signals the transition from pretreatment assessment to planning, and this is collected only in systems designed specifically to monitor flow through the RT process. Administrative databases may also lack information about other elements of the patient's care that are necessary to interpret waiting times for RT. For example, planned deferral of the start of postoperative RT because of delayed wound healing is indistinguishable from unscheduled delay unless the date when the patient is ready to be treated is recorded prospectively. Finally, the retrospective approach does not provide the real-time information needed to fine-tune the performance of an RT program. Prospective collection of the pertinent information is the preferred approach for tracking patients through the system. This approach has now been adopted by the Ontario RT system (see "A Canadian Case Study" in this chapter).

Causes of Waiting Lists for Radiotherapy

Kinetics of Waiting Lists

When demand for RT exceeds supply, waiting times inevitably increase and a waiting list for RT starts to grow. In theory the waiting list will then continue to grow for as long as demand continues to exceed supply. In reality, waiting lists for RT do not grow indefinitely. When waiting times for RT become longer than the referring physicians believe is acceptable, they may begin to offer their patients alternative treatments in circumstances in which RT would normally have been their first choice. For example, when long waiting lists for RT developed in Ontario in the early 1990s, there was a significant decline in the use of primary RT in the management of head and neck cancers, followed by a rebound when waiting lists decreased after a major reinvestment in facilities.[15,16] It has also been shown that there is a significant negative association between the prevailing waiting time for RT and the proportion of patients receiving postoperative RT following a partial mastectomy for breast cancer.[17] Furthermore, tumor progression or deterioration in patients' general condition during the delay may render them ineligible for RT that would initially have been appropriate, and these cases drop off the list. Decreasing referrals and increasing drop-offs from the waiting list serve to reduce demand for RT. As demand declines, the balance between supply and demand is eventually restored; the waiting list then ceases to grow, waiting times stabilize at a higher level, and RT utilization rates stabilize at a lower level. This phenomenon has been referred to as *implicit rationing* because it limits utilization without explicitly limiting access to care.[18]

Even when average supply is equal to average demand for RT, random fluctuations in referral rates may produce transient peaks in demand that exceed supply, and this may be sufficient to cause a substantial waiting list.[19] This risk can be reduced by forward planning that provides a buffer of reserve capacity or by building flexibility of capacity into the system. The smaller the functional unit, the greater is the impact of random fluctuations, and the more reserve capacity is required to avoid a waiting list.[19]

Even in the absence of any shortfall in supply, quite long delays may develop in a complex process such as RT planning, simply because of the many serial steps involved. Process mapping and redesign can be useful in streamlining health systems and can reduce delays in some situations. For example, a French proton therapy center applied such an approach to reduce average wait times by 4 or more weeks and to increase the annual number of treatment sessions from 4000 in 2007 to 4500 in 2009.[20] Investigators at the University of Michigan examined streamlining the referral to treatment process for patients requiring palliative radiation for bone and brain metastases. They standardized processes and cut the number of individual steps to begin treatment from 27 to 16. The proportion of patients receiving consultation, simulation, and treatment within the same day was increased from 43% to nearly 95%.[21] However, no amount of fine-tuning will have any impact on waiting times for RT if total demand exceeds total supply.

Consequences of Waiting Lists for Radiotherapy

Delays in starting RT are a source of great concern both to the patients and to those involved in their care. Box 12-2 summarizes the potential adverse effects of waiting list for RT. Delays have both direct and indirect effects on the well-being of patients, and waiting lists also have broader economic and social consequences. It is useful to classify the direct effects of delay on the well-being of individual patients as *nonstochastic* or *stochastic*.[22] We use these terms as they have been used in the field of radiation protection, in which they provide a useful distinction between the effects of radiation that depend on chance and those that do not. The nonstochastic effects of delay include the psychological distress resulting from the delay and the physical symptoms as a result of the untreated cancer. They occur in most cases and often increase in intensity with time, although they may not occur at all before some initial threshold period has been exceeded. The stochastic effects of treatment delay include the development of metastases and failure to achieve local control with radiation. These are all-or-nothing phenomena. Their probability increases as a function of time, but their severity is independent of time,

BOX 12-2 The Effects of Waiting Lists for Radiotherapy

DIRECT EFFECTS OF DELAY IN RT ON THE WELL-BEING OF PATIENTS

- 1.0 Nonstochastic effects
  - 1.1 Persistence or worsening of symptoms while waiting for treatment
  - 1.2 Psychological distress
- 2.0 Stochastic effects
  - 2.1 Decreased probability of local control
  - 2.2 Increased probability of spread beyond the irradiated field
  - 2.3 Decreased probability of cure because of 2.1 and 2.2
  - 2.4 Increased probability of complications due to compensatory increases in dose and/or volume

INDIRECT EFFECTS OF WAITING LISTS FOR RT ON THE WELL-BEING OF PATIENTS

- 3.0 Decreased probability of being referred for RT when it is appropriate
  - 3.1 Omission of necessary RT
  - 3.2 Exposure to less effective or more toxic alternatives to RT
- 4.0 Re-referral to a distant center for RT with loss of continuity of care
- 5.0 Decreased quality of practice of radiation oncology
  - 5.1 Risk of cutting corners to treat more patients (e.g., hypofractionation)
  - 5.2 Decreased quality of personal care because of the imperative to maximize technical productivity
  - 5.3 Decreased scope for innovation

ECONOMIC EFFECTS OF WAITING LISTS

- 6.0 Decreased efficiency of RT programs
  - 6.1 Decreased net benefits of RT (see 1.0 and 2.0)
  - 6.2 Increased costs associated with care for patients during delay
- 7.0 Decreased overall efficiency of cancer treatment programs
  - 7.1 Decreased benefits of RT because of treatment delayed or denied
  - 7.2 Increased costs because of the requirement for additional care during delay or use of more expensive alternatives to RT

OTHER SOCIETAL EFFECTS OF WAITING LISTS

- 8.0 Legal liability of providers for failure to provide adequate access to care
- 9.0 Decreased public confidence in the healthcare system

and there is no lower limit of waiting time below which they will not occur. Waiting lists may also have indirect adverse effects on patient care, mediated by changes in medical practice. In addition to their effects on health outcomes, waiting lists have important economic and societal implications.[22]

Measuring the Direct Effects of Delays in Radiotherapy

Some of the direct effects of delays in RT are self-evident. Delays in cancer treatment cause psychological distress and patients who are symptomatic wait longer for relief. There are also good reasons to believe that delays may adversely affect the long-term outcomes of RT. Delays provide an opportunity for tumor progression. There is abundant evidence that the probability of local control decreases as tumor volume increases and that the risk of metastasis increases over time.[23] These arguments are probably sufficient to persuade most radiation oncologists that unnecessary delays in RT should be avoided. However, in a publicly funded health system, in which waiting lists are endemic and widespread, many different specialties may each use their own waiting list problems to try to lever additional funding from a limited overall pool. In this context, direct evidence that delays in RT have an adverse effect on clinical outcomes is necessary to ensure that the needs of the RT sector are given appropriate priority.

Given the scant direct evidence that was available about the impact of delay on outcomes in the early 1990s, we initially used a mathematical modeling approach to estimate the risks of treatment delay.[22] The model was based on radiobiological principles that had been validated in experimental systems, and it incorporated the best available clinical information about tumor doubling times and the relationship between tumor volume and local control in the context of cancer of the tonsil.[22] The model predicted a decrease in local control rates of between approximately 10% per month of delay in the start of RT. Others have since made similar predictions.[24,25] However, although this approach was credible to radiation oncologists, it was not readily understood by those outside the field and had no impact on public policy. To make the case for increased resources, we therefore needed to provide direct clinical evidence of the adverse effects of delay.

Measuring the magnitude of the stochastic effects of treatment delay is not straightforward. It is inherently difficult to measure the risk of treatment failure as a result of delay because local failures caused by delay are absolutely indistinguishable from treatment failures resulting from other causes. The problem is analogous to that of defining the risk of carcinogenesis associated with low-dose radiation. One cannot simply count the cancers resulting from radiation because they are usually indistinguishable from the many other cancers that may occur because of causes other than radiation. Rates of failure must, therefore, be compared in groups of patients who have been exposed to longer and shorter delays, and the challenge is to ensure that those groups are comparable with respect to all other relevant prognostic factors. A randomized trial would be the best way of creating truly comparable groups, but it would be unethical to randomize patients to timely RT versus delayed RT, because there is no conceivable benefit in delay. Comparisons of the outcomes of RT in nonrandomized groups of patients who have waited longer or shorter periods of time are subject to all the biases that may affect any retrospective observational study. However, in this context, such studies are important because they represent the best available direct source of information.[25,26]

Recent systematic reviews have identified a growing number of observational studies that have investigated the association between treatment delay and the outcome of radiotherapy in certain clinical situations.[27] Figure 12-4 summarizes the results of the 20 high-quality studies included in a recent published meta-analysis.[27] Most of these studies had been done in the context of head and neck cancers and breast cancer. In these two disease groups, meta-analysis have showed a significant increase in the risk of local recurrence in patients who waited longer for RT.[27] A large population-based outcomes study, not included in this meta-analysis, recently confirmed that delay was associated with a higher risk of local failure following postlumpectomy RT for breast cancer.[28] We found no evidence of a threshold below which delay was free of risk. Moreover, although there was less evidence of an association between delay and local control in sites other than breast and head and neck, there was insufficient data available to conclude that delay in RT is free of this risk in any situation. We found no significant association between delay in RT and

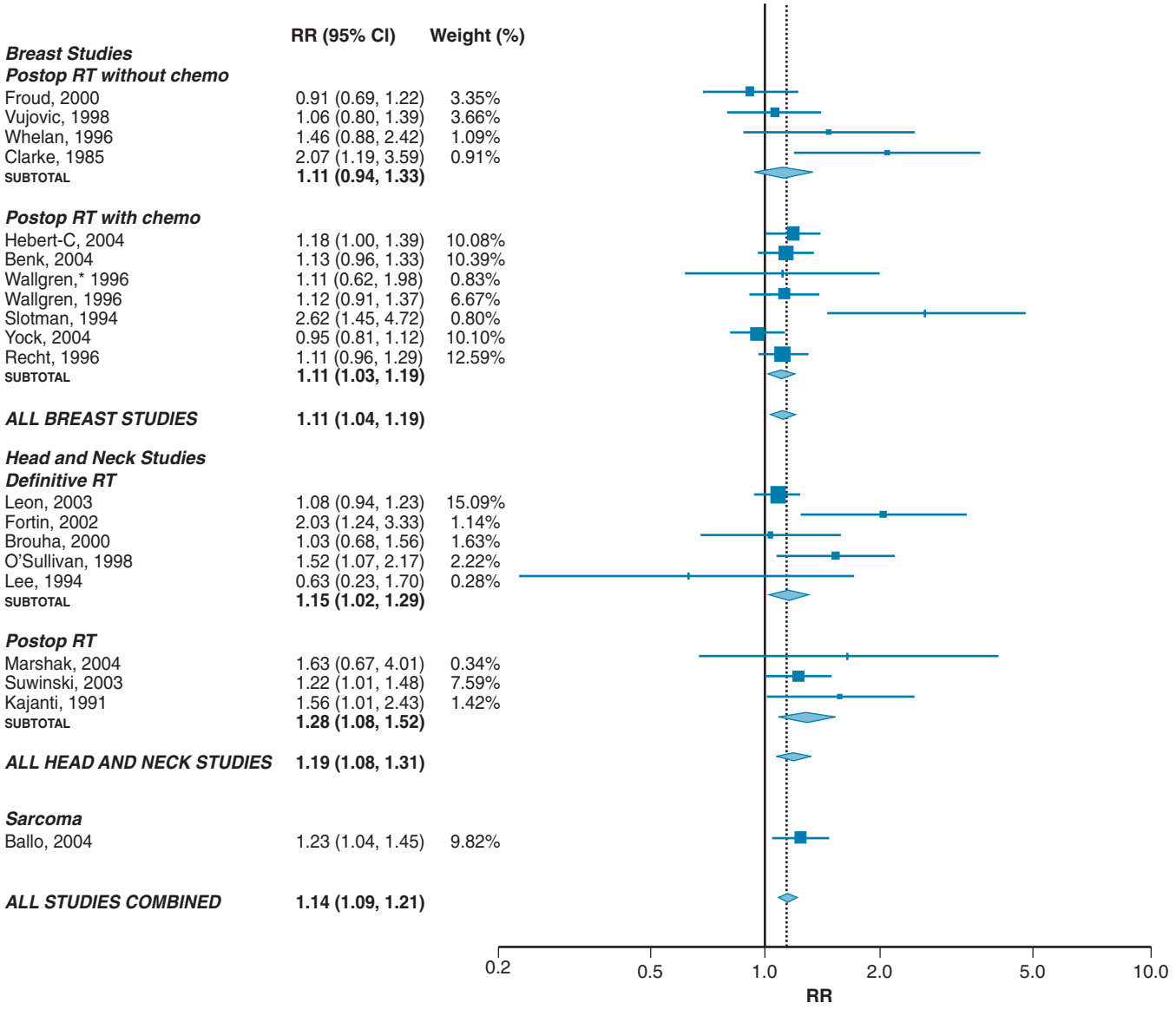

Figure 12-4 The association between delay in RT and the risk of local recurrence. The plot shows the results of a meta-analysis that included 20 high-quality studies that compared rates of local recurrence following RT.
(From Chen Z, King W, Pearcey R, et al: The relationship between waiting time for radiotherapy and clinical outcomes: A systematic review of the literature. Radiother Oncol 87:3-16, 2008.)

the risk of distant metastasis, although there was less information available about this outcome.[27] There was a small but significant decrease in survival with increasing delay in head and neck cancers.[27]

The relative risk of local recurrence of 1.1 per month of delay in starting postoperative RT for breast cancer translates into an absolute increase in recurrence rate of about 1% per month of delay in a population with a baseline rate of local recurrence of 10%.[27] Although this is a small risk for any individual it has the potential to cause an important increase in the number of recurrences at the population level. The increase in the relative risk of recurrence by 1.15 per month of delay in patients undergoing definitive RT for head and neck cancers translates into an absolute increase in risk of recurrence of 3% in a population with a baseline risk of failure of 20%, or an absolute increase of 6% in a population with a baseline risk of failure of 40%.[27] Interestingly, these findings are consistent with those predicted by the mathematical models described previously.[22,24] Thus, a few weeks delay in RT may have an adverse effect on outcome that is sufficient to cancel out all the improvements in outcome achieved by advances in the practice of RT over the last 20 years.[24,25] Given that there is no theoretical reason to believe that there is a threshold below which delay is safe, we have recommended that it would be prudent to adopt the principle that delays in RT should be as short as reasonably achievable (ASARA), modeled on the ALARA principle that guides risk management in the field of radiation protection.[25]

Indirect Effects of Waiting Lists for Radiotherapy on Patient Care

Box 12-2 summarizes the indirect effects of waiting lists on patient care and population health. The phenomenon of implicit rationing by which waiting lists reduce the use of RT

has already been described and the consequences of underutilization of RT will be discussed later in this chapter. Waiting lists may also increase the use of alternative treatments that may be less effective, more morbid, and more expensive than RT. There is evidence that long waiting lists may cause radiation oncologists to modify the way they prescribe RT. A study from the Queensland Radium Institute, for example, showed a significant negative correlation between waiting times and the number of fractions prescribed per course, as a result primarily of decreases in palliative fractionation as waiting times increased.[29] We have found a similar association between prevailing waiting time and the choice of fractionation for bone metastases in Ontario.[30] There are obviously serious risks in deviating from accepted practice in radiation oncology for the sole purpose of getting more patients treated. However, in circumstances in which randomized trials have demonstrated that shorter courses of RT are equivalent to longer courses of treatment, adoption of the more parsimonious approach has the potential to reduce overall workload and greatly increase the availability of RT, without adversely affecting outcomes.[31] The challenge is to ensure that shorter-than-standard courses of RT are used only in circumstances in which they have been shown to be medically appropriate. Explicit standards of care are required to prevent deterioration of quality in an attempt to maintain accessibility.

Societal Effects of Waiting Lists for Radiotherapy

Waiting lists for RT are potentially costly (Box 12-2). Patients require both care and counseling during delays and the costs of alternative treatments may be considerably higher than those of RT. Waiting lists have sometimes caused patients to be referred to distant centers for RT with loss of continuity of care and support for patients and added costs to the health system. The inability to provide timely RT may also be frustrating and distressing for the staff of RT programs. Waiting lists also expose RT providers to legal liability. In Quebec, a class action suit was launched against the hospitals responsible for providing RT, on behalf of approximately 10,000 women who had to wait long periods for adjuvant RT following surgery for breast cancer. At trial, the judge accepted the evidence that delay was associated with an increase in the risk of local failure and the case was ultimately settled with financial compensation for women who had waited for longer than 12 weeks to begin postoperative RT following lumpectomy.[32] Chronic waiting lists for RT and other important medical services eventually became an important political issue. Waiting lists are often used as evidence of the need for change, both by advocates of privatization of the health system and by those who favor reinvestment in the public system. By the early 2000s, public opinion polls showed that "wait times" for medical care had become the greatest concern of most Canadian voters, and there were increasing demands that government should set waiting time standards.

A Canadian Case Study

Why did waiting lists for RT become such a widespread problem around the world in the 1990s? Was there an increase in demand or a decrease in supply or both? Ontario's experience serves as a useful case study. Analysis of historical data showed that three different factors conspired to cause a huge increase in demand for RT over the critical period.[16] First, the incidence of cancer increased inexorably by approximately 3% per year, resulting primarily from the aging of the Ontario population.[16] Second, there was a dramatic increase in the number of patients referred for RT for breast cancer (consistent with the evidence-based trend toward breast conservation surgery[16]), for rectal cancer (consistent with the evidence-based adoption of postoperative RT and chemotherapy[31]), and for prostate cancer (as a result of a large increase in the number of early cases detected following the widespread adoption of prostate-specific antigen [PSA] screening[16]). Third, there was a significant increase in the average number of fractions prescribed per course of RT. This was driven by an increase in the number of fractions per curative or adjuvant course, which outweighed a concomitant but smaller decrease in the number of fractions per palliative course of RT.[16] There was no decrease in treatment capacity. In fact, the number of treatment machines in the province increased faster than the incidence of cancer.[16]

The demographic trends responsible for increasing cancer incidence and the changing patterns of practice that were responsible for Ontario's waiting list crisis are international phenomena, which explains why waiting lists developed more or less simultaneously in many other countries at the about same time. Countries where most or all of the RT system was publicly funded were hardest hit. The fact that the United States did not experience similar problems probably reflects the much greater reserve capacity available in the large private sector in the United States and also its ability to increase capacity rapidly in response to increased demand. In the private sector, increased demand represents an opportunity to increase revenues. When demand begins to outgrow supply, providers titrate additional resources into the system until demand is once again saturated. In contrast, in a publicly funded system operating on a fixed global budget there is rarely any reserve capacity, and it may be impossible to expand capacity rapidly. Increasing capacity often requires expanding facilities and acquisition of new equipment, and approval processes for new capital projects in publicly funded systems may take years to complete. These built-in delays may make it impossible ever to catch up on a growing problem once it becomes established. Only accurate forecasting of the future need for RT, linked to a proactive planning process for facilities, equipment, and personnel, can provide a way of avoiding similar problems in the future in slow-to-react public systems.

In Ontario, additional steps were used to prospectively monitor waiting times for radiotherapy as an indicator of quality of care. Prospective data collection was required to overcome the limitations to the retrospective analysis of waiting times, because such analyses are "blind" to patients who dropped off the waiting list before they were treated. Further, the data used in retrospective analyses may lack the information necessary to define the rate-limiting steps in the RT process or may lack information about other elements of the patient's care that are necessary to interpret waiting times for RT or to fine-tune the performance of an RT program. Prospective collection of the pertinent information is the preferred approach for tracking patients through the system. Figure 12-5 illustrates how this approach was adopted by the Ontario RT system using the framework presented previously (see Figure 12-1). Definitions were developed for overall wait times (and by waiting period) as indicators of performance, and the CARO definitions were used to set standards of performance as described. Methods were developed to prospectively collect wait-time data for each treating center, and proportion of patients meeting performance standard were routinely monitored and publicly reported. To improve wait times, investment in infrastructure was made. Further, each cancer center evaluated its treatment processes relevant to wait times and implemented process improvements (e.g., by running appropriate processes in parallel rather than sequentially). Patients with delays that were medically indicated (e.g., delayed wound healing) or with personal circumstances requesting delay were identified prospectively and accounted for in the analyses. As a result, analyses now reveal that the vast majority of patients meet wait-time standards across the province.[33]

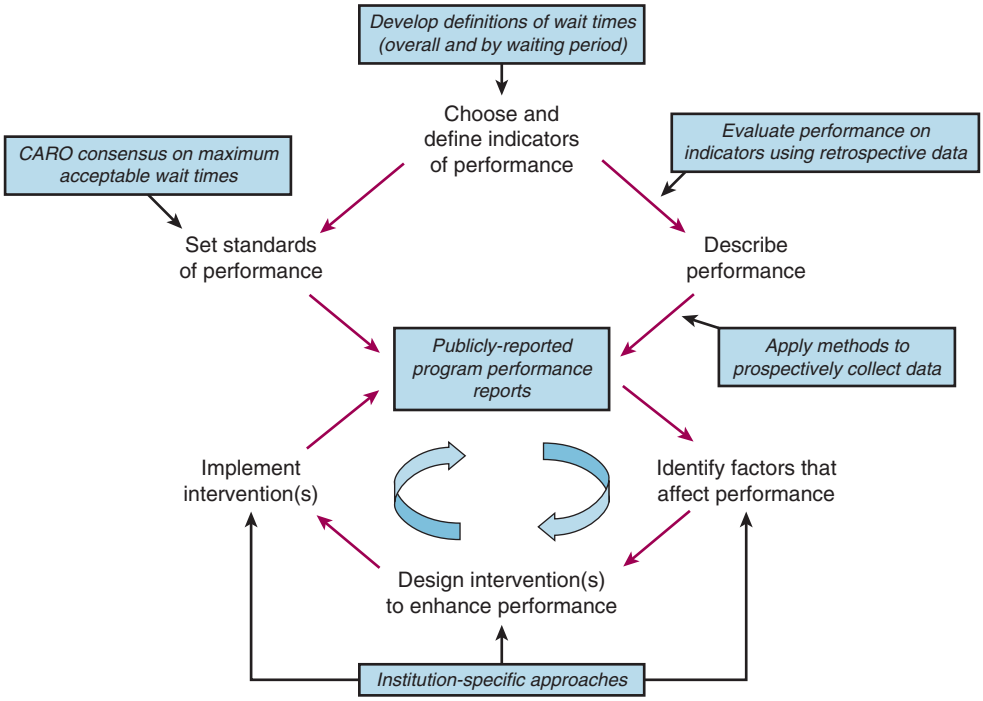

Figure 12-5 An illustration of the use of HSR to improve quality of care with regard to radiation wait times.

Measuring Access to Radiotherapy

Limitations of Waiting Times as an Indicator of Access to Radiotherapy

The existence of a long waiting list for RT is a symptom of inadequate access to RT. The duration of the waiting time for RT may be directly related to the probability of an adverse outcome, and waiting times may therefore serve as a quantitative measure of the quality of care. The length of a waiting list, however, provides no information about the magnitude of the shortfall between supply and demand, and waiting times cannot, therefore, serve as a quantitative measure of accessibility. The absence of a waiting list does not mean that access is optimal. Waiting lists develop only in response to supply-side problems in the availability of services. Waiting times are entirely insensitive to demand-side problems with respect to spatial accessibility, accommodation, affordability, or awareness (see Box 12-2). Problems in those dimensions of accessibility in fact reduce demand and may serve to reduce or avoid waiting lists. Thus, the absence of a waiting list does not imply that access is optimal. To ensure appropriate access to RT, it is also necessary to monitor RT utilization rates.

Defining Accessibility of Radiotherapy

The best quantitative measure of the accessibility of any service is the rate of its appropriate utilization, that is, the proportion of patients that need a service who actually receive it. The term *need* is used here as defined by Cuyler,[34] who states that "the need for medical care exists when an individual has an illness for which there is effective and acceptable treatment."

$$\text{Accessibility} = \frac{\text{Number of patients who need and receive treatment}}{\text{Total number who need treatment}}$$

Accessibility can have any value between 0 and 1, where 1 corresponds to optimal access. These values can also be multiplied by 100 and expressed as a percentage. Thus, to determine the accessibility of RT directly, we must measure both the utilization of RT and need for RT in the cancer population. In practice, the number of patients in a population who receive RT is relatively easy to determine, but the number who need RT is usually unknown. Proxy measures of need therefore have to be chosen.

Measuring Accessibility of Radiotherapy

The *incidence* of cancer (i.e., number of new cases diagnosed in the population of interest, over the period of interest) may be used as the denominator for describing the rate use of RT in the initial management of the disease. The best way to establish the proportion of cases that are treated with RT is to follow all of them forward in time from the date of diagnosis and find out if and when the patient received RT. The approach was first used in the Netherlands,[35] and we subsequently used it to describe the use of RT in Ontario.[15] The estimated rate of use of RT in the initial management of cancer depends on the cutoff point in time used to define initial RT. If a short cutoff point is chosen to define initial RT (e.g., RT within 3 months of diagnosis), the indicator will miss some patients who receive adjuvant RT following surgery. If a longer cutoff point is chosen (e.g., RT within 1 year), the indicator will include almost all patients who receive RT as part of their initial management, but it will also wrongly include some patients who are actually receiving RT for an early recurrence following primary surgery. The best cutoff point depends on the specific disease under consideration. For practical purposes, we have chosen to use the proportion of incident cases treated within 1 year of diagnosis to describe the initial use of RT in the general cancer population.[15] Figure 12-6, *A* describes variations in the use of RT in the initial management of cancer in Ontario in terms of this indicator ($R_{1\ year}$).

The incidence of cancer is a less suitable denominator for describing the utilization of palliative RT because a high proportion of incident cases will never develop indications for palliative RT, and many of those who ultimately do need

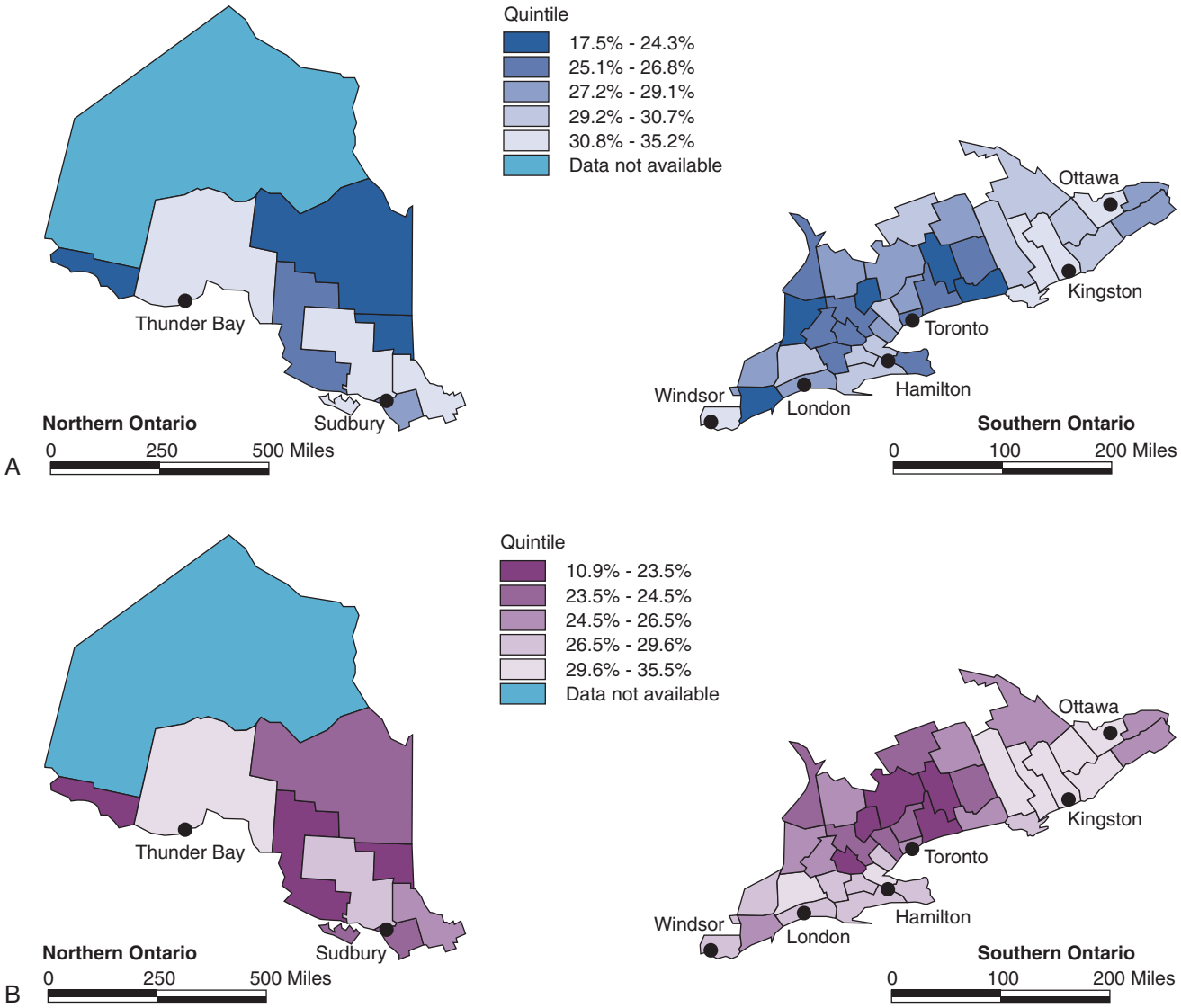

Figure 12-6 Geographic variations in the use of RT in Ontario. **A,** Intercounty variations in the rate of use of RT in the initial management of cancer within 1 year of diagnosis. **B,** Intercounty variations in the use of palliative RT in the last 2 years of life among patients who died of their cancer. The location of the provincial RT centers is shown for comparison.
*(**A,** Adapted from Mackillop WJ, Groome PA, Zhou Y, et al: Does a centralized radiotherapy system provide adequate access to care? J Clin Oncol 15:1261–1271, 1997; **B,** adapted from Huang J, Zhou S, Groome P, et al: Factors affecting the use of palliative radiotherapy in Ontario. J Clin Oncol 19:137–144, 2001.)*

palliative RT will not require it until years after the diagnosis. It is preferable to describe the use of palliative RT among patients who die of their cancer. This can be accomplished by identifying patients who died of their disease in a population-based cancer registry and following them back in time to identify those who received RT within a defined interval before death.[36] Figure 12-6, *B* describes variations in the use of palliative RT in the last 2 years of life among patients who died of their disease in Ontario. The same approach lends itself well to the description of the rates of use of other types of care in the terminal phase of the illness.

What Factors Affect the Rate of Radiotherapy in the General Cancer Population?

Figure 12-6 illustrates geographic variations in the rate of use of RT in Ontario, with the highest rates being observed in the counties where RT facilities are located.[15] It has generally been found that rates of RT use are higher in urban than in rural areas,[37] and that proximity to an RT facility is associated with higher utilization rates.[15] Taken together, these observations suggest that spatial accessibility is an important determinant of the accessibility of RT.

In studying geographic variations in practice, it is obviously important to be able to distinguish systematic variation from variations because of chance alone. Modeling techniques have been developed that can be used to isolate the systematic component of variation.[15] Multivariate analysis is helpful in distinguishing the impact of health system-related factors from other factors that are legitimately involved in determining patients' eligibility for RT. These include differences in cancer incidence, stage distribution, evolution of evidence supporting use of radiotherapy, patient functional status, and patient preference. Patient functional status and preference are important factors but are usually not available in administrative health data. Patient preference plays a significant role in observed rates of RT in cases in which there is more than one

TABLE 12-1 Factors Affecting the Use of Palliative Radiotherapy in Ontario*

	Odds Ratio	95% Confidence Interval
MEDIAN HOUSEHOLD INCOME		
Low, <Can $20,000	1.00	—
Medium, Can $20,000-$50,000	1.09	1.04-1.15
High, >Can $50,000	1.17	1.11-1.24
RT DEPARTMENT IN DIAGNOSING HOSPITAL		
No	1.00	—
Yes	1.35	1.30-1.40
PROXIMITY OF PATIENT'S HOME TO NEAREST RT CENTER		
No RT center in county of residence	1.00	—
RT center in county of residence	1.24	1.21-1.27
REGION		
Northeast Ontario	0.84	0.79-0.90
Toronto	0.88	0.84-0.92
Windsor	0.90	0.84-0.97
Ottawa	1.00	—
London	1.02	0.97-1.07
Northwest Ontario	1.04	0.96-1.13
Kingston	1.17	1.11-1.26
Hamilton	1.20	1.14-1.26

**From a logistic regression that controlled for age, sex, and primary site.*

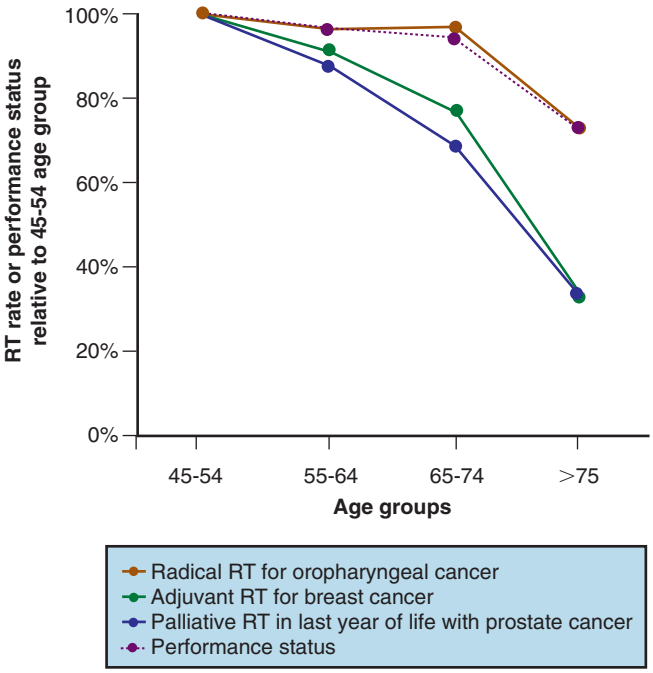

Figure 12-7 The effect of age on the use of RT. The proportion of patients who received RT for specified indications is shown for older age groups and compared with the rate observed in patients between 45 and 54 years old. The expected decline in performance status with increasing age is shown for comparison.
(Adapted from Tyldesley S, Zhang-Salomons J, Groome P, et al: Association between age and the utilization of radiotherapy in Ontario. Int J Radiat Oncol Biol Phys 47:469–480, 2000.)

standard-of-practice treatment. An example is treatment of low-risk prostate cancer.

Measurements of RT use have revealed unexpected inequities in access to care. One example is from a study investigating factors associated with use of palliative RT among patients who died of their cancer in Ontario (Table 12-1). In multivariate analysis, rates of use of palliative RT proved to be significantly lower among patients in whom the diagnosis was made in a hospital without an RT facility,[36] which confirms the concern of others that lack of awareness of the indications among other health professionals for RT may also be a significant factor in determining accessibility.[37] Additionally, even in the context of a publicly funded health system, the socioeconomic status of the patient influences the likelihood of receiving palliative RT. Figure 12-7 shows that rates of use of palliative and adjuvant RT decrease with increasing age and that this decrease is far greater than can be explained due to declining performance status.[38]

Measuring the Need for Radiotherapy

Given that the use of RT varies widely, it is important to ask what proportion of patients with cancer need RT. In the past, it was often stated that approximately 50% of patients with cancer should receive RT at some point in the course of the illness, but that recommendation was based almost entirely on expert opinion.[39] Two more objective methods have since been developed for estimating the need for RT.

Evidence-Based Requirements Analysis

Evidence-based requirements analysis (EBRA) is an objective method that has been used to estimate the need for RT. The indications for RT are first identified by systematic review. Next, an epidemiologic approach is used to estimate how frequently each indication for RT occurs in the population of interest. Finally, the results of the systematic review and the epidemiologic analysis are combined to estimate the overall need for RT. In this context, the term *need* can be equated with the *appropriate rate* of utilization of RT,[34] and the two terms may be used interchangeably. Tyldesley et al discovered this method and used it first to estimate the need for RT in patients with lung cancer.[40] We have subsequently refined the method and used it in several other major cancer sites.[41] The strengths of the method are: (1) that it is transparent in that all the assumptions involved are explicit; and, (2) that it is flexible, and models can be adapted to reflect the case mix in any community of interest or to explore the implications of changes in the indications for RT. The main weaknesses of the approach are that it is complex and time consuming and like any other type of modeling, its results are only as good as the information on which it is based. EBRA can be expected to produce valid results when it is applied to major cancers where the indications for RT are well defined and there is sufficient epidemiologic information available to estimate the frequency with which each indication occurs. Delaney et al extended the use of this method to measure the need for RT across the whole spectrum of malignant disease, and it is now being widely used to predict requirements for RT equipment.[42]

Criterion-Based Benchmarking

An alternative way of estimating the appropriate rate of the use of RT is to use a series of observations to derive a "benchmark." In the business world, *benchmarking* has been defined as "measuring products against the toughest competitors or those recognized as industry leaders."[43,44] In the field of health care, the equivalent is to measure outcomes against the best achieved anywhere or against those achieved in recognized centers of excellence. The same concept may be applied in setting benchmarks for the appropriate rate of utilization of any given treatment. The rate observed under certain specific conditions may be equated with the appropriate rate of

utilization—in other words, with the need for treatment. Benchmarks for the utilization of RT should be set in communities in which there is unimpeded access to RT and expert decision making about the use of RT. To ensure unimpeded access, there should be no financial barriers, referring physicians should be aware of the indications for RT, and patients should have convenient access to a nearby RT center that has sufficient capacity to provide prompt treatment. To ensure optimal decision making, decisions about the use of RT should be made by experts practicing in a multidisciplinary setting, and ideally the decision to treat should not affect their remuneration. If these criteria are met, it is reasonable to expect that the observed rate of utilization of RT will approximate the appropriate rate. We call this approach criterion-based benchmarking (CBB).[44]

We have been able to select a few communities in Ontario that meet most of the listed criteria and have used them to set benchmarks for the appropriate rate of utilization of RT for lung cancer.[44] Figure 12-8 shows that in this context, estimates of the appropriate rate of RT generated by this method are similar to those derived from the evidence-based approach. The CBB method has several strengths: (1) It is an inductive method that is grounded in observations in the real world; (2) it is applicable to both rare and common cancers because it does not require an accurate, comprehensive catalog of indications for treatment or detailed information about case mix; (3) it is relatively inexpensive and can be repeated easily if the indications for treatment change; and (4) it can be validated by replication in different communities. It also has several weaknesses: (1) It assumes that optimal structures and processes are associated with optimal practice, and this has not been proved; (2) the structures and processes that support optimal access and optimal decision making are not well defined; and (3) it requires a detailed knowledge of the structures in place in communities that are candidates to be benchmarks and this information may not readily be available. This CBB approach has been adopted by Ontario's provincial cancer agency and is now used for RT system planning. It is also used in the ongoing evaluation of the performance of the RT system performance by the Cancer Quality Council of Ontario which routinely reports on rates of RT use in relation to benchmarks established for the major malignant diseases.

Once utilization and need have been measured, it is straightforward to calculate the level of unmet need. Consider the data shown for lung cancer in Figure 12-8. It was estimated that approximately 41.6% of cases of lung cancer need RT as part of their initial management but the observed rate of RT use was only was 32.5%. Thus, only 32.5/41.5 = 78.3% of cases who needed RT actually received it. The ~22% shortfall between the observed rate and the appropriate rate represents an important opportunity for improving outcomes of lung cancer.

The Consequences of Underutilization of Radiotherapy

Adequate access to RT is a necessary component of any comprehensive cancer control program. At present, many patients who might benefit from RT have no access to the treatment that they need. This is a global problem that affects both developed and developing countries, but it is most prevalent and severe in low-resource settings where RT services are either nonexistent, or so limited as to be essentially nonexistent[43,45] (see discussion later in this chapter).

The consequences of lack of access to RT are most devastating for patients who have a radiocurable condition for which no other curative treatment is available (e.g., those with locally advanced cervical cancer). In situations such as this, the lack of access to RT inevitably translates into an avoidable and often unpleasant death. In contrast, failure to provide adjuvant RT when it is indicated, does not make death inevitable but does increase the risk of local recurrence and may also compromise long-term outcomes. Many patients who do not get palliative RT when they need it to relieve their pain or other symptoms will continue to suffer, whereas others who are more fortunate, must accept the lesser benefits and perhaps greater toxicity of alternative treatments.

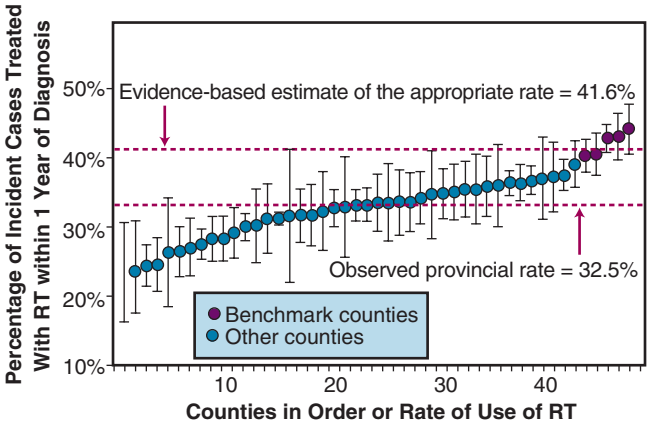

Figure 12-8 Evidence-based estimates and benchmarks of the appropriate rate of use of RT in the initial management of lung cancer. The rates of RT in the initial treatment of lung cancer are shown for each county in Ontario. The *error bars* represent the 95% confidence limits for these observations. Benchmark counties are those where cancer centers with relatively short waiting lists were located. The evidence-based estimate of the appropriate rate and the overall provincial rate are shown as *horizontal lines*; the distance between the lines represents the unmet need for RT.
(Adapted from Barbera L, Zhang-Salomons J, Huang J, et al: Defining the need for radiotherapy for lung cancer in the general population: a criterion based, benchmarking approach. Med Care 41:1074–1085, 2003.)

Beyond its effects on the patients themselves, the lack of access to RT may have serious consequences for their families and their communities. The unnecessary death of a young man or woman may have devastating economic as well as social consequences for their surviving family. The broader economic consequences of failure to use RT vary depending on the patient's condition and the socioeconomic status of the community. In rich countries, in which a range of other services are more readily available, failure to use RT when it is indicated may lead to the increased use of other, less cost-effective treatments, with a consequent overall increase in the cost of care. Even in poor countries where no alternative treatments are available, it may ultimately cost more not to treat a curable young patient than it would have cost to provide the necessary RT because failure to treat him or her results in the loss of a productive member of society.

STUDYING THE QUALITY OF RADIOTHERAPY

This section introduces the concept of quality in health care, describes what HSR has taught us so far about the quality of RT, and identifies what we still need to learn.

Concepts of Quality and Effectiveness in Health Care

In the field of HSR, the term *efficacy* is used to describe the extent to which a treatment achieves its objectives in the controlled setting of a clinical trial. The term *effectiveness* is

reserved for describing the extent to which a health program meets its stated objectives in the real world. The term *quality* is used to describe the effectiveness of the care provided, relative to the effectiveness of the best possible care. In this context, the term *quality* is therefore synonymous with the term *attainment factor* as defined previously.

Almost 40 years ago, Donabedian[46] defined *quality* as "a property of, and a judgment upon, some definable unit of health care, and that care is divisible into at least two parts: technical and interpersonal." The quality of technical care is measured by the extent to which "the application of medical science and technology maximizes its health benefits without correspondingly increasing its risks." The quality of interpersonal care is measured by "how well the physician-patient interaction meets the socially defined norms of the relationship."[46] Although others may define it somewhat differently today, there is universal agreement that quality is a multidimensional concept that embraces both the technical and personal elements of care.

Donabedian[46] also provided an approach for evaluating and improving quality, which Kramer and Herring soon astutely recognized as being appropriate for use in radiation oncology.[47] Donabedian's approach was to analyze the quality of programs in terms of *structure*, *process*, and *outcome*. The term *process* is used here to describe the way that care is delivered. In the context of radiation oncology, it includes pretreatment assessment, medical decision making, planning, delivery of RT, and supportive care during RT, and so on. The term *structure* is used broadly to include facilities, equipment, human resources, and organizational structures. The term *outcome* is used here, as in clinical practice, to describe the consequences of the care that has been provided. It is reasoned that: (1) optimal *process* is necessary for optimal *outcome*; (2) adequate *structure* is necessary, though not sufficient, for optimal *process*; and (3) *outcomes* may be enhanced by identifying and correcting deficiencies in structure, or deficiencies in process. This became the philosophy of the U.S. Patterns of Care Study that was established by Kramer in 1970. It operates on the premise that practice variations exist, differences in process and outcome can be measured, and deficiencies can be corrected.[47] The Patterns of Care Study (PCS) continues this important work today under the new title of Quality Research in Radiation Oncology (QRRO).

Studies of the Structure of Radiotherapy Programs

Two different types of research are being undertaken in this area. First, there are descriptive studies of the physical and organizational structures that prevail in RT programs around the world. In some instances, the observed structures are compared with predetermined standards. In others, the description of structures has been linked to studies of process and outcome with the goal of establishing which types of structure are associated with the best results. These studies may rely on mail surveys or involve on-site visits, but they are all cross-sectional or retrospective in design. Second, there is the field of technology evaluation, which is essentially prescriptive rather than descriptive in intent. It seeks to establish prospectively the usefulness of new technologies in patient care and thus contributes information that is important in setting standards for equipment in an RT program.

Descriptive Studies of the Structure of Radiotherapy Programs

In a highly technical specialty like radiation oncology, optimal care can be provided only when the necessary technological infrastructure is in place, including the correct mix and quantity of equipment and the correct mix and quantity of personnel. Nationwide surveys of RT facilities have now been done in many different countries. In the United States, the PCS/QRRO has taken the lead in describing the basic structural characteristics of radiation oncology facilities for the entire country. Its comprehensive survey of the structure of U.S. facilities serves as the starting point for national surveys of treatment processes and outcomes and permits stratified sampling of different types of facilities.[48] In addition to evaluating equipment and personnel, PCS/QRRO has described the structure of RT facilities in the following terms: (1) whether they have resident training programs or not, (2) volume of new cases treated per annum, (3) whether they were headed by a full-time or part-time radiation oncologist, and (4) participation in clinical trials.

In Europe, a variety of government,[49] agencies,[50] and individual investigators[51] have conducted national surveys of RT program infrastructure, primarily as a basis for planning. Most national surveys reveal considerable diversity with respect to the level of technology and expertise that is available in different RT centers, particularly with respect to brachytherapy. The European Society for Radiotherapy and Oncology (ESTRO) has more recently taken the lead describing and comparing the infrastructure of RT programs across Europe in a project called Quantification of Radiation Therapy Infrastructure and Staffing (QUARTS), funded by the European Commission.[52] QUARTS involves an international survey of equipment and personnel, the establishment of guidelines for levels of staffing and equipment, and the estimation of future needs based on projected incidence and estimates of the need for RT.

International comparisons of radiotherapy structure have been performed by the International Atomic Energy Agency (IAEA). These studies have covered Europe, Asia, Africa, and Latin America.[53-56] A common theme has been wide variation in the supply of RT resources with undersupply a common international problem, especially in low-income (gross national income [GNI] per capita US$1,035 or less) and middle-income countries (GNI per capita US$1036-$12,615).[53-55,57] A strong relationship exists between a lower national economic status and the degree of greater undersupply of RT equipment.[58] At its extreme, 29 of 52 African countries, with a total population of 198 million people, have no known external beam RT facility.[53]

The concept of program structure embraces not only physical infrastructure but also organizational structures including systems of funding, management, and governance. These elements of structure in radiation oncology may also have important effects on processes, but they have generally received less attention than the physical elements of structure. Funding arrangements at European RT centers listed in the ESTRO directory were investigated as part of an international study of palliative RT.[59] A broad range of funding mechanisms for RT departments is described, including a global budget, per-case payments, fee-for-service, and all possible combinations thereof. RT centers in Spain, the United Kingdom, and the Netherlands were mainly funded by a global budget plus or minus per-case payments, whereas the majority of centers in Germany and Switzerland received most of their funding through a fee-for-service arrangement.[59]

Prescribing Technology Assessment

New technologies are being developed rapidly, and our specialty needs to develop better ways of evaluating them and of determining their appropriate place in routine clinical practice.[60,61] Wherever possible, new treatment techniques should

be evaluated in randomized clinical trials, but it is clear that this approach only lends itself to the study of relatively common presentations of relatively common diseases. A large component of the practice of radiation oncology, however, is directed toward patients who have one of the many less common cancers or one of the infinite range of unusual presentations of a common cancer. In neither of these situations is there ever going to be "level 1 evidence" to guide our practice, and it would be impossible for a new approach to treatment to achieve their full potential if we demanded level 1 evidence for its use in every situation. On the other hand, if we choose to make our decisions about the acquisition and use of new technologies based only on the manufacturers' claims of enhanced precision, we may expose our patients to added risks and added costs without real benefits.[60]

Studies of Process in Radiotherapy

The term *quality assurance* (QA) is used to describe processes intended to avoid error in medical care, that is, to ensure that every patient gets the right treatment delivered the right way. Much of what has been written about QA in radiation oncology concerns the avoidance of error in delivering RT, but avoidance of error in case selection for RT deserves equal attention. The term *error* is used here to describe a deviation from appropriate care. Operationally, deviations from appropriate care can only be identified when the boundaries of appropriate care have been defined. Any QA program therefore falls into two parts: setting standards (i.e., deciding what is appropriate) and ensuring compliance with standards (i.e., making sure that every patient is treated appropriately). Some processes in a RT program have the potential to affect every patient, whereas others concern specific groups of patients. We deal first with research in the area of general QA before considering the process of care for specific groups of patients with cancer.

Research on Quality Assurance Processes in Radiotherapy

The RT community has long recognized the importance of routine QA because of the potential for a malfunctioning or wrongly calibrated machine to cause systematic errors in the treatment of a large number of patients. Detailed guidelines and protocols have therefore been developed for commissioning, maintenance, and calibration of treatment machines.[61] However, neither the existence of such guidelines nor an organizational commitment to adhere to them is sufficient to guarantee patient safety. A seminal study undertaken some years ago by Horiot et al on behalf of the European Organization for Research and Treatment of Cancer (EORTC) revealed that some centers made systematic errors in radiation dosimetry.[62] It also showed that feedback of the results of the initial survey diminished the frequency of such errors when the study was later repeated.[63]

Although QA on equipment reduces the chance of systematic error, the requirement for individualization of treatment plans creates the added risk of random error caused, for example, by lapses in human judgment or miscommunication. It has been shown that although well-defined care paths or intervention-specific guidelines can minimize the frequency of this type of error, it does not eliminate them. Real-time audit is necessary to avoid rare but potentially serious errors in the context of routine practice,[64] and even in the controlled setting of clinical trials.[65] The general rule that emerges from these analyses is that human errors cannot all be avoided, but the vast majority can be detected before they have any adverse impact on the patient. Understanding why errors occur is now recognized as the key to development of better processes for their avoidance in future, and the epidemiology of medical errors is therefore a growing field of study.[66] Because actual errors are rare, it is important also to investigate near-misses[67] and this is the approach that is now widely being used in the field of RT.[68,69] Although several recent accidents have heightened awareness of the dangers of RT,[70] serious errors that result in harm to patients are exceptionally rare in comparison to error rates in other fields of medicine.[71] The low error rates in RT were not achieved by chance; they reflect a long-standing awareness of the dangers of RT and a tradition of commitment to QA that antedates the intense media attention directed to medical error over the last decade. Nonetheless, new technologies bring new risks of error and there is a need for continuing research in field of QA in RT.

Research on Practice Patterns in Radiotherapy

During the past 30 years, there have been numerous studies of patterns of care in radiation oncology using methods primarily developed by the PCS.[72] Many different clinical situations have been studied. Most work has been done in the major sites in which RT plays an important role in curative treatment, but there have also been a number of studies of the practice of palliative RT, particularly in the context of bone metastasis. Striking variations in practice have been discovered in every situation that has been studied in detail. Practice has been shown to vary at many different points in the pathway of care: in pretreatment assessment; in fundamental aspects of the RT prescription, including target volumes, treatment techniques, and dose and fractionation; in decisions about adjunctive systemic treatment; in the planning process; in treatment delivery; in the way that treatment details are recorded; in supportive care during and after treatment; and in arrangements for long-term follow-up.

Why Study Practice Variations in Radiotherapy?

Practice variations have been identified in every field of medicine where anyone has taken the trouble to look for them. As we have seen, radiation oncology is no exception. In the era of evidence-based medicine, practice variations represent a threat to the credibility of any medical specialty; it is difficult to defend variations in patient care except insofar they reflect variations in the needs of individual patients or unavoidable variations in the availability of resources. Practice variations in radiation oncology represent not only a threat but also an opportunity for improving practice and outcomes. The opportunities to improve the quality of care depend on the state of knowledge in the particular clinical situation under study. If optimal practice has already been established or can be established for the purposes of the study, deviations from the optimal represent opportunities for improving quality of care. It then becomes important to understand why practice deviates from the optimal, to design interventions that will improve practice. If, on the other hand, optimal practice has not yet been established, practice variations represent an opportunity for learning. Studies of practice patterns may identify controversies that should be addressed in clinical trials. In certain specific circumstances, it may be possible to explore the relationship between treatments and outcomes to determine which approach is superior. The scope and limitations of this type of study are discussed in Relating Structure and Process to Outcomes.

Why Does Practice Vary in Radiation Oncology?

In an ideal world, cancer treatment would be guided only by precise classification of the case and the application of scientific knowledge about the optimal treatment of that class of cases, taking into account the patient's personal values and preferences. In the real world, however, other environmental

factors may influence patient care. Treatment options are often constrained by the resources available. Scientific knowledge is variably disseminated and may be interpreted differently by individual physicians, depending on their training, experience, and work environment. Moreover, financial considerations have the potential to influence medical decisions, whenever there is more than one defensible treatment option available. We now review what is known about the impact of each of these factors on the practice of RT.

Impact of Program Structure on the Practice of Radiotherapy. Consistent with Donabedian's concept, there is abundant evidence that physical and organizational structures determine processes in RT (see Figure 12-12). If the total availability of personnel and equipment is not adequate to permit prompt access to RT, referring physicians may choose alternative forms of treatment. Many studies have revealed that radiation oncologists' choices of investigations, treatment techniques, and fractionation schemes are influenced by the resources available. The PCS has consistently found significant associations between the structural characteristics of facilities and the quality of processes involved in patient care. For example, in a now-classic study of work-up and treatment procedures in head and neck cancers,[73] the PCS found significantly poorer compliance with its criteria of appropriateness of assessment, treatment, and other aspects of care among patients treated at facilities headed by a part-time, rather than a full-time, radiation oncologist (Figure 12-9, *A*), and at nontraining facilities compared with training facilities (Figure 12-9, *B*).

Impact of Scientific Evidence on the Practice of Radiotherapy. Practice varies most where there is least evidence available. Decision making about the use of RT has been shown to be highly variable in the context of adjuvant RT. This is most evident where the value of RT has not been confirmed in randomized trials. Although many indications for RT are supported by the results of randomized trials, there have been far fewer formal comparative studies of the details of RT prescriptions and techniques. Not surprisingly, technical practice of RT is even more variable than clinical decision making in radiation oncology. Even in situations in which there have been several consistent published reports that appear to indicate that one approach is superior to another, it has been shown that physicians may interpret these data differently and therefore may still vary widely in their treatment recommendations.[74]

There has been much interest in enhancing the practice of medicine through the synthesis and dissemination of scientific knowledge in the form of treatment guidelines. Guidelines are clearly valuable for reference purposes, but it is not clear to what extent they have actually succeeded in modifying practice in the general population. For example, we observed no impact of a provincial guideline promoting shorter fractionation for postlumpectomy RT over and above changes attributable to prior reports of randomized trial evidence supporting this practice.[75] Changes in practice have sometimes been reported after the introduction of treatment guidelines, but it is usually impossible to conclude that the guidelines themselves were responsible for those changes.[76]

The existence of treatment guidelines does not guarantee appropriate clinical decision making. Misclassification of patients may lead to selection of an inappropriate care path or treatment plan. This may be caused by inadequate or inaccurate pretreatment assessment or misinterpretation of the results of an adequate assessment. If QA is directed only at the avoidance of errors in delivery of RT, patients remain at risk of receiving the wrong treatment, albeit flawlessly delivered. Clear specification of eligibility criteria for RT and real-time audit of compliance with those criteria is required to avoid this type of error.

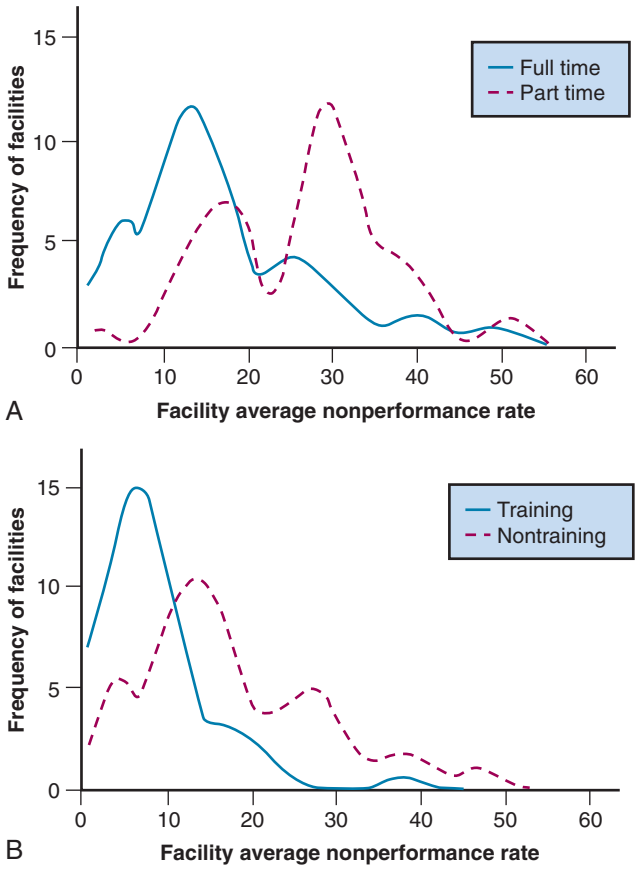

Figure 12-9 Relationships between the structural characteristics of RT programs and quality of practice. **A,** Nonperformance rates for part-time and full-time facilities. **B,** Frequency polygons of nonperformance scores for training and nontraining facilities.
(Adapted from MacLean CJ, Davis LW, Herring DF, et al: Variation in work-up and treatment procedures among types of radiation therapy facilities: the patterns of care process survey for three head and neck sites. Cancer 48:1346–1352, 1981.)

Scientific evidence appears to vary in its impact depending on the practice environment and also on the demographic characteristics of the patients. In 2001, the U.S. Commission on Cancer reported that breast-conserving surgery was still used in less than 50% of U.S. patients with stage 1 and 2 breast cancer and that variations in its use were not consistent with existing practice guidelines.[77] Breast conservation was more rapidly and completely adopted in urban than in rural areas and there were large geographic variations in its adoption across the United States, with much higher rates in the northeast than elsewhere. Older patients and patients from lower socioeconomic groups were less likely than others to have a partial mastectomy, and those who did were less likely to receive postoperative RT. There is also evidence that the characteristics of physicians and their type of practice influence the extent to which they rely on guidelines or other published information in reaching treatment decisions. Reliance on published information in decision making is greater in academic centers and decreases the longer the physician has been in practice.[78] Local policies may affect practice more than national guidelines. A study from the United Kingdom, for example, showed that much of the variation in the use of postoperative RT for breast cancer was attributable to variations in the local management protocols of surgical units.[79]

Impact of Physicians' Beliefs on the Practice of Radiotherapy. There is abundant evidence that physicians' beliefs

about appropriate treatment are shaped by factors other than universal knowledge. Physicians' views about the indications for RT are strongly influenced by their training and experience. Because the key decisions about referral are usually made by surgeons, the views of the surgical community are a major determinant of the role that RT plays in cancer care at the population level. It has repeatedly been shown that surgeons are less likely to recommend RT than radiation oncologists, particularly when a choice has to be made between primary RT and primary surgery. For example, in comparison to radiation oncologists, urologists are less likely to recommend primary RT for prostate cancer,[80] and otolaryngologists are less likely to recommend RT for laryngeal cancer.[81] Medical oncologists today have acquired a significant role in initiating referrals to radiation oncology, but their views about the indications for RT also differ significantly from ours.[74]

Impact of Financial Incentives and Disincentives on the Practice of Radiotherapy. There is evidence that funding mechanisms may affect case selection for RT. For example, a study based on administrative claims data from Pennsylvania showed that the patient's health insurance status was associated with the chance of receiving RT following partial mastectomy. Postoperative RT was given in only 45% of patients with Medicaid compared with greater than 75% of patients with private insurance and Medicare and similar observations have been made elsewhere.[82] Funding arrangements have also been shown to influence choices of fractionation in some studies. Lievens has explored the effects of funding on patterns of palliative RT in Belgium.[83] She found that fractionated courses of RT were prescribed more frequently than single treatments for bone metastases, at least in part because the funding mechanism in place at that time penalized the use of single fractions. In 2001, a new mechanism of funding of palliative RT was introduced in Belgium, which removed the disincentive to single treatments. Since that time, there has been a trend to reduce the number of fractions prescribed in all except 3 of the 23 centers that responded to her most recent survey. Many of those centers reported that the change in the fee schedule was a significant factor in their decision to change practice.[83] Lievens et al have also shown significant associations between funding models and the practice of palliative RT in an international survey of RT centers across Europe. They found that centers funded by a global budget or per-case payment used a significantly lower number of fractions per course and were less likely to use shielding blocks than were centers funded by fee-for-service. The growing evidence that funding may shape the way that RT is practiced suggests that it may be possible to improve practice by appropriately manipulating reimbursement systems. However, there is also a high risk that poorly designed fee schedules may compromise quality of care.[84] It has also been pointed out that, under per-case funding arrangements, profits may be inversely related to quality, making it important to set clear baseline quality standards.[85]

Role of Quality Indicators in the Practice of Radiotherapy

Assessment of quality of care allows healthcare providers to examine their clinical performance against established standards of care, allows payers to assess the quality of care they are purchasing, and is an increasingly important area of HSR.[86] As described previously, the general framework (see Figure 12-1) for a program of HSR describes how quality indicators may be used to assess quality of care and to improve health system performance. Quality indicators may be selected, defined, validated, and applied to target observed variations in practice by evaluating actual practice against targeted performance and to conduct explanatory studies aimed at identifying factors that are associated with better or worse performance.

Quality indicators specific to radiation oncology have been developed across the framework of structure, process, and outcome domains of quality of care and across a spectrum of clinical settings.[86-88] A recent comprehensive review by Albert and Das summarizes the current scope of quality indicator development and application in radiation oncology.[89]

The setting of radiation utilized in the curative management of prostate cancer can be used to illustrate these general principles of quality measurement. Prostate cancer has a high incidence and is commonly managed with either external-beam radiotherapy or brachytherapy as definitive treatment. The RT is highly technical, and continuous advances in technology require consideration in the definition and application of quality indicators in this setting.[88] In Canada, RT is delivered exclusively in 37 publicly funded cancer centers across the country, staffed by approximately 400 radiation oncologists. A Canadian HSR team undertook a modified Delphi process to identify existing candidate quality indicators for measuring the quality of technical medical care and to develop consensus on a suite of quality indicators based on best available evidence.[88] This process identified a suite of 25 quality indicators covering all aspects of prostate cancer radical RT management: pretreatment assessment, external beam RT, brachytherapy, androgen deprivation therapy, and follow-up.

These selected quality indicators were then used as criteria in an audit of patterns of practice, and to develop benchmarks of performance in highest-performing centers.[90] Thirty-two of 37 RT centers (84%) participated, providing 810 cases in total. Analysis of these cases revealed that compliance with 12 pretreatment assessment indicators varied considerably across indicators: from 56% (sexual function documented) to 96% (staging bone scan obtained in high-risk patients). For cases treated with external-beam radiotherapy (EBRT), 100% of EBRT cases were treated using three-dimensional conformal radiotherapy (3DCRT) or intensity-modulated radiotherapy (IMRT) techniques with computed tomography (CT) or magnetic resonance imaging (MRI) planning, whereas 81% of planned cases recorded dose-volume histograms for planning target, rectum, and bladder volumes. For patients treated with conventional fractionation, the dose to the prostate was >70 Gy in 100% of low-risk patients, was >70 Gy in 92% of high-risk cases, but was >74 Gy in only 78% of intermediate-risk patients treated without androgen ablative therapy (ADT). ADT therapy was used in 92% of high-risk cases. Figure 12-10 illustrates that centers varied with regard to how many indicators they were fully compliant on; no center was fully compliant on fewer than 4 of 16 indicators, and no center was fully compliant on all indicators.[90] Given that each quality indicator was selected as representing a minimum standard of care,[88] these data suggest room for improvement in quality of care, particularly for indicators such as dose, in which variation can affect cancer outcome.

Studies of Outcomes in Radiotherapy Programs

It is important to appreciate that although outcomes may seem to be the ultimate measure of quality, one cannot fine-tune the operation of a cancer program by measuring the long-term outcomes by which we usually judge the success of cancer treatment. It may take a decade to measure the 5-year recurrence-free rates associated with a particular pattern of practice. Any feedback from audit of outcome comes far too slowly to permit optimization of the program performance. Quality improvement programs in oncology largely have to operate on the principle that if you get the structure and the process right, the outcomes will look after themselves. That being said, there is some value in measuring outcomes and the opportunity to do this should not be overlooked.

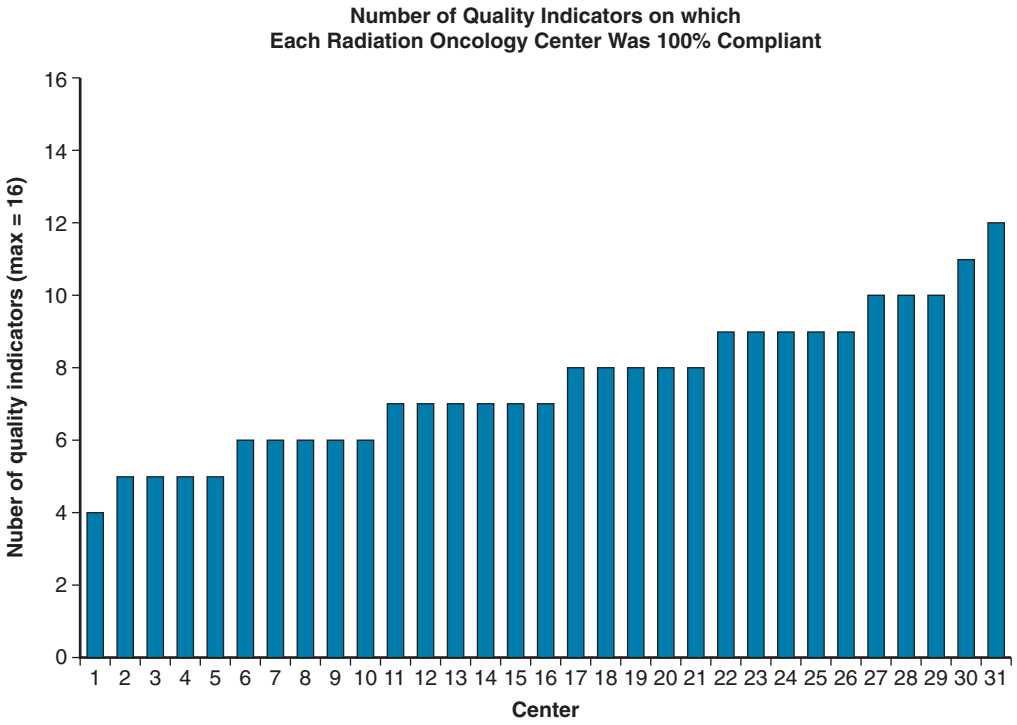

Figure 12-10 Center performance on a suite of 16 quality indicators across Canadian radiotherapy centers. The graph shows the number of indicators on which all cases sampled from that center met the specific quality indicator (demonstrating 100% compliance on that indicator). *(Data taken from Brundage et al: Radiother Oncol, 107:339–345, 2013.)*

Surprisingly, it may be easier to measure outcomes than processes in the general population. Accurate information about vital status is usually available in cancer registries, and it may be quite straightforward to measure survival at the population level. Hospital records and billing files may provide information about subsequent surgical procedures that can sometimes provide surrogate measures of local control by RT. For example, survival without subsequent laryngectomy has been used as a surrogate for local control in measuring the success of radical RT for laryngeal cancer, and survival without subsequent cystectomy has been used as a surrogate for local control after radical RT for bladder cancer (Figure 12-11). The high statistical power of population-based studies also makes it possible to detect and quantify rare but serious late effects that it might be impossible to detect based on the analysis of experience of any individual institution.[91]

Large variations in outcome have been observed among different countries and among different regions, demographic groups, and institutions within the same country. The challenge lies in distinguishing the component of variation in outcome attributable to differences in quality from the inevitable variations in outcome due to differences in case mix.

International variations in cancer outcomes are inevitably multifactorial in origin, and it is difficult to attribute them to any individual aspect of health system performance. Nonetheless, such comparisons have proved to be useful.[92,93] Figure 12-12 shows international variations in cancer survival as a function of proportion of gross domestic product spent on health care. It demonstrates a remarkably clear relationship between investment in health care and cancer survival. It is impossible to determine whether the worse outcome observed in countries that spent less on health care was the result of more advanced stage of disease at diagnosis, higher levels of comorbidity, poorer access to care, or poorer quality of care. However, despite these uncertainties the message is clear that you get what you pay for. These results had a direct influence on public policy in the United Kingdom and were used to justify an expansion in the budget of the National Health Service's cancer programs by almost $1 billion, permitting a massive expansion in the equipment and staffing of its radiation oncology programs.

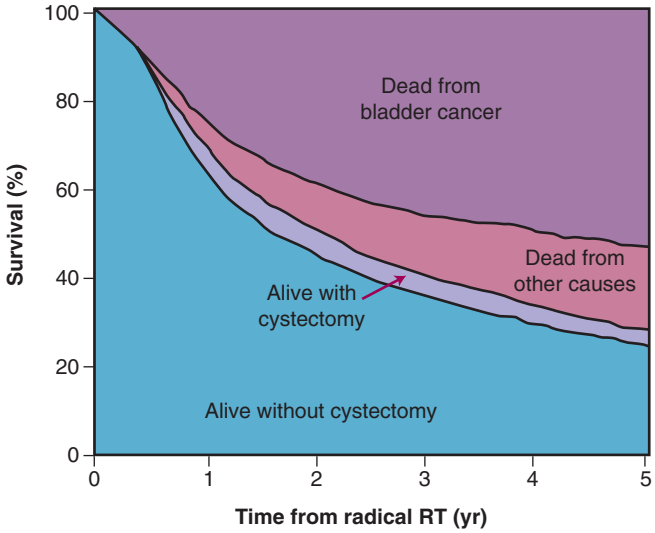

Figure 12-11 Outcome of radical RT for bladder cancer in Ontario. The graph illustrates the results of a population-based study of the outcome of radical RT for bladder cancer in Ontario. The curves show the probability of survival and cystectomy-free survival in 1370 patients who received radical RT for bladder cancer between 1982 and 1994. Deaths from cancer are differentiated from deaths from other causes. *(Adapted from Hayter CRR, Paszat LF, Groome PA, et al: A population-based study of the use and outcome of radical radiotherapy for invasive bladder cancer. Int J Radiat Oncol Biol Phys 45:1239–1245, 1999.)*

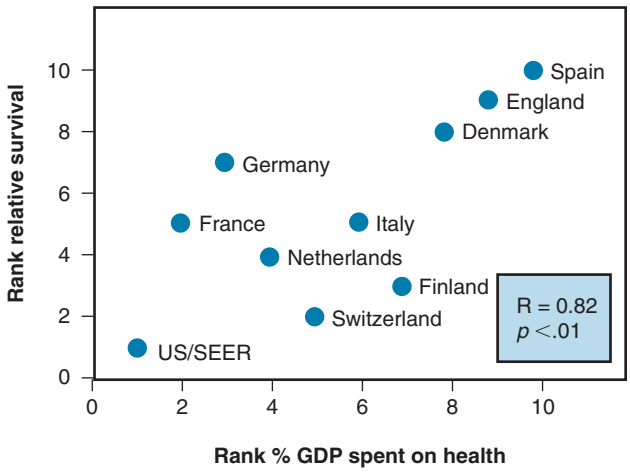

Figure 12-12 Correlation between relative survival and expenditure on health care. The scatter plot shows the relationship between relative survival for all cancer in female patients and the percentage of gross domestic product (GDP) spent on health care in 10 developed countries. *(Adapted from Evans BT, Pritchard C: Cancer survival rates and GDP expenditure on health: A comparison of England and Wales and the USA, Denmark, Netherlands, Finland, France, Germany, Italy, Spain, and Switzerland in the 1990s. Public Health 114:336–339, 2000.)*

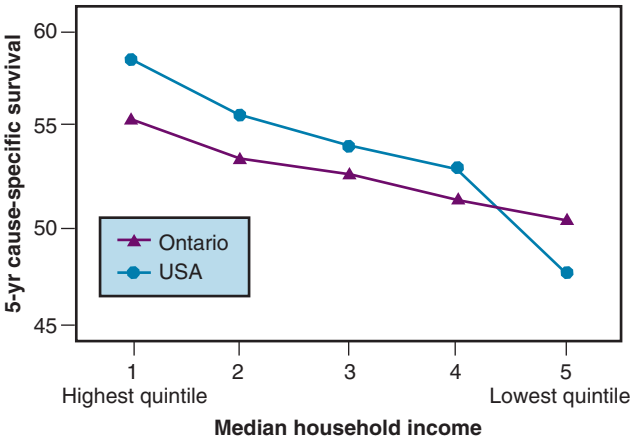

Figure 12-13 Associations between socioeconomic status (SES) and cancer survival in the United States and Canada. The graph shows 5-year, cause-specific cancer survival as a function of SES for all cancers combined (excluding prostate) in the Canadian province of Ontario and in the regions of the United States covered by the Surveillance, Epidemiology, and End Results (SEER) cancer registries. *(Data from Boyd CJ, Zhang-Salomons J, Groome PA, et al: Associations between community income and cancer survival in Ontario and the United States. J Clin Oncol 17:2244–2255, 1999.)*

It has also been shown that cancer outcomes are worse in residents of poorer communities than in residents of richer communities within the same country.[92] Figure 12-13 shows variations in 5-year survival among patients from richer and poorer communities in Canada and the United States. There is a clear gradient in survival across socioeconomic strata in both countries. Some, but not all, of the observed variation is the result of more advanced stage at diagnosis among the poorer groups, probably reflecting differences in access to care.[92] Differences in quality of care may be responsible for some of the observed differences in survival not explained by differences in stage mix. These differences in outcome represent potential opportunities for improving overall outcomes at the population level.

Before we can develop strategies for reducing these disparities, further studies are needed to explore their causes. Although the socioeconomic status–survival gradient is steeper in the United States, there is still a significant difference in outcome among residents of richer and poorer communities in Canada. This may seem somewhat surprising because Ontario has a single-payer, universal healthcare system with no parallel private healthcare sector, and in theory the rich do not have better access to care or quality of care than the poor. Clearly, however, the removal of financial barriers to access to care does not in itself abolish differences in outcome between rich and poor.[92]

Interregional comparisons within the same country may also be informative. When dissimilar populations are compared, it is necessary to control for differences in case mix, but in the absence of any major interregional variations in socioeconomic status, systematic variations in case mix are unlikely. Under these circumstances, variations in outcome, which exceed those expected because of chance alone, may reasonably be attributed to variations in access or quality. Figure 12-14 shows the observed 5-year survival for several major cancer sites in eight different regions of Ontario. Once the observed variations are reduced to take account of the expected variation because of chance alone, the best observed outcomes may be used as a benchmark for the achievable outcome. Figure 12-14 shows that, after adjusting for variation because of chance alone, there were no residual geographic variations in the outcome of cancers of the pancreas, colon, or cervix, but there remained important geographic variations of survival for head and neck cancers, Hodgkin disease, and testicular cancer. Table 12-2 shows the observed 5-year survival for the province as a whole compared with the estimated achievable survival for several diseases in which geographic variation in outcome exceeded that because of chance alone. Although such studies can demonstrate the potential to improve outcome by improving quality, they do not reveal where the defects in quality lie. Further studies are required to identify specific defects in the underlying processes and structures.

Relating Structure and Process to Outcomes

Whether you begin with variations in outcome and work back to try to find their causes or begin with variations in process and work forward to try to identify their consequences, there are significant problems that must be addressed before a causal relationship between process and outcome can be established. We will discuss these problems and describe how they should be addressed in the context of outcomes research.

Limitations of "Outcomes Research"

Studies that examine treatment and outcome in the context of routine care are often today referred as "outcomes research." This type of study should *not* generally be used to try to evaluate the efficacy of treatment. It is notoriously difficult to control for bias in retrospective reviews of institutional experience.[94] Comparisons of outcomes achieved in contemporaneous groups of patients who have received different types of treatment at the same institution are inevitably confounded by "treatment selection bias." Comparisons of outcomes between groups of patients who received different treatments more or less contemporaneously at different institutions are less subject to treatment selection bias but are vulnerable to "referral bias" resulting from interinstitutional differences in case mix.[94,95] The use of "historical controls" (i.e., the comparison of outcomes between patient groups who have received different treatment at different points in time) is also fraught with hazard.[96] Case mix may change systematically over time; investigations may change, resulting in "stage migration"; and collateral aspects of care may also change. It is possible to

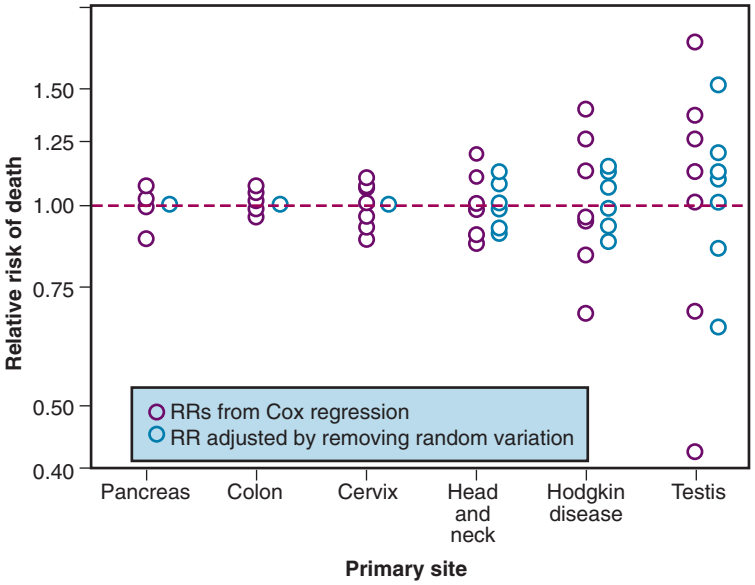

Figure 12-14 Interregional variations in cancer survival in Ontario. The scatter plot shows the relative risk of death from cancer in seven geographic regions of Ontario derived from a Cox regression that controlled for age, sex, and socioeconomic status. The *purple circles* represent the observed variations in survival. The *blue circles* represent the remaining variation after subtraction of the expected random component of variation. *(Adapted from Zhang-Salomons J, Groome PA, Mackillop WJ: Estimating the best achievable cancer survival by eliminating regional variations in Ontario. Clin Invest Med 363[Suppl 22], 1999.)*

TABLE 12-2 Observed versus Achievable 5-Year Survival for Selected Cancer Sites in Ontario*

Primary Site	Achievable 5-Year Survival Rate (95% Confidence Interval)	Observed 5-Year Survival Rate (95% Confidence Interval)	
		All Ontario	Worst Region
Head and neck	64% (63-65)	60% (59-61)	54% (49-59)
Hodgkin disease	88% (86-90)	86% (84-87)	81% (73-89)
Testis	97% (97-98)	95% (94-96)	92% (89-95)
Central nervous system	32% (31-34)	28% (27-29)	27% (24-30)
Rectum	52% (51-54)	50% (49-51)	48% (45-51)
Stomach	21% (20-22)	20% (19-21)	15% (12-17)
Lung	18% (18-19)	15% (15-16)	12% (11-13)
Ovary	49% (47-51)	46% (44-47)	40% (33-48)
Prostate	77% (76-77)	75% (74-75)	71% (69-72)
Bladder	74% (72-75)	73% (72-74)	68% (65-71)

**The best achievable survival was estimated from the highest observed survival in any of the seven regions in Ontario, by subtracting deviations from the provincial average that are expected, as a result of random variation. Cox regression was used to control for age, sex, and socioeconomic status. This model assumes that there are no systematic variations in case mix among the regions.*

reduce the impact of these types of bias by controlling for known prognostic factors, but these usually leave much of the variance in outcome unaccounted for. For these reasons, none of these types of retrospective, observational studies can substitute for prospective, experimental studies (i.e., randomized controlled trials) in the evaluation of efficacy of treatment. The credibility of our discipline is weakened to the extent that we rely on these less valid methods in situations in which a randomized trial is possible.

Legitimate Roles of "Outcomes Research" in Evaluating Effectiveness

It is important to recognize that there are some aspects of medical practice that cannot be evaluated in randomized trials and must be explored using observational methods.

There are some important aspects of treatment that cannot and should not be studied in a randomized trial. It may be important, for example, to know how much outcomes are affected by deviation from standard practice, such as by delay in initiation of RT, protraction of overall treatment time, the use of lower-than standard doses, or reliance on antiquated equipment. However, one cannot ethically randomize patients to receive nonstandard versus standard treatment when the only real purpose of the exercise is to measure the adverse consequences of the nonstandard approach. We can therefore only learn about this type of issue by investigating the impact of inadvertent or unavoidable deviations from standard practice in retrospective, observational studies of the type discussed previously.[25,26]

It is important to be cautious in the interpretation of "negative findings" in studies that attempt to explore the consequences of deviations from standard practice. Studies that fail to show a statistically significant difference in outcome between nonstandard and standard treatments often lack the statistical power that would be necessary to rule out small but clinically important adverse effects. When patient safety is on the table, the absence of evidence of adverse effects should never be misconstrued as evidence of their absence.

When a Randomized Trial Is Not Feasible. Some issues should ideally be addressed in a randomized trial, but either cannot, or will not, be addressed in this way. Rare clinical problems are often impossible to study in randomized trials because it is difficult to sustain enthusiasm for any trial or maintain the infrastructure necessary to support it over

a protracted period of slow accrual. Large well-organized, multicenter clinical trial groups have a greater chance of success in this situation than any individual institution, but there are limits to what any group can do. Nearly all of what we know about the relationship between treatment and outcome in rare situations has to come from observational studies. In other situations, a clinical trial may be theoretically feasible but is rendered impossible by entrenched opposing views about treatment that effectively preclude recruitment to any trial. One such example was the controversy regarding the primary management of more advanced cancers of the larynx. The issue was hotly debated for decades and opinions were highly polarized. The depth of the controversy is clearly illustrated in the results of an international mail survey of patterns of care in laryngeal cancer done in the early 1990s.[81] This showed, for example, that most otolaryngologists in Canada, the United Kingdom, and Scandinavia regarded primary RT, reserving surgery for salvage, as the standard approach for T3 glottic cancer, whereas most of their counterparts in the United States and Australia favored primary laryngectomy.

Under these circumstances, it may be possible to learn about the relative effectiveness of the competing approaches by comparing the outcome they achieve at the population level. The rationale for this approach is that variations in practice driven by differences in physicians' beliefs, or any other factors unrelated to the characteristics of the patients, can be treated as a natural experiment. For example, Groome et al performed a study comparing the outcomes of treatment for locally advanced laryngeal cancer between Ontario, Canada, and the United States. They found that primary laryngectomy was used much more frequently in the United States than in Ontario,[97] consistent with the results of the previous mail survey.[81] Survival at 5 years proved to be identical in the two populations, whereas laryngectomy-free survival was significantly higher in Ontario than in the United States. These observations lend support to the position that primary RT, reserving surgery for salvage, permits retention of natural voice without compromising survival.

Evaluating the Adoption and Generalizability of the Results of Clinical Trials. Randomized clinical trials are unquestionably the best way of comparing the efficacy of a new treatment with the previous standard treatment. However, clinical trials rarely involved more than a small fraction of potentially eligible cases. Therefore, it cannot be taken for granted that the benefits observed in the context of the trial will be reproduced when the treatment is adopted in the general population. It has therefore been argued that population-based "phase IV" studies should be carried out as new treatments are introduced into routine practice to evaluate their effectiveness in the real world.[98,99] Box 12-3 describes some of the unique advantages of phase IV studies.

Many phase IV studies have used temporal changes in practice to evaluate the effectiveness of RT. For example, Pearcey et al studied the impact of the rapid adoption of concurrent cisplatin-based chemoradiotherapy (C-CRT) in 1999 on population-based outcomes of cervical cancer in Ontario.[99] Use of C-CRT increased from <10% of RT cases diagnosed from 1992 to 1998 to >60% in those from 1999 to 2001. There was no observable change in survival for the subgroup of patients treated with surgery alone. Among those treated with primary RT with or without chemotherapy, survival significantly increased from 58.6% in 1995 to 1998 to 69.8% in 1999 to 2001 ($p < 0.01$). The magnitude of change in survival was in keeping with randomized trials. These findings supported the population-based effectiveness of C-CRT for cervical cancer.

An important assumption of a phase IV study is the comparability of treatment groups. This may often be assured through ecological comparisons such as in Pearcey et al's study of C-CRT for cervical cancer.[99] Over modest time periods, the spectrum of cases in the population usually does not change sufficiently to threaten study validity. This stability is not always the case, however, as demonstrated by Gupta et al's study of the impact of C-CRT on head and neck cancer population outcomes in Ontario,[100] which showed an increase in survival from 43.6% in the preadoption cohort to 51.8% in the postadoption cohort. However, the survival increase for oropharynx cancer was greater than predicted based on randomized trials of C-CRT (38.8% preadoption and 57% postadoption). The observed findings were in keeping with known increases in incidence of the prognostically favorable oropharyngeal cancer associated with human papillomavirus (HPV) over the study period. Notably, the survival increase for all other head and neck sites combined was in keeping with randomized trials (45.6% preadoption and 48.3% postadoption).

Phase IV studies provide information on treatment adoption and its consequences that is not available through any other means. For example, in the study of adoption of C-CRT for head and neck cancers, it was possible to study the impact of C-CRT on hospitalization rates in the general population. There was a significant increase in hospitalizations after C-CRT adoption for head and neck cancers (23.4% versus 43.3%), but no increase in treatment-related deaths. Additionally, the adoption of C-CRT was far more gradual for head and neck cancers than for cervical cancer. In both cases, however, when superiority of one treatment over another was demonstrated in randomized trials, practice changed.

In the case of equally effective options, this may not always be the case. Ashworth et al studied fractionation of post-lumpectomy radiation for invasive breast cancer in Ontario before and after the publication of the Ontario Clinical Oncology Group (OCOG) trial that demonstrated equivalence of 16- and 25-fraction schedules.[75] They found that after completion of the OCOG trial, shorter fractionation schedules increased from 48% to 71% of cases, though large intercenter variation existed, including two of nine centers treating the majority of patients with longer schedules.

BOX 12-3 Proposed Roles of Phase IV, Population-Based Outcomes Studies

1. To describe uptake of new therapy.
   - What is the prevalence or incidence of eligible cases?
   - What proportion of eligible patients has received therapy?
   - Are quasi-eligible patients receiving therapy?
   - To what extent is therapy appropriately delivered (i.e., complete versus partial adoption)?
2. To evaluate the association among a change in practice or policy and outcomes.
   - Is there benefit at the population level?
   - Is the magnitude of benefit commensurate with that observed in clinical trials?
   - Are there previously unrecognized (or underrecognized) adverse events?
3. To explore the real-world economic ramifications of a new medical therapy.
4. To provide an empirical process to determine which aspects of the randomized controlled trial design are associated with a minimal efficacy-effectiveness gap.
5. To provide a measure of the societal benefit of medical research.

From Booth CW, Mackillop WJ: Translating New Medical therapies into Society Benefit: The role of population-based outcome studies. [commentary] JAMA *300:2177–2168, 2008.*

There are a number of statistical techniques available to minimize treatment selection bias and confounding in observational studies of effectiveness. These include multivariable model risk adjustment, propensity score methods, stratification, time series analysis, matching, restriction, and instrumental variable analysis. A full discussion of the relative merits of these techniques is beyond the scope of this chapter. As a general rule, validity is strengthened when multiple techniques produce comparable results.

STUDYING THE EFFICIENCY OF RADIOTHERAPY

Health economics is the area of specialization within the field of economics that concerns itself with all economic aspects of health and health care. Much of health economics deals with health-related issues on a higher plane than HSR. Macroeconomic analysis of the societal impact of health and health care at the national and international levels lies well beyond the scope of HSR. On the other hand, microeconomic analysis of the costs and benefits of specific healthcare programs lies squarely within the domain of HSR. We briefly describe how health economic analysis fits into HSR, introduce the methods that are commonly used, and illustrate their relevance to radiation oncology.

The resources available for health care in any society are finite. What is achievable for patients with cancer depends on the size of the total healthcare budget, on how much of that total budget is directed to cancer care, and on how efficiently the available resources are used in providing cancer care. Health economics aims to provide the information necessary to make rational choices about how to deploy funding for health care and how to make the best possible use of the funds available. Economic analyses are useful at many levels in the health system. High-level decisions about allocation of resources to different healthcare programs are increasingly based on a comparison of their impact on health in relation to their cost. These decisions are most clearly visible in publicly funded systems, but in the private sector decisions made by insurers about which services will be reimbursed are based on similar considerations and have a similar effect. Information about the benefits of RT in relation to its costs is, therefore, required to ensure that an appropriate slice of the cancer budget is allocated to radiation oncology. Economic analyses are also needed to optimize the internal efficiency of RT programs. To ensure that we get the maximum value per dollar invested in RT, it is important that we should be aware of the relative costs of alternative approaches for providing RT.

Health economics involves much more than the measurement of healthcare costs, which most economists would regard as no more than accounting. However, economic analysis does require the measurement of costs, and a number of useful studies have been done in comparing alternative approaches for measuring the cost of RT,[101] and in defining units of workload to which costs can be assigned.[102] In assessing the overall costs of RT, it is important to consider not only the direct costs of providing treatment but also the indirect costs of supportive care for complications of RT. It is important to specify the perspective from which an economic analysis is carried out. If the analysis is being conducted from the perspective of the RT provider, it may be appropriate to focus primarily on direct costs, whereas if the perspective is that of the health system as a whole, indirect costs incurred in other sectors must also be considered. If the analysis is being conducted from the societal perspective, loss of productivity as a consequence of the treatment needs to be included and balanced against loss of productivity as a result of the untreated disease.

Economic analyses typically consider the benefits of health care as well its costs. Four different types of study are usually distinguished: cost minimization studies, cost-benefit studies, cost-effectiveness studies, and cost-utility studies.

Cost minimization studies, often simply called cost studies, compare the costs of alternative treatments or processes, on the explicit or implicit assumption that each produces similar health outcomes. In RT, this type of study has provided information pertinent to decisions about the acquisition of new equipment,[103] about the decision to purchase or lease equipment,[104] about service contracts,[105] and so on. In some instances, simple cost comparisons have been done between slightly different approaches to treatment, such as high-dose rate versus low-dose rate brachytherapy.[106]

In cost-benefit analysis, the health benefits of treatment are described only in terms of their dollar value; health outcomes are considered only insofar as they have an impact on costs or affect the productivity of those affected. This type of analysis may be useful in some circumstances in demonstrating to policy makers that apparently expensive programs of treatment or prevention may in fact be cost neutral or even save money when the overall financial consequences of providing the program are compared to those of not providing it. However, the idea that the benefits of health care can be adequately described in terms of the money they save is counterintuitive to most clinicians, and this type of analysis has not been widely used in the field of radiation oncology.

Cost-effectiveness studies compare alternative treatments or processes with respect to their effectiveness, as well as their cost. Effectiveness is usually described in terms of a single objective outcome measure, such as survival. This is useful in that it enables us to put a dollar value on the outcomes achieved by RT, and it has often revealed that RT is relatively inexpensive in relation to the benefits it delivers.[107,108]

Because cost-effectiveness analysis describes the benefits of treatment in terms of a single measure of outcome, it does not provide a satisfactory way of describing and comparing the value of treatments that are associated with different types of health benefit, such as radical RT for cervical cancer and palliative RT for bone metastases. Survival alone is an inadequate measure of palliative RT, and quality of life is an inadequate measure of the effectiveness of curative treatment. The concept of utility, a measure of the relative value of different life states, is useful in reducing the benefits of treatment to a common currency. If utility can be measured, and there is still some question as to whether this is really possible, years of survival can be adjusted for relative value and outcomes expressed as quality-adjusted years of life (QALYs). This measure is sensitive to both duration of survival and quality of life. Cost per QALY can be used to compare the value of treatment in curative and palliative contexts. The value of other forms of medical care has been measured in cost per QALY, and this permits comparison of the value of RT with the value of other treatments both in oncology and in other spheres of medicine.[109,110]

Information about the relative benefits of RT in different clinical contexts could be used as a basis for assigning priorities to one type of case over another in circumstances in which resources are insufficient to provide RT for everyone who needs it. This type of explicit rationing has not, to our knowledge, been used to control access to RT in any of the countries where access to RT is constrained by inadequate supply. Although this approach would serve to mitigate the adverse effects of inadequate access to RT and maximize the societal benefits of the available resources, it seems to have little appeal to policy makers. It has, however, been proposed that cost-effectiveness or cost-utility analysis be used as the basis for selecting the most effective components of care for inclusion

in healthcare programs. In the future, as both the demand for health services and the cost of care continue to increase across the developed world, we anticipate that decisions about which services will be provided within publicly funded systems or managed care programs will increasingly be based on these types of economic analysis. Research in the economics of radiation oncology is likely to be of increasing practical importance in optimizing the effectiveness of RT programs in the future.

SUMMARY

In the past, radiation oncologists and their traditional partners in physics and radiobiology have devoted most research efforts to creating the knowledge necessary to optimize the outcomes of RT in the individual patient. There is a lot of evidence to suggest that we currently fall far short of making the benefits of that research available to all the patients who might benefit from it. It has been demonstrated that in many parts of the world, access to RT is both inadequate and inequitable and that the quality of RT is variable and often suboptimal. These deviations from optimal practice cause us to fall far short of achieving what is theoretically achievable for patients with cancer today within the limits of existing scientific knowledge and technology. Deviations from optimal practice represent real opportunities for enhancing the results of RT, without placing reliance on the uncertain outcome of the slow process of basic research, which frequently promises much but delivers little. Although fundamental and clinical research must continue, a greater proportion of our efforts should be devoted to enhancing our understanding of the factors that influence access to RT and determine the effectiveness and efficiency of RT programs. RT provides major health benefits for a large proportion of patients with cancer, and even a small incremental gain in health system performance would be expected to translate itself into large societal benefits.

HSR in radiation oncology is still a relatively new field, and it offers new investigators a great opportunity to make a real difference. There are a number of good opportunities for training in health services and policy research, and the funding for HSR has greatly increased in recent years. There is real need for radiation oncologists to become involved in leadership roles in HSR because the clinician's insights are vital in choosing the right research questions. Getting the right answers, however, may require a high level of methodologic expertise in areas that are unfamiliar to most radiation oncologists. Success in HSR often depends on building effective collaborations with scientists in other fields such as epidemiology, health economics, and the social sciences. Those who enter the field should also be aware that getting the most out of HSR requires a degree of diplomacy and academic ability. Clinicians involved in HSR need to remember that in the pursuit of the goal of evidence-based management of healthcare programs, they need to influence health system managers as well as their peers. Investigators need to learn the skill of working collaboratively with the health system managers and policy makers who hold the power to implement some of the changes necessary to optimize outcomes, while keeping some control of the research agenda.

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