Int. J. Radiation Oncology Biol. Phys., Vol. 49, No. 4, pp. 973–985, 2001

0360-3016/01/$–see front matter

PII S0360-3016(00)01401-2

CLINICAL INVESTIGATION **Lung**

ESTIMATING THE NEED FOR RADIOTHERAPY FOR LUNG CANCER: AN EVIDENCE-BASED, EPIDEMIOLOGIC APPROACH

SCOTT TYLDESLEY, M.D., F.R.C.P.C.,*†‡ CHRIS BOYD, M.SC.,* KARLEEN SCHULZE, M.MATH.,* HUGH WALKER, PH.D.,*§ AND WILLIAM J. MACKILLOP, M.B., CH.B., F.R.C.P.C.*†‡§

*Radiation Oncology Research Unit, §Departments of Oncology, and Community Health and Epidemiology, Queen's University, †Kingston Regional Cancer Centre, and ‡Kingston General Hospital, Kingston, Ontario, Canada

Background and Objectives: Current estimates of the proportion of cancer patients who will require radiotherapy (RT) are based almost entirely on expert opinion. The objective of this study was to use an evidence-based approach to estimate the proportion of incident cases of lung cancer that will require RT at any point in the evolution of the illness.

Methods: A systematic review of the literature was undertaken to identify indications for RT for lung cancer, and to ascertain the level of evidence that supported each indication. An epidemiologic approach was then used to estimate the incidence of each indication for RT in a typical North American population of lung cancer patients. The effect of sampling error on the estimated appropriate rate of RT was calculated mathematically, and the effect of systematic error, was estimated by sensitivity analysis.

Results: It was shown that 53.6% ± 3.3% of small-cell lung cancer (SCLC) cases develop one or more indications for RT at some point in the course of the illness, 45.4% ± 4.3% in their initial treatment, and 8.2% ± 1.5% later for recurrence of progression. Overall, 64.3% ± 4.7% of non–small-cell lung cancer (NSCLC) cases require RT, 45.9% ± 4.3% in their initial treatment, and 18.3% ± 1.8% later in the course of the illness. The proportion of NSCLC cases that ever require RT is stage dependent; 41.0% ± 5.5% in Stage I; 54.5% ± 6.5% in Stage II; 83.5% ± 10.6% in Stage III; and 65.7% ± 7.6% in Stage IV. In total, 61.0% ± 3.9% of all patients with lung cancer will develop one or more indications for RT at some point in the illness, 44.6% ± 3.6% in their initial treatment, and 16.5% ± 1.5% later for recurrence or progression.

Conclusion: This method provides a rational starting point for the long-term planning of radiation services, and for the audit of access to RT at the population level. We now plan to extend this study to the other major cancer sites to enable us to estimate the appropriate RT treatment rate for the cancer population as a whole. © 2001 Elsevier Science Inc.

Radiotherapy, Needs assessment, Lung cancer, Treatment guidelines.

INTRODUCTION

The delivery of radiotherapy (RT) requires specialized personnel, equipment, and facilities. It takes a long time to commission new facilities and train the staff to operate them. RT systems, therefore, require careful, long-term planning. An estimate of the number of patients that will need treatment should be the starting point for this planning process. The future incidence of cancer can usually be projected with considerable accuracy. The challenge is to establish what proportion of incident cases will require RT. That depends on the indications for RT that are accepted by the community, and on the proportion of incident cases in the community that will develop one or more of these indications. It has been estimated that 50–60% of incident cancer cases will require RT at some point in the evolution of the illness (1–6). However, these estimates rely heavily on expert opinion and the assumptions on which they are based are not explicitly stated.

Observed RT utilization rates vary widely. Very protracted follow-up is necessary to estimate the proportion of incident cases that receive RT at any point in their lives, and this has rarely been done at the population level (7). How-

Reprint requests to: Dr. W. J. Mackillop, Kingston General Hospital, Radiation Oncology Research Unit, Apps Level 4, 76 Stuart Street Kingston, Ontario, Canada K7L, 2V7. E-mail: william.mackillop@cancercare.on.ca

Dr. Tyldesley was a Health Policy Research Fellow at the Radiation Oncology Research Unit at Queen's University. He is now a Staff Radiation Oncologist at the Vancouver Cancer Clinic.

Preliminary results of this work were presented at the Annual Meetings of the Canadian Association of Radiation Oncologists, in 1998 and 1999.

Supported in part by grants from the National Cancer Institute of Canada, with funding from the Canadian Cancer Society and Cancer Care Ontario (W.J.M.). Fellowship support for S. Tyldesley was provided by the Terry Fox Fellowship Fund of the National Cancer Institute of Canada, and the Shane Fellowship from the Order of the Eastern Star.

Accepted for publication 22 August 2000.

ever, the proportion of incident cases that receive RT as part of their initial management has been measured in several countries and reported rates range from about 20% to over 50% (7–10). RT utilization rates also vary significantly within countries; in both Sweden and Australia, rates are known to be higher in urban, than in rural areas (9, 10). In Ontario, Canada, we have shown that the proportion of incident cases receiving RT varies widely from one county to the next, with the highest rates being reported in the counties where the provincial RT centers are located (7). We suspect that the low rates observed in some areas reflect inadequate access to care, but it remains possible that the higher rates observed in other areas represent overutilization, and that the lower rates might be appropriate. It is also possible that the inter-regional variations in rates may be an appropriate response to variations in case mix (7). Thus, without a means of calculating appropriate RT rates, it is all but impossible to interpret variations in RT utilization.

We have developed an evidence-based process for determining the appropriate rate of use of RT in a given population. Our approach is straightforward: we first define the indications for RT based on a systematic review of the literature; we then estimate the incidence of each indication in the population of interest, and sum them to determine the total number of cases that should receive RT. The resources required to treat each indication may then be factored into the model. The term "Epidemiologically Based Needs Assessment" has been used to describe this approach, which has been used previously in other contexts, but not in the field of RT (11, 12). Our goal is to create a comprehensive model for estimating the RT requirements of any population. We are proceeding step-wise, beginning with the most common malignant diseases. This report illustrates the method as applied to lung cancer.

We included in our analysis all the indications for RT for lung cancer that are described in current North American clinical practice guidelines. However, we recognize that some of these are accepted universally, whereas others are not. The model is, therefore, structured in such a way that it can be modified to fit with any specific guidelines that may have been adopted in a particular community. The information about case mix that is used to estimate the need for RT, should ideally be provided by contemporaneous observations in the population of interest. In practice, however, a lot of the necessary information may prove to be unavailable. In this study, we have aimed to define the appropriate rate of use of RT for lung cancer in a "typical" North American population. We have, therefore, relied mainly on data from American and Canadian cancer registries, although where necessary, we have borrowed information from other developed countries. The model is structured in such a way that readers may substitute descriptors of case mix that are more specific to their own community, where this information is available.

Table 1. Levels of evidence supporting indications* for radiotherapy

I	Large randomized trials with clear-cut results (and low risk of error)
II	Small randomized trials with uncertain results (and moderate to high risk of error)
III	Nonrandomized contemporaneous controls
IV	Nonrandomized, historic controls
V	No controls, case-series only

*Sackett's criteria (Ref. 23).

METHODS AND MATERIALS

Identifying indications for radiotherapy

Borrowing the definition provided in the American Heritage Dictionary, we define an indication for RT as a set of clinical parameters that suggest that RT is necessary, expedient, or advisable (13). We first searched for guidelines and recommendations for the use of RT for lung cancer in textbooks, on Medline, and on the internet. Secondary searches were done to follow up on additional references identified in the primary searches. The sources we most frequently used included the following: The American Society of Clinical Oncology Clinical Practice Guidelines (14); the National Comprehensive Cancer Network Clinical Practice Guidelines (15, 16); American College of Radiology's Appropriateness Criteria (17); the National Cancer Institute's Physician Data Query Treatment Options (18); the British Columbia Cancer Agency's Cancer Management Manual (19); Cancer Care Ontario Clinical Practice Guidelines (20); the UK Royal College of Radiology's Clinical Oncology Information Network Guidelines (21); and the Scottish Intercollegiate Guidelines Network's National Clinical Guidelines (22). The level of evidence that supported each guideline was classified using Sacket's System, which is shown in Table 1 (23).

Describing indications for radiotherapy

The variables used to define specific indications included: histology; clinical stage; pathologic stage; status of resection margins; symptoms; performance status; and history of and/or response to other treatment. In some situations, RT was recognized as an option, but its risks and benefits were such that some patients would accept treatment while others would decline. In this situation, which was described by Eddy, as "an option with preferences split" (24), patients' preferences were included in defining the indication for RT. In all other situations, it was assumed that every patient would accept RT if it was recommended.

Estimating the incidence of indications for radiotherapy

Once we had identified the variables that defined each indication, we used this information to construct a tree diagram that segregated the cancer population into patients that had indications for RT, and those that did not. Figure 1 illustrates this approach in an imaginary population of cancer cases. Each terminal branch of the tree

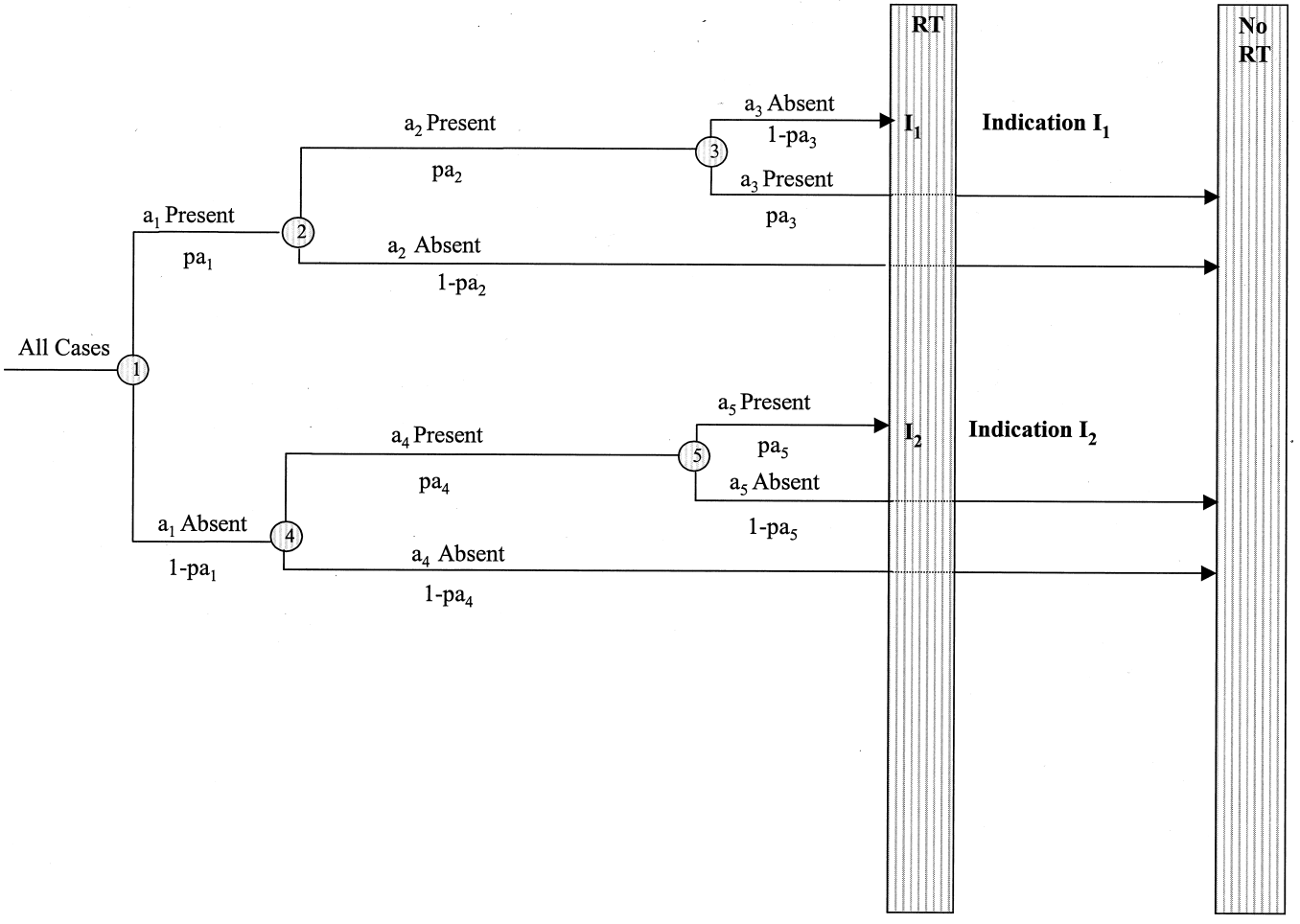

Fig. 1. Estimating the proportion of cases with an indication for RT. Fig. 1 illustrates how a tree diagram was used to estimate the proportion of incident cases with indications for RT. The five branch points in this diagram segregate this imaginary population of cancer cases into six subgroups based on the presence or absence of attributes a_1, a_2, a_3, a_4, and a_5. In this illustration, two of the subgroups represented by the terminal branches of the tree have indications for RT. The first indication, I_1, is defined by the presence of attributes a_1 and a_2, and the absence of attribute a_3. The proportion of this population that has indication I_1 is given by $pI_1 = pa_1.pa_2.(1 - pa_3)$. The second indication, I_2, is defined by the absence of attribute a_1, and by the presence of attributes a_4 and a_5. The proportion of this population that has indication I_2 is given by pI_2, $= (1 - pa_1).pa_4.pa_5$. The proportion of the total population that has any indication for RT is given by $pI_{total} = pI_1 + pI_2$.

represents a group of patients that is sufficiently well characterized that it can be determined whether RT is indicated or not. The proportion of the overall cancer population that ends up in a given terminal branch is the product of the proportions that took the path in that direction at each previous branch point. The branch points 1, 2, 3, 4, and 5 in Fig. 1 segregate the population into subgroups based on the presence or absence of attributes, a_1, a_2, a_3, a_4, and a_5, respectively. The proportion of the total population that exhibits attribute $a_1 = pa_1$, and the proportion of the population that does not exhibit attribute $a_1 = 1 - pa_1$. The proportion of the a_1-positive cases that also exhibit attribute $a_2 = pa_2$, and the proportion that do not exhibit attribute $a_2 = 1 - pa_2$, and so on. In this illustration, two of the terminal branches of the tree correspond to subgroups that have an indication for RT, and the other four terminal branches correspond to subgroups that do not have an indication for RT. The first indication for RT, I_1, is defined by the presence of attributes a_1 and a_2 and by the absence of attribute a_3. The proportion of the total population that has indication I_1 for RT is given by $pI_1 = pa_1 \cdot pa_2 \cdot (1 - pa_3)$. The second indication for RT, I_2, is defined by the absence of attribute a_1, and by the presence of attributes a_4 and a_5. The proportion of the total population that has indication I_2 is given by $pI_2 = (1 - pa_1) \cdot pa_4 \cdot pa_5$. Thus, the proportion of the total population that has any indication for RT, pI_{total}, is given by

$$pI_{total} = pI_1 + pI_2 = [pa_1 \cdot pa_2 \cdot (1 - pa_3)] + [(1 - pa_1).pa_4 \cdot pa_5]$$

pI_{total} represents our estimate of the Appropriate Rate of

Table 2. Classification of the quality of the sources of information used to estimate the prevalence of indications for radiotherapy

Quality of source	Source type
α	Population-based registry
β	Report of a random sample from a population
δ	Comprehensive mult-institutional database
ϕ	Comprehensive single-institutional database
γ	Multi-institutional reports on selected groups of cases (e.g. multi-institutional clinical trials)
μ	Single-institution reports on selected groups of cases (e.g. single-institutional clinical trials or retrospective series)
σ	Expert opinion

Radiotherapy (ARR), in this population of cancer patients. It may also be multiplied by 100 and expressed as a percentage of the total population.

Estimating the incidence of attributes that define indications for radiotherapy

Thus, the complex task of defining the incidence of indications for RT resolves itself into the simpler task of defining the incidence of specific attributes in the cancer population. For many attributes, several different sources of information were available. In estimating the appropriate rate of use of RT in a specific population, it is important that the estimates of the incidence of the indication-defining attributes should be based on observations in the same population or in a similar population. The goal of the present study was to measure the requirement for RT in a "typical" North American population. Several sources of information were often available. The sources that best matched the attributes of the subpopulation of interest were selected. We then used the classification system shown in Table 2 to rank our sources based on how well they represented the population or subpopulation of interest. We assigned the highest value to information from North American population-based cancer registries such as, the Surveillance Epidemiology and End Results registries (SEER) (25), and the Ontario Cancer Registry (OCR) (26), because these were free of the problems of referral and selection bias that may affect other sources. For the same reason, we also gave a high value to sources based on a random sample of the population. Multi-institutional databases such as the National Cancer Data Base (NCDB) (27) were ranked below the population-based sources because, although they contain a great deal of useful information about a large number of cases, they are potentially subject to referral bias. These large databases unfortunately did not provide all the necessary information, and we also relied on a variety of other sources that may have been less representative of the population as a whole. Comprehensive reports of the entire experience of an individual institution were ranked higher than reports of highly selected groups of cases involved in clinical trials because, although both types of source are subject to referral bias, the latter is also subject to treatment selection bias, while the former is not. Where we identified two or more sources of information of equivalent quality based on the criteria in Table 2, we selected the one with the largest sample size for use in the main model.

Estimates of error

Systematic error. At branch points where two or more estimates of proportion of equivalent quality were identified, we used the estimate derived from the largest sample in the main model. However, we used sensitivity analysis to calculate the impact of using the alternative estimates on the Appropriate Radiotherapy Rate; that is, we did separate analyses using the lowest and highest estimates of the proportion of cases expressing the attribute of interest at each such branch point.

Random error. The sampling error associated with each estimate of proportion contributes to the total sampling error in pI_{total}. In the example shown in Fig. 1, where $pI_{total} = pI_1 + pI_2$, the variance in the overall Appropriate Radiotherapy Rate, var pI_{total}, is given by:

$$var\ pI_{total} = var\ pI_1 + var\ pI_2$$

and the standard error of $pI_{total} = \sqrt{\text{var } pI_{total}}$.

The variance associated with pI_1, var pI_1, was estimated using a modified delta calculation (28), as follows: var $(pI_1) = \{[\text{var } (pa_1 \cdot pa_2)] \cdot \text{var } (1 - pa_3)\} + [\text{var } (pa_1 \cdot pa_2) \cdot (1 - pa_3)^2 + [\text{var } (1 - pa_3).(pa_1 \cdot pa_1)^2]$,
where $\text{var}(pa_1 \cdot pa_2) = [\text{var}(pa_1) \cdot \text{var}(pa_2)] + [\text{var}(pa_1) \cdot (pa_2)^2] + [\text{var } (pa_2) \cdot (pa_1)^2]$.

The variance associated with pI_2 is estimated similarly.

In the "Results" section below, we have provided the 95% confidence intervals on the appropriate radiotherapy rate calculated as $\pm$ is 1.96 standard error of pI_{total}.

RESULTS

Indications for radiotherapy for lung cancer

We identified 16 different indications for RT in the initial phase of management of lung cancer, and 8 additional indications for RT for progression or recurrence. Table 3 summarizes these indications, and provides two or more references in support of each. The code letters provided in the first column of Table 3 are used to identify the indications for RT in the tree diagrams that are presented below. Table 3 also indicates the best level of evidence that was available to support each indication, based on the classification described in Table 1 (23).

For ease of presentation, the overall tree diagram that we used to determine the frequency of indications for RT for lung cancer has been broken down into separate components dealing with small-cell lung cancer (SCLC), and with each stage grouping of non–small-cell lung cancer

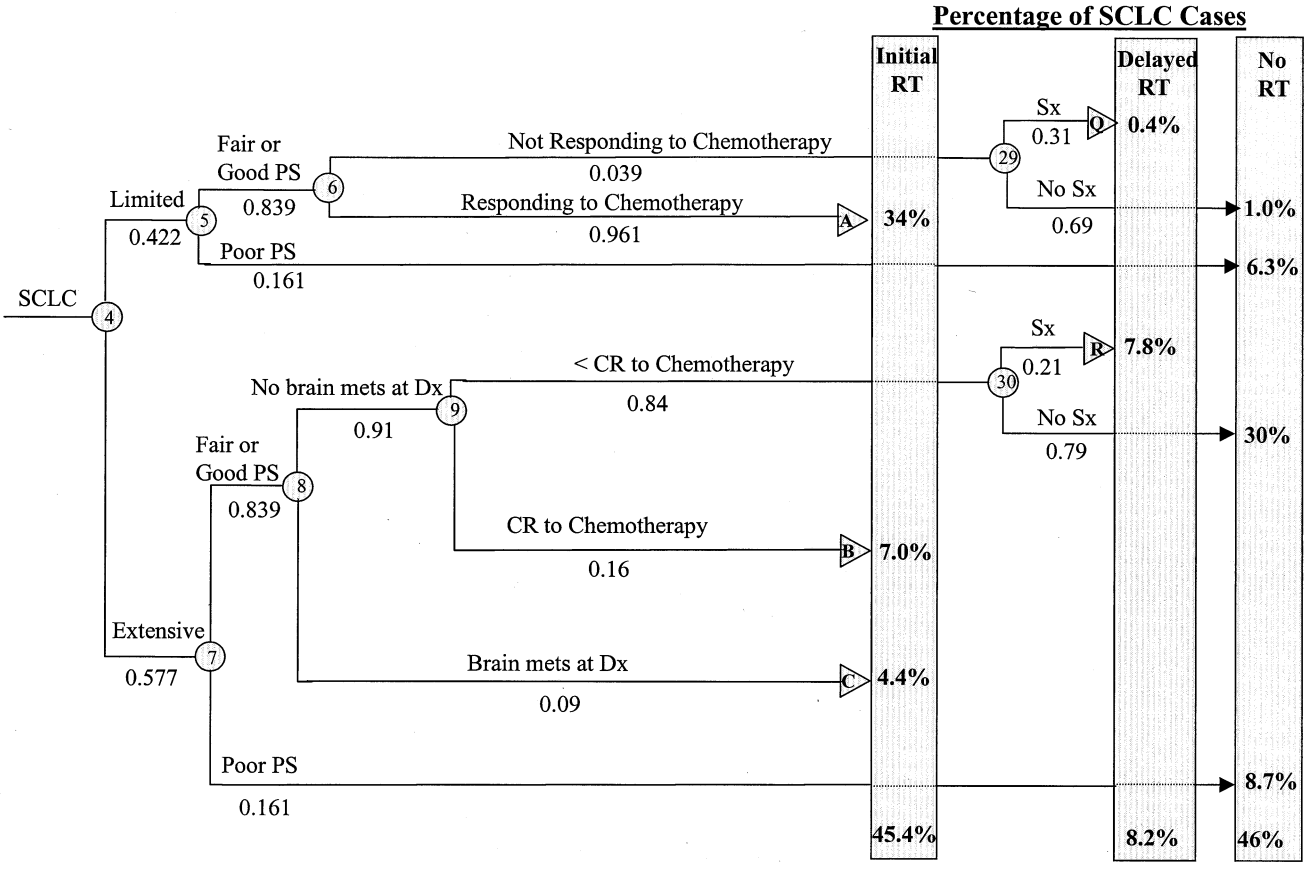

Fig. 2. Indications for radiotherapy (RT) for small-cell lung cancer (SCLC). This figure shows the tree diagram that was used to estimate the proportion of SCLC cases with indications for RT. The source of the information used at each numbered branch point is given in Table 4. Each terminal branch that corresponds to an indication for RT, is identified by a letter which identifies it in Table 3. The percentage of cases with early or delayed indications for RT appear in separate columns on the right; the percentage of cases with any indication for RT is given at the bottom of each column. Abbreviations: PS = performance status; Dx = diagnosis; CR = complete response; Sx = symptoms that may benefit from RT.

(NSCLC). We will deal with each of these components in turn, before presenting the overall model.

Small-cell lung cancer

Figure 2 illustrates how patients with SCLC were segregated into subgroups with indications for RT on the basis of the extent of the disease, their performance status, response to chemotherapy, and symptomatic status. Each indication for RT is represented by a terminal branch that ends in one of the two shaded columns corresponding to initial and delayed RT. Each indication is labeled with a code letter that identifies it in Table 3. The quality of the supporting evidence varies from indication to indication. For example, there is Level 1 evidence to support the use of thoracic RT following a response to chemotherapy in patients with limited stage disease (Indication A), but only Level 3 evidence to support the use of prophylactic cranial irradiation in patients who have a complete response to chemotherapy for extensive disease (Indication B).

Each branch point on the tree diagram in Fig. 2 is labeled with a code number that identifies it in Table 4. Table 4 provides references to the sources used to estimate the proportion of cases that take a given path at each branch point. Table 4 also indicates the quality of each estimate using the classification system outlined in Table 2. The quality of the estimates varies from one branch point to the next. At Branch Point 4, the model uses α level estimates of the proportion of cases with limited stage disease, whereas at Branch Point 9, the model uses γ level estimates of the proportion of extensive stage cases that have a complete response to chemotherapy.

Using the process described in the "Methods" and illustrated in Fig. 1, we estimate that 53.6% ± 3.3% of SCLC cases will require RT at least once in their lives, 45.4% ± 3.0% as part of their initial management, and 8.2% ± 1.5% later in the course of the illness.

Stage I and II non–small-cell lung cancer

Figure 3 shows the tree diagrams used to identify the indications for RT for Stages I and II NSCLC. As above, each indication is represented by a terminal branch on the right of the diagram that ends in one of the shaded columns

Table 3. Indications for radiotherapy: Levels and sources of evidence

Legend key*	Clinical scenario	Treatment indicated	Level of evidence†	references
A	SC, Limited, No op, CT with PR or CR	TRT + CI	I	16, 18, 19, 20, 21, 22
B	SC, Extensive, CT with CR	CI	III	18, 19, 21
C	SC, Extensive, brain mets	CI	I	16, 18, 19, 21
D	NSC, Stage I, Post op, RI or R2	TRT	III	15, 17, 19, 21, 22
E	NSC, Stage I, No op	TRT	III	15, 17, 18, 19, 21, 22
F	NSC, Stage II, Post op, pN0-1, R1-2	TRT	III	15, 17, 21, 22
G	NSC, Stage II, Post op, pNx: R0	TRT	III	15, 17, 20, 21
H	NSC, Stage II, No op	TRT	III	15, 19, 18, 21, 22
I	NSC, Stage III, Post op, any pT/pN2-3, R0	TRT	I	15, 17, 19, 18, 21, 22
J	NSC, Stage III, Post op, pT1-4/pN2-3, R1-2	TRT	III	15, 17, 19, 21, 22
K	NSC, Stage III, Post op, pT3/pN0-1, R1-2	TRT	III	15, 17, 19, 21, 22
L	NSC, Stage III, No op, good PS, no Sx, accepts RT	TRT	I	14, 15, 17, 18, 19, 20, 21, 22
M	NSC, Stage III, No op, good PS, Sx	TRT	I	14, 15, 17, 18, 19, 20, 21, 22
N	NSC, Stage III, No op, poor PS, Sx	TRT	III	14, 15, 18, 19, 20, 21, 22
O	NSC, Stage III, No op, poor PS, Sx, accepts RT	TRT	I	14, 19, 20
P	NSC, Stage IV, fair PS, Sx	PRT	IV	14, 17, 18, 19, 22
Q	SC, Limited, CT, NR, relapse, Sx	PRT	III	16, 18, 19, 21, 22
R	SC, Extensive, CT, PR or NR, relapse, Sx	PRT	III	16, 18, 19, 21, 22
S	NSC, Stage I, Post op, RO, relapse, Sx	PRT	III	15, 17, 18, 22
T	NSC, Stage II, Post op, RO, relapse, Sx	PRT	III	15, 17, 18, 22
U	NSC, Stage III, Post op, pT3/pN0-1, relapse: Sx	PRT	III	17, 18
V	NSC, Stage III, good PS, No Tx, Progression, Sx	PRT	III	14, 15, 17, 18, 19, 22
W	NSC, Stage III, poor PS, No Tx, Progression, Sx	PRT	III	14, 15, 17, 18, 19, 22
X	NSC, Stage IV, Good PS, No Tx, Progression, Sx	PRT	III	14, 15, 18, 19, 22

*The letters in the legend key column identify each indication for RT in Figs. 1–6: Indications A through P describe radiotherapy RT as a component of initial management; Indications Q through X describe RT for progression or relapse.

†The level of evidence that supports each indication was classified using the criteria in Table 1.

Abbreviations: SC = small cell; NSC = non–small cell; Post op = cancer-directed surgery was done; No op = no cancer-directed surgery was done; pT and pN = pathologic T and N categories as defined by UICC/AJCC; R indicates the presence or absence of residual tumour following surgery as defined by UICC/AJCC (R0 = no residual tumour, R1 = microscopic residual tumour, R2 = macroscopic residual tumour); Sx = symptoms that may benefit from RT; mets = metastases; CT = chemotherapy; CR = complete response; PR = partial response; NR = no response; TRT = thoracic RT; CI = cranial irradiation; PRT = any palliative RT.

corresponding to initial or delayed RT, and labeled with a code letter that links it to Table 3. The variables used to define indications for RT were, the operability of the case, the type of surgery performed, the pathologic T and N categories, and the status of the resection margins in the operated cases. Each branch point in the diagram is identified with a code number that links it to Table 4.

We will not reiterate the information provided in the diagrams and tables except to point out some simplifications and approximations that were made in constructing the model. The assessment of operability in NSCLC is complex, and involves consideration of both resectability and medical tolerance for the required procedure. However, it is the actual rate of surgery in the population of interest that determines the need for radiation. The rates of surgery used in the model were, therefore, based on the observed rates in the SEER registries (25). The American College of Radiology deems that RT is highly appropriate following surgery that has not involved mediastinal dissection in patients who have undergone surgery for Stage II NSCLC (17). In the SEER registries, approximately 28% of patients with resected Stage II NSCLC did not have a surgical lymph node dissection and that figure was used in the model.

Figure 3 shows that 41.0% ± 5.5% of Stage I cases will require RT at some point in the illness, 27.2% ± 1.8% as part of their initial management and 13.8% ± 5.6% for later progression or recurrence, and that 54.5% ± 6.5% of Stage II cases will require RT at some point, 37.1% ± 4.7% as part of their initial management, and 17.4% ± 4.5% for later progression or recurrence.

Stage III non–small-cell lung cancer

Figure 4 shows the tree diagram used to define the indications for RT for Stage III NSCLC. Subgroups of cases requiring RT were defined based on age, performance status, operability, pathology findings, symptoms, and patient preferences. As above, the evidence to support each indication for RT is provided in Table 3 and sources used to define proportions at each branch point are given in Table 4.

Most of the model is self-explanatory. We will only comment here on those aspects of it where we made approximations. To be considered for radical treatment, whether surgery or RT, most guidelines require that a Stage III NSCLC patient should have an adequate performance status, adequate pulmonary function, and weight loss of less than 5%. We were unable to estimate the proportion of incident cases that had each of these attributes. We, therefore, considered all cases with ECOG performance status of

Table 4. The prevalence of attributes used to define indications for radiotherapy

Legend key*	Population or subpopulation of interest	Attribute	Proportion of populations with this attribute†	Quality of information‡	References
1	All incident cases	Post-mortem Dx	**0.027**, 0.029	***α***, α	**25**, 27
2	All histologies	Small cell	**0.152**, 0.150	***α***, α	**25**, 27
3a	All NSC	Stage 1	**0.263**	***α***	**25**
3b	All NSC	Stage II	**0.049**	***α***	**25**
3c	All NSC	Stage III	**0.316**	***α***	**25**
3d	All NSC	Stage IV	**0.372**	***α***	**25**
4	All SC	Limited	**0.42**	***α***	**25**
5	Limited SC	Good PS	**0.84**	***α***	**29**
6	Limited SC	Progression on CT	**0.039**	***γ***	**35**
7	Extensive SC	Good PS	**0.84**	***α***	**29**
8	Extensive SC	Brain mets at Dx	**0.09**	***λ***	**36**
9	Extensive, SC, CT	Less than CR	**0.84**, 0.85, 0.9, 0.9	***γ***, γ, γ, γ	**37**, 38, 39, 40
10	NSC, Stage I	No. op	**0.32**	***α******	**25**
11	NSC, Stage I, Post op	+ ve margins	**0.02**, 0.04, 0.03, 0.15	***μ***, μ, μ, μ	**41**, 42, 43, 44
12	NSC, Stage I	Contraindication	**0.185**	***α***	**29**
13	NSC, Stage II	No op	**0.15**	***α***	**25**
14	NSC, Stage II, Post op	No MLND	**0.28**	***α***	**25**
15	NSC, Stage II, Post op	+ ve margins	**0.02**, 0.04, 0.03, 0.06	***μ***, μ, μ, μ	**41**, 42, 43, 44
16	NSC, Stage II	Contraindication to RT	**0.185**	***α***	**29**
17	NSC, Stage III	Good PS	**0.839**	***α***	**29**
18	NSC, Stage III	No op	**0.814**	***α***	**25**
19	NSC, Stage III, Post op	pT3, pN0-1	**0.193**	***α***	**25**
20	NSC, Stage III, Post op, pT1-4, pN2-3	+ ve margins	**0.38**	***γ***	**45**
21	NSC, Stage III, Post op, pT3, pN0-1	+ ve margins	**0.06**	***μ***	**44**
22	NSC, Stage III, good PS	Sx at Dx	**0.64**	***ϕ***	**32**
23	NSC, Stage III, good PS, No op, No Sx	Preference for RT	**0.52**	***μ***	**46**
24	NSC, Stage III, fair or poor PS	Contraindications to RT	**0.51**	***α***	**29**
25	NSC, Stage III, fair PS	Sx at Dx	**0.64**	***ϕ***	**32**
26	NSC, Stage III, poor PS, No Sx	Preference for RT	**0.52**	***μ***	**46**
27	NSC, Stage IV	Contraindications to RT	**0.08**	***α***	**29**
28	NSC, Stage IV	Sx at Dx	**0.38**, 0.29	***γ***, γ	**30**, 31
29	Limited SC	Delayed Sx	**0.31**, 0.202	***γ***, γ	**47**, 48
30	Extensive SC, < CR to CT	Delayed Sx	**0.21**, 0.25, 0.122	***γ***, γ, γ	**39**, 49, 50
31	NSC, Stage I, Post op	Delayed Sx	**0.21**	***γ***	**51**
32	NSC, Stage II, Post op	Delayed Sx	**0.29**, 0.25	***γ***, γ	**52**, 53
33	NSC, Stage III (pT3 PN0), Post op	Delayed Sx	**0.21**, 0.29, 0.25	***γ***, γ, γ	**51**, 52, 53
34	NSC, Stage III, good PS, No op	Delayed Sx	**0.54**	***ϕ***	**32**
35	NSC, Stage III, poor PS, No op	Delayes Sx	**0.54**	***ϕ***	**35**
36	NSC, Stage IV, good PS	Delayed Sx	**0.54**	***ϕ***	**32**

*The numbers in the legend key column refer to the branch-points in Fig. 2–6.

†The proportions shown in bold type were used in the main analysis.

‡The quality of each source of information was classified using the system shown in Table 2.

Abbreviations: Dx = diagnosis; NSC = non-small cell; SC = small cell; No op = no cancer-indicated surgery; Post op = cancer-directed surgery was done; MLND = Mediastinal lymph node dissection; + ve margins = positive margins; − ve margins = negative margins; CT = chemotherapy; CR = complete response; PS = performance status, Sx = symptoms that may benefit from RT.

3 or 4 to be ineligible for radical treatment. The proportion of patients with an ECOG performance status of 3 or 4 was obtained from a registry-based study done in the United Kingdom (29). The best management for potentially resectable clinical Stage III patients is unknown, but it is deemed reasonable to attempt resection in such cases (14, 18). In the model, we used the actual surgery rate observed in the SEER registries.

The use of RT in pathologic Stage III NSCLC patients without positive margins was listed as an indication for RT in some guidelines (15, 17–19, 21, 22), but not in others (20). However, most guidelines suggested that evidence was insufficient to support postoperative RT for pN0–1 patients (19–22). Therefore, RT for pT3/PN0–1 patients with negative margins was not included as an indication for early RT, whereas, RT for pT1–4/N2–3 patients with negative margins was included as an indication for early RT. It was thought that patient preferences would be particularly important in determining the proportion of patients for whom this indication would be appropriate; however, we were unable to find any data dealing with patient preference for this particular indication.

Overall, it was estimated that 83.5% ± 10.6% of Stage

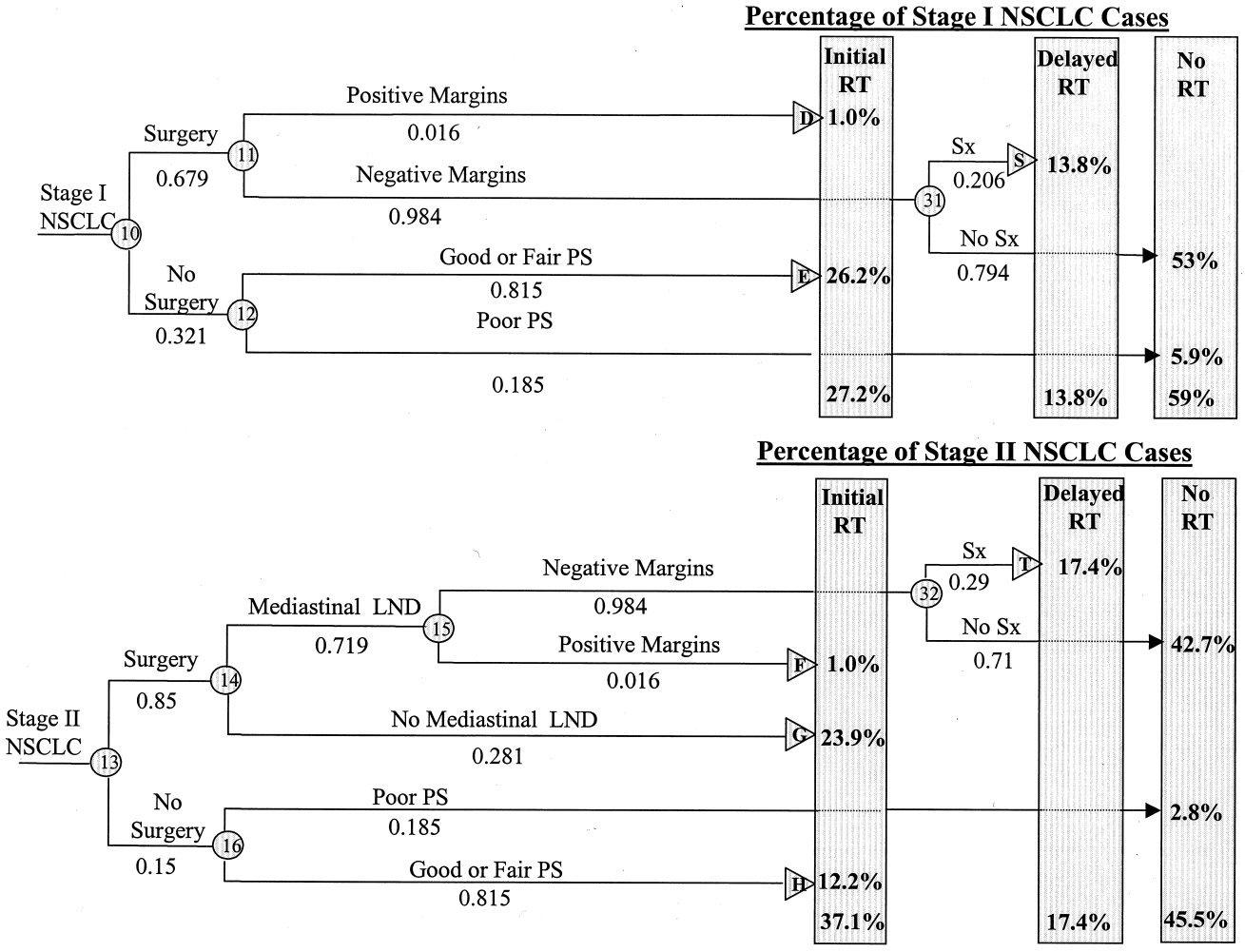

Fig. 3. Indications for radiotherapy (RT) for Stage I and II non–small-cell lung cancer (NSCLC). This figure shows the tree diagrams used to identify indications for RT for Stage I and Stage II NSCLC. The source of the information used at each numbered branch point is given in Table 4. Each terminal branch that corresponds to an indication for RT is identified by a letter, which identifies it in Table 3. The percentage of cases with early or delayed indications for RT appear in separate columns on the right; the percentage of cases with any indication for RT is given at the bottom of each column. Abbreviations: PS = performance status; LND = lymph node dissection; Sx = symptoms that may benefit from RT.

III NSCLC cases would benefit from RT at some point in their illness, 75.7% ± 10.5% as part of their initial management, and 7.7% ± 1.1% later for progression or recurrence.

Stage IV non–small-cell lung cancer

Figure 5 shows the diagram used to identify indications for RT for Stage IV NSCLC, based on performance status and the presence or absence of symptoms that might benefit from RT, either at diagnosis or at progression. Most guidelines acknowledge that RT has a role in the palliation of symptoms, such as hemoptysis, chest pain, cough, and postobstructive atelectasis and pneumonia (14, 17, 19, 21, 22), and in the palliation of symptoms from brain, spinal cord and bone metastases (14, 18, 19, 21, 22). The extent to which the use of chemotherapy alters the need for RT is unclear; however, the sensitivity analyses included a prospective series in which patients were managed with chemotherapy in addition to RT. The proportion of cases requiring RT in two prospective trials of multi-agent chemotherapy for Stage IV nonsmall cell lung cancer were included in the sensitivity analyses (30, 31). The particular indications for RT were not listed in these studies, however, we have assumed that RT was prescribed for symptoms from either metastatic or local sites such as those outlined in the guidelines.

For Stage IV patients who do not have an indication for RT at diagnosis, the RT indications described above would also apply at the time of relapse or progression. The source used for such delayed indications was a prospective series in which initially asymptomatic unresectable patients were offered RT at the time of progression of non–small-cell lung cancer for "significant respiratory symptoms. . .despite adequate analge-

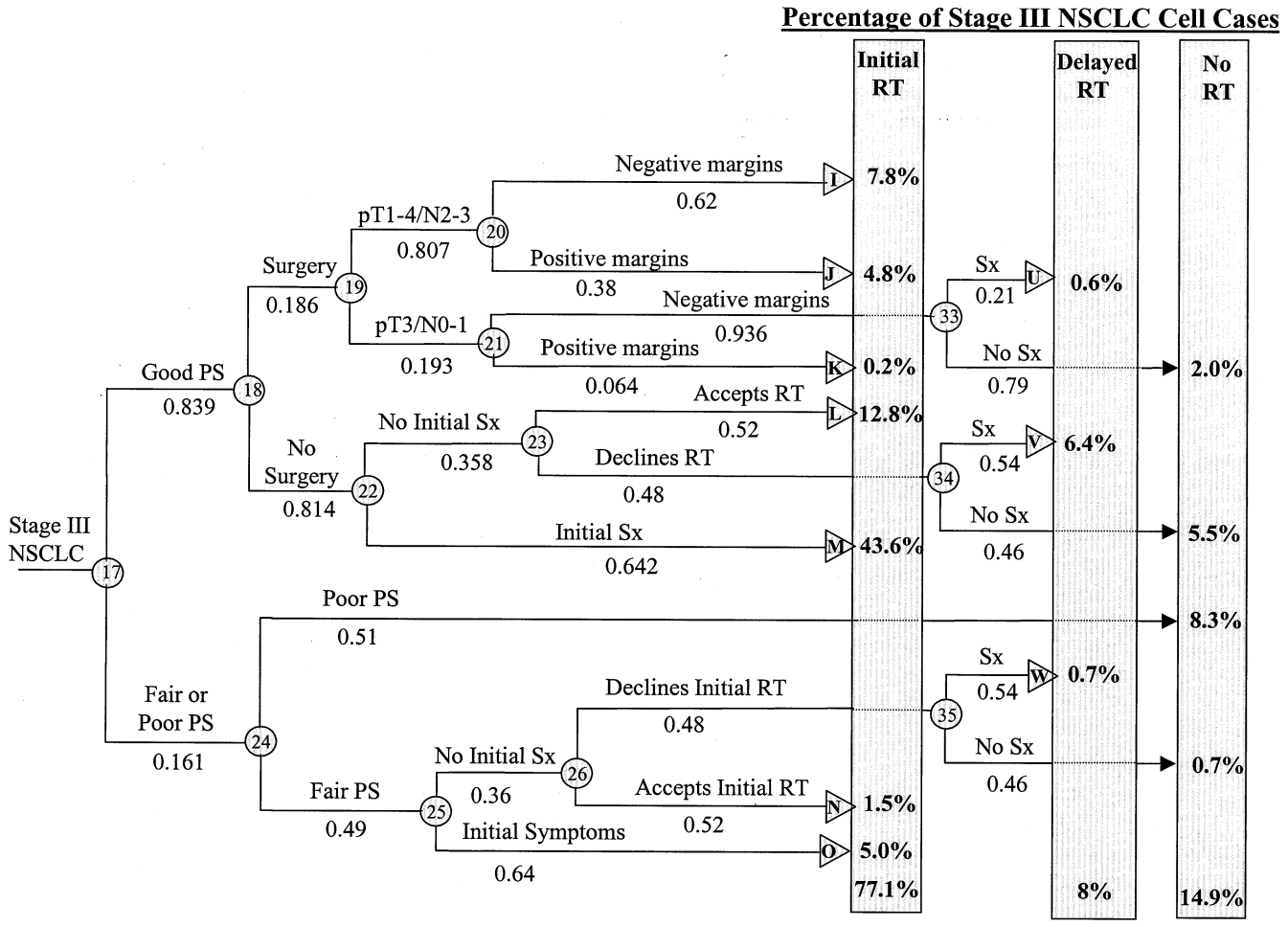

Fig. 4. Indications for radiotherapy (RT) for Stage III non–small-cell lung cancer (NSCLC). This figure shows the tree diagram used to identify indications for RT for Stage III NSCLC. The source of the information used at each numbered branch point is given in Table 4. Each terminal branch that corresponds to an indication for RT is identified by a letter, which identifies it in Table 3. The percentage of cases with early or delayed indications for RT appear in separate columns on the right; the percentage of cases with any indication for RT is given at the bottom of each column. Abbreviations: PS = performance status; Sx = symptoms that may benefit from RT.

sia, cough suppressant or antibiotics" or "major involvement of a main bronchus with significant stenosis" (32).

The model indicates that 65.7% ± 7.6% of Stage IV NSCLC cases require RT at some time in the illness, 35.0% ± 7.6% at the time of diagnosis, and 30.8% ± 1.1% at some time later in the course of the illness.

Estimated appropriate radiotherapy rate for lung cancer

The estimated appropriate treatment rates for the subgroups of cases as shown in Figs. 2 through 5 were integrated to estimate the overall requirement for RT for lung cancer (Fig. 6). Registries include patients diagnosed only at the time of postmortem, who are obviously not candidates for RT. The model, therefore, begins by identifying the proportion of cases diagnosed during life. The near identical distribution of histologies seen in two cancer registries was used to define the proportion of SCLC and NSCLC cases (25, 26). The SEER and NCDB databases were then used to subdivide the NSCLC cases into stage groups (25, 27).

The model indicates that 64.3% ± 4.7% of NSCLC cases will require RT, 45.9% ± 4.3% at the time of diagnosis, and 18.3% ± 1.8% later in the course of the illness.

When estimates for SCLC and NSCLC are combined, the model indicates that 60.1% ± 3.9% of all patients with lung cancer will have one or much indications for RT at some point in the illness, 44.6% ± 3.6% at the time of diagnosis, and 16.5% ± 1.5% later for progression or recurrence.

A multiway sensitivity analysis that used the *highest* estimate at each branch point where two or more equally good estimates were available, resulted in the estimates 61.4% of cases would require RT, 45.2% at diagnosis, and 16.2% later in the course of the illness. A second multiway sensitivity analysis that used the *lowest* estimate at each such branch point resulted in estimates that 58.6% of cases would require RT, 41.4% at diagnosis, and 17.2% later in the course of the illness. The ranges of 58.6–61.4% in the overall RT rate, and of 41.4–45.2% in initial rate, represent

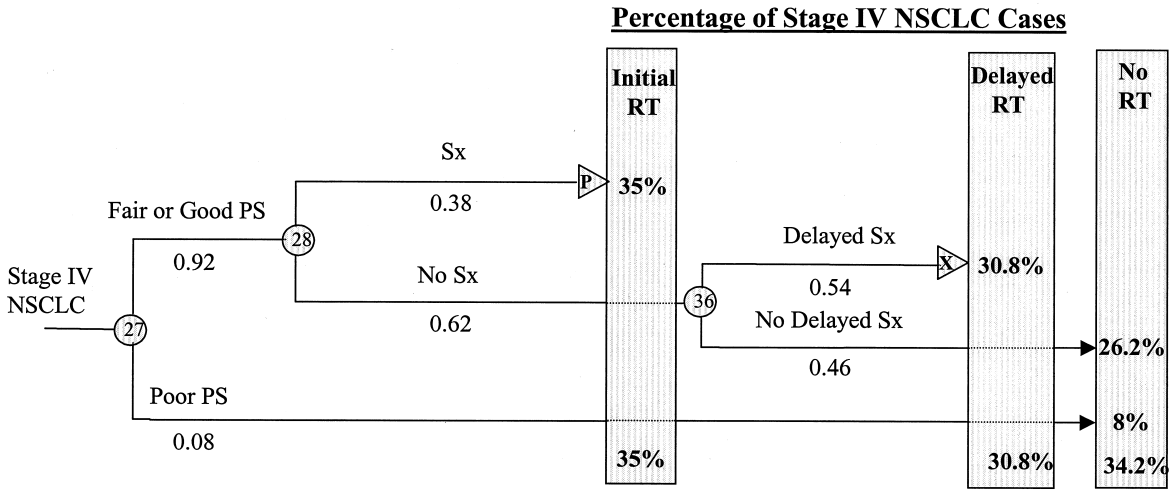

Fig. 5. Stage IV non–small-cell lung cancer (NSCLC) probability tree. This figure shows the tree diagram used to identify indications for radiotherapy (RT) for Stage IV NSCLC. The source of the information used at each numbered branch point is given in Table 4. Each terminal branch that corresponds to an indication for RT is identified by a letter, which identifies it in Table 3. The percentage of cases with early or delayed indications for RT appear in separate columns on the right; the percentage of cases with any indication for RT is given at the bottom of each column. Abbreviations: PS = performance status; Sx = symptoms that may benefit from RT.

the plausible ranges of these values, based on the best available epidemiologic data.

DISCUSSION

Cuyler has stated that "a need for medical care exists when an individual has an illness or disability for which there is an effective and acceptable treatment" (33). Before "needs" can be measured, "illness," therefore, has to be defined objectively in terms of observable characteristics, and "effectiveness" has to be demonstrated scientifically. Our method for estimating a population's need for RT starts from those principles. We used an evidence-based approach to define indications for RT, and an epidemiologic approach to measure the incidence of those indications. We will briefly discuss what we perceive to be the strengths and the weaknesses of this methodology.

The method has several inherent strengths. First, it is relatively objective and relies less on expert opinion than methods that have been used to estimate RT requirements in the past. Second, it is transparent; all the assumptions involved in the model are explicitly stated. Third, it is flexible; it can be adapted to differences in case mix among regions, to changes in case mix over time, and to any particular treatment guidelines. Fourth, it is detailed enough to permit audit of the use of RT in particular clinical situations, as well as overall treatment rates.

The method also has its weaknesses. As with any model that synthesizes information from different sources, the product is only as good as the raw material. No amount of modeling can make up for deficiencies in the primary data, and in some aspects of this model, we relied on imperfect information. First, many indications for RT proved not to be supported by Level 1 evidence. However, most were supported by a large amount of Level 3 evidence, and it was striking how frequently guidelines created independently by different organizations identified the same indications for treatment. Nonetheless, a few indications were included in some guidelines but not in others, reflecting continuing controversy about the usefulness of RT in these contexts. In such situations, modeling does nothing to resolve the underlying controversy, but the implications of including or excluding any given indication, can at least be determined by sensitivity analyses. Second, there were weaknesses in the way that we measured the incidence of indications for treatment. The main problem that we faced was that no single database contained sufficient information to define the incidence of all the indications for RT. We, therefore, had to use several different sources of information to estimate the proportion of patients with attributes that define indications for RT. In making choices about which source of information to use, we attempted to select the source of information that best represented the population as a whole, but the quality of the information available varied widely. For example, population-based registries provided excellent information about histology and the stage of the disease, but usually contained no information about the prevalence of symptoms or positive surgical margins, nor about the patient's performance status or symptoms. We, therefore, most often had to rely on reports from individual institutions or on results of clinical trials to provide this type of information, and these sources may well not have been truly representative of the population as a whole. Perhaps the greatest deficiency in the model was that, although we were able to estimate the number of cases in which RT should be recommended, we had little information about the proportion of patients who would actually consent to treatment under those circumstances. Unless this deficiency in our knowledge base is corrected, this method

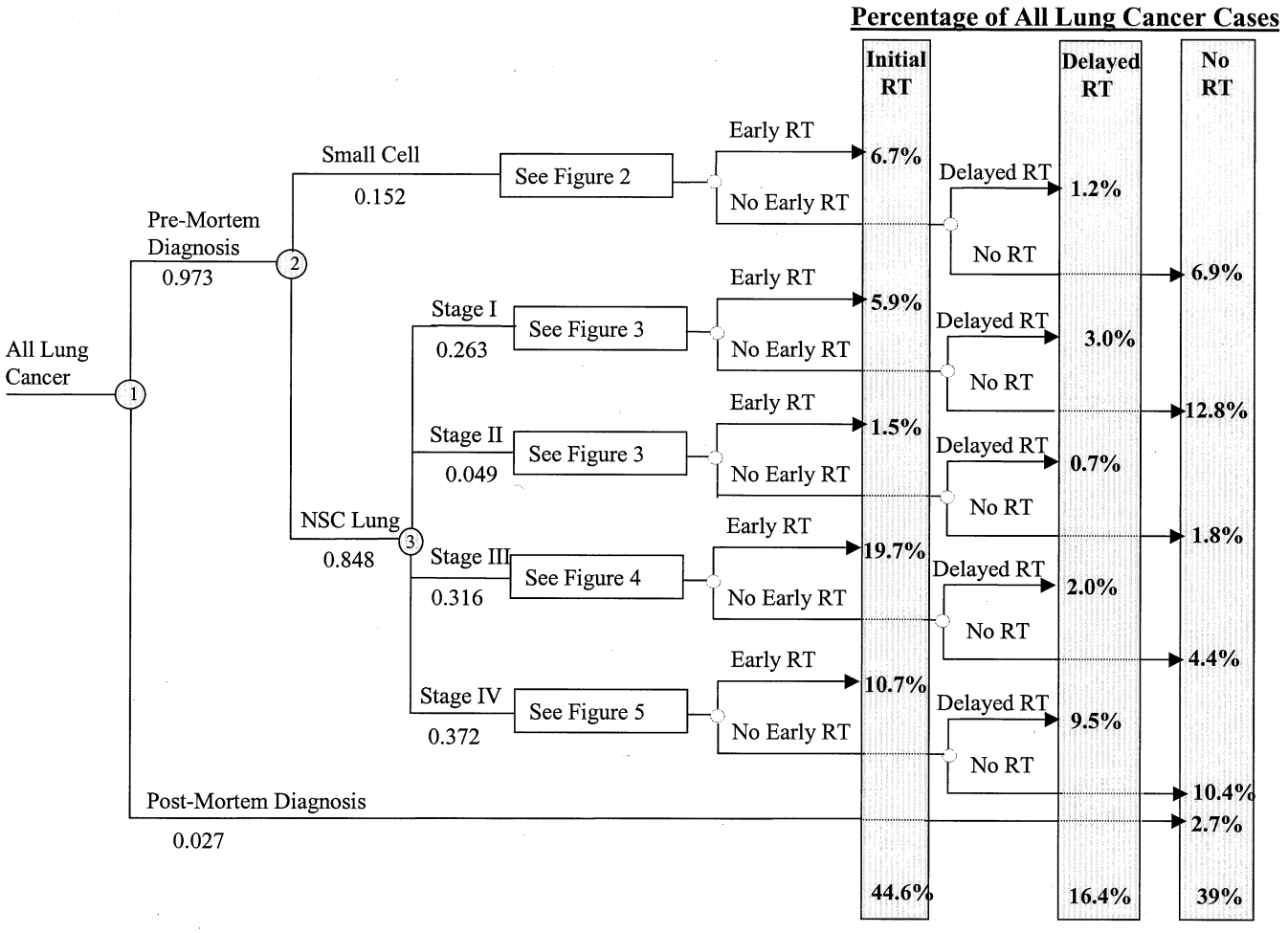

Fig. 6. Overall lung cancer probability tree. This figure shows the tree diagram that integrates the information provided in Figs. 2–5 to estimate the proportion of the total population of incident cases of lung cancer with any indication for radiotherapy (RT). The source of the information used at each numbered branch point is given in Table 4. Each terminal branch that corresponds to an indication for RT is identified by a letter, which identifies it in Table 3. The percentage of cases with early or delayed indications for RT appear in separate columns on the right; the percentage of the total population with any indication for RT is given at the bottom of each column.

will inevitably lead us to overestimate the need for RT to a greater or lesser degree.

Notwithstanding the limitations of our approach, we believe that it provides a reasonable way of assessing the need for RT at the population level. Note that we use the term, "needs assessment" here to describe the process of estimating a population's total requirement for treatment and not, as it is sometimes used, to describe the process of measuring the gaps between what is and what ought to be (34). Our method provides a rational basis for the long-term planning of radiation services, which has been lacking in the past. Market forces can be relied upon to ensure a plentiful supply of RT for those who are able to pay for it, in the fee-for-service situation. However, the long waiting lists for RT that developed across Canada in the late 1980s reflect the need for much more careful planning to ensure adequate access to care in publicly funded systems, and we expect that our approach will prove useful in averting similar problems in the future.

The existence of a "need" for RT as defined by the presence of an illness for which effective treatment is available, does not automatically imply that this service should be provided by any public, or private, insurance scheme. The level of care that can be provided must inevitably be determined by the resources that are available. In publicly funded health-care systems, this depends on how much society as a whole is willing, and able, to spend on health care. In private insurance schemes, it depends on how much the insured population is willing to pay. The same synoptic approach that we have used to estimate the proportion of cases that will require RT also lends itself to the estimation of the total cost, and the total benefits of providing RT for cancer. We are currently using the framework of the model for lung cancer to estimate the costs and benefits of treating patients for each indication outlined above. This approach should enable us to catalog the costs and benefits of RT in different situations in a way that will ultimately

facilitate valid judgements about the priority that should be given to providing RT in each of these situations.

Work is also underway on applying this method to other cancer sites. Our long-term goal is to provide an estimate of the need for RT in a typical cancer population, and to provide a model which can be readily adapted to the case mix, and treatment policies adopted in any particular community.

REFERENCES

1. Intersociety-Council for Radiation Oncology. Radiation Oncology in integrated cancer management. Report to the Director of the National Cancer Institute, Washington, DC: 1991.
2. Ontario Cancer Treatment, and Research Foundation. A plan for radiation treatment, province of Ontario, 1995–2000. Toronto, Ontario: OCTRF; 1995.
3. Duncan W, Jenkin D. The Radiation Oncology Commission: A Report to the Ontario Treatment and Research Foundation, and the Ontario Cancer Institute. Toronto, Canada: OCTRF; 1990.
4. The Committee for Radiation Oncology Studies. Criteria for Radiation Oncology in multidisciplinary cancer management. Report to the Director of the National Cancer Institute, Washington, DC: 1981.
5. Frodin JE, Jonsson E, Moller T, *et al*. Radiotherapy in Sweden. A study of present use in relation to the literature and an estimate of future trends. *Acta Oncol* 1996;35(8):967–979.
6. Cleton FJ, Coebergh JWW, (ed for Steering Committee on Future Health Scenarios). Cancer in the Netherlands. Dordrecht, the Netherlands: Kluwer Academic; 1991.
7. Mackillop WJ, Groome PA, Zhang-Salomoms J, *et al*. Does a centralized radiotherapy system provide adequate access to care? *J Clin Oncol* 1997;15(3):1261–1271.
8. Mackillop WJ, Dixon P, Zhou Y, *et al.* Variations in the management and outcome of non-small cell lung cancer in Ontario. *Radiother Oncol* 1994;32:105–115.
9. Denham JW. How do we bring an acceptable level of radiotherapy services to a dispersed population? *Australas Radiol* 1995;39:171–173.
10. Lote K, Moller T, Nordman E, *et al*. Resources of productivity in radiation oncology in Denmark, Finland, Iceland, Norway and Sweden during 1987. *Acta Oncol*1991;30:555–561.
11. Wright J. Health needs assessment in practice. London, UK: BMJ Publishing Group; 1998.
12. Sanderson C, Hunter D, McKee M, *et al*. Limitations of epidemiologically based needs assessment: The case of prostatectomy. *Med Care* 1997;35(7):669–685.
13. American Heritage Dictionary of the English Language. 3rd ed. Boston: Houghton Mifflin; 1996.
14. American Society of Clinical Oncology. Clinical practice guidelines for the treatment of unresectable non-small cell lung cancer. *J Clin Oncol* 1997;15(8):2996–3018.
15. Ettinger DS, Cox JD, Ginsburg RJ, *et al*. NCCN non-small-cell lung cancer practice guidelines. *Oncology* 1996;10(Suppl. 11):81–111.
16. Demetri G, Elias A, Gerhenson D, *et al*. NCCN small-cell lung cancer practice guidelines. *Oncology* 1996;10(Suppl. 11):179–194.
17. American College of Radiology Task Force on Appropriateness Criteria. Appropriateness criteria for imaging and treatment decisions in radiation oncology. Reston, VA: American College of Radiology; 1996.
18. National Cancer Institute. CancerNet. A service of the National Cancer Institute: PDQ Cancer Information Summaries: Treatment. Monograph on line. Accessed Dec/99. (url: http://cancernet.nci.nih.gov/pdq/pdq_treatment.shtml).
19. British Columbia Cancer Agency. Cancer Management Manual. Monograph on line. Accessed Dec/99. (url: http://www.bccancer.bc.ca/cmm/lung/).
20. Cancer Care Ontario Practice Guidelines Initiative. Lung Cancer Clinical Practice Guidelines. Monograph on line. Accessed Dec/99. (url: http://hiru.mcmaster.ca/ccopgi/lungcpg.html).
21. The Royal College of Radiologists' Clinical Oncology Information Network. Guidelines on the non-surgical management of lung cancer. *Clin Oncol* 1999;11:S1–S51.
22. Scottish Intercollegiate Guidelines Network. Management of Lung Cancer. Monograph on line. Accessed Mar/00. (url: http://www. Show.scot.nhs.uk/sign/html/htmltxt23.htm).
23. Sackett, DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest* 1989;95(Suppl. 2):2S–4S.
24. Eddy DM. A manual for assessing health practices and designing practice policies. Philadelphia, PA: American College of Physicians; 1992.
25. Nattinger AB, McAuliffe TL, Schapira MM. Generalizability of the surveillance, epidemiology, and end results registry population: Factors relevant to epidemiologic and health care research. *J Clin Epidemiol* 1997;50:939–945.
26. Clarke EA, Marrett LD, Kreiger N. Cancer registration in Ontario: A computer approach. In: Jensen OM, Parkin DM, Maclennan R, *et al.*, editors. Cancer registration principles and methods, Lyon, France: International Agency for Research on Cancer; 1991. p. 246–257.
27. Fry WA, Menck HR, Winchester DP. The national cancer data base report. *Cancer* 1996;77:1947–1955.
28. Bishop YMM, Fienberg SE, Holland PW. Discrete multivariate analysis. Theory and practice. Cambridge, MA: The MIT Press; 1975.
29. Brown JS, Eraut D, Trask C, *et al.* Age and the treatment of lung cancer. *Thorax* 1996;51:564–568.
30. Ruckedeschel JC, Finkelstein DM, Ettinger DS, *et al*. A randomized trial of the four most active regimens for metastatic non-small cell cancer. *J Clin Oncol* 1986;4:14–22.
31. Rapp E, Pater JLP, Willan A, *et al*. Chemotherapy can prolong survival in patients with advanced non-small cell lung cancer—Report of a Canadian multicenter randomized trial. *J Clin Oncol* 1988;6(4):633–641.
32. Carrol M, Morgan SA, Yarnold JR, *et al*. Prospective evaluation of a watch policy inpatients with inoperable non-small cell lung cancer. *Eur J Clin Oncol* 1986;22(11):1353–1356.
33. Culyer AH. Need and the National Health Service: Economics and social choice. New Jersey: Rowman and Littlefield; 1976.
34. Eyles J, Birch S, Chambers S, *et al.* A needs-based methodology for allocating health care resources in Ontario, Canada: Development and an application. *Soc Sci Med* 1991;33(4): 489–500.
35. Murray N, Coy P, Pater JL, *et al*. Importance of timing of thoracic irradiation in the combined modality treatment of limited-stage small-cell lung cancer. *J Clin Oncol* 1993;11(2): 336–344.
36. Abrams J, Doyle LA, Aisner J, *et al*. Staging, prognostic factors, and special considerations in small cell lung cancer. *Semin Oncol* 1988;15(3):261–277.
37. Ettinger D, Finkelstein D, Abeloff M, *et al*. A randomized comparison of standard chemotherapy versus alternating chemotherapy and maintenance versus no maintenance for extensive-stage small-cell lung cancer: A phase III study of the

eastern cooperative oncology group. *J Clin Oncol* 1990;8(2): 230–240.
38. Gatzemeier U, Pawel J, Laumen R, *et al*. Etoposide/vincristine-based chemotherapy with of without carboplatin in extensive-stage small cell lung cancer. A prospective randomized phase III trial. *Semin Oncol* 1994;21(3):31–35.
39. Evans WK, Feld MD, Murray N, *et al*. Superiority of alternating non-cross-resistant chemotherapy in extensive small cell lung cancer. *Ann Intern Med* 1987;107(4):451–458.
40. Roth BJ, Johnson DH, Einhorn LH, *et al*. Randomized study of cyclophosphamide, doxorubicin, and vincristine versus etoposide and cisplatin versus alternation of these two regimens in extensive small cell lung cancer: A phase III trial of the Southeastern Cancer Study Group. *J Clin Oncol* 1992;10(2): 282–291.
41. Kaiser L, Fleshner P, Keller S, *et al*. Significance of extramucosal residual tumor at the bronchial resection margin. *Ann Thorac Surg* 1989;47:265–269.
42. Dienemann H, Trainer C, Hoffmann H, *et al*. Incomplete resections in bronchial carcinoma: Morbidity and prognosis (German). *Chirurg* 1997;68(10):1014–1019.
43. Jeffery R. Survival in bronchial carcinoma. *Ann Roy Coll Surg Engl* 1972;51:55–58.
44. Harpole D, Healey E, DeCamp M, *et al*. Chest wall invasive non-small cell lung cancer: Patterns of failure and implications for a revised staging system. *Ann Surg Oncol* 1996;3(3):261–269.
45. Rusch V, Albain K, Crowley J, *et al*. Neoadjuvant therapy. A novel and effective treatment for stage IIIb non-small cell lung cancer. *Ann Thorac Surg* 1994;58:290–295.
46. Brundage MD, Davidson JR, Mackillop WJ. Trading treatment toxicity for survival in locally advanced non-small cell lung cancer. *J Clin Oncol* 1997;15(1):330–340.
47. Osterlind K, Hansen HH, Hansen HS, *et al*. Chemotherapy versus chemotherapy plus irradiation in limited small cell lung cancer. Results of a controlled trial with 5 years follow-up. *Br J Cancer* 1986;54:7–17.
48. Souhami RL, Geddes DM, Spiro SG, *et al*. Radiotherapy in small cell cancer of the lung treated with combination chemotherapy: A controlled trial. *BMJ* 1984;288:1643–1648.
49. Ihde DC, Mulshine JL, Barnett S, *et al*. Prospective randomized comparison of high-dose and standard-dose etoposide and cisplatin chemotherapy in patients with extensive-stage small-cell lung cancer. *J Clin Oncol* 1994;12(10):2022–2024.
50. Chahinian AP, Propert KJ, Ware JH, *et al*. A randomized trial of anticoagulation with warfarin and of alternating chemotherapy in extensive small-cell lung cancer by the Cancer and Leukemia Group B. *J Clin Oncol* 1989;7(8):993–1002.
51. Van Houtte P, Rocmas P, Smets P, *et al*. Postoperative radiation therapy in lung cancer: A controlled trial after resection of curative design. *Int J Radiat Oncol Biol Phys* 1980;6:983–986.
52. Medical Research Council Lung Cancer Working Party. The role of post-operative radiotherapy in non-small cell lung cancer: A multicentre randomized trial in patients with pathologically staged T1–2, N1–2, M0 disease. *Br J Cancer* 1996; 74(4):632–639.
53. The Lung Cancer Study Group. Effects of postoperative mediastinal radiation on completely resected stage II and stage III epidermoid cancer of the lung. *N Engl J Med* 1986;315:1377–1381.