

ESTRO project

Towards evidence-based guidelines for radiotherapy infrastructure and staffing needs in Europe: the ESTRO QUARTS project

Søren M. Bentzen^{a,*}, Germaine Heeren^b, Brian Cottier^c, Ben Slotman^d,
Bengt Glimelius^{e,f}, Yolande Lievens^g, Walter van den Bogaert^g

^aGray Cancer Institute and the Cancer Centre, Mount Vernon Hospital, Northwood, UK, ^bESTRO Office, Brussels, Belgium, ^cDepartment of Health, National Health Services Analysis Unit, Clatterbridge Centre for Oncology, UK, ^dRadiotherapy Department, Vrije Universiteit Medical Centre, Amsterdam, The Netherlands, ^eDepartment of Oncology, Radiology and Clinical Immunology, University Hospital, Uppsala, Sweden, ^fDepartment of Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden, ^gDepartment of Radiotherapy, University Hospital Gasthuisberg, Leuven, Belgium

Abstract

Background and purpose: Adequate and equitable access to radiotherapy (RT) must be a reasonable health care goal for the EU. However, there are large variations among the EU countries and even regional variations within countries in the provision of RT. In this report, we combine the best available evidence on the indications for RT with national epidemiological data to arrive at estimates for the appropriate level of RT infrastructure in the 25 EU countries.

Patients and methods: Data from three systematic overviews of the best available evidence for the indication for RT in 23 main cancer types are combined with epidemiological data from the EUCAN and GLOBOCAN databases on the crude incidence of each of these cancers in the 25 EU countries. Together with published benchmarks for accelerator throughput this allows estimation of the number of linear accelerators per million people required to facilitate appropriate RT utilization rates in each country. Where possible, the estimates are compared with the detailed data available from Sweden.

Results: The crude incidence of the main cancer types shows large variation among the 25 EU countries. This reflects in part differences in exposure to aetiological risk factors and partly differences among the countries in population age structure. Correspondingly, the estimate of the required number of linear accelerators per million people showed considerable variation: ranging from 4.0 in Cyprus to 8.1 in Hungary. The average for the 25 countries was 5.9 per million people. These estimates were compared with available national guidelines and actual data on RT infrastructure and large shortfalls were found in many countries. Implications for health economics and capacity planning are briefly discussed.

Conclusions: The QUARTS project has developed a model that establishes a direct and transparent link between epidemiological data and indications for RT based on the best available evidence. Comparison of the model estimates with current levels of RT infrastructure has revealed major inequalities in provision of RT in the 25 EU countries. Continuation of this study is recommended as a way of improving RT provision on rational grounds throughout the European community and as a model for health care planning in the EU.

© 2005 Elsevier Ireland Ltd. All rights reserved. Radiotherapy and Oncology 75 (2005) 355-365.

Keywords: Guidelines; Radiotherapy infrastructure; Epidemiology; Health economics; Health care policy

Cancer remains second only to cardio-vascular disease as a cause of death in the European Union. Life style changes together with the ageing of the population in the EU mean that cancer *incidence* is still going up. The good news is that there are strong signs that cancer *mortality* is on the decline in many EU countries [8,34]. This means that early detection and improved treatment is beginning to have a demonstrable effect on cancer survival [42]. Of those cancer patients who are cured it is estimated that 49% are cured by surgery, 40% by radiotherapy (RT) alone or combined with other

modalities and 11% by chemotherapy alone or combined with other modalities [38,39]. Radiotherapy is also a highly effective option for palliation and symptom control in many cases of advanced or recurrent cancer [14,21].

Adequate and equitable access to RT must be a reasonable health care goal for the EU. However, there are large variations among the EU countries and even regional variations within countries in the provision of RT [7,38,39]. Even among socio-economically similar countries the number of linear accelerators per million people varies by nearly

a factor of 2: from 3.2 in England to 6.1 in France (data from QUARTS see below). In the UK, this number varies among the regions and ranges from 2.13 to 6.02 per million people with the highest provision in the London region [7]. There are reasons to believe that these variations in RT provision, also affect the utilization of this treatment modality: the proportion of patients receiving RT varied from 22 to 58% among regions in the British audit [7]. Another symptom of inadequate provision of RT is the fact that waiting times for RT have become unacceptably long in several EU countries, which again is likely to have a detrimental effect on treatment outcome [10,23,32,46].

Radiotherapy is a relatively inexpensive component of cancer care: as an example, the estimated total cost of radiotherapy in Sweden in 2001 was only 5.6% of the estimated total cost of cancer care [31]. Still, in a climate of managed care, the large variability in RT provision seen among and within countries raises the question whether the high RT provision level is too high, i.e. not cost-effective, in some regions/countries? Or whether the lower levels are too low and thus disfavour patients living in these areas? Even if the current level of RT provision in a given country appears to be adequate, there is a need to plan ahead and make sure that provision is sufficient also in the future. However, due to the highly specialised staff required to prescribe, plan and deliver RT as well as the required capital investment in treatment units and the buildings housing them, changing the RT capacity requires long term planning and investment in education and infrastructure. Traditionally, long-term forecasts for RT requirements have been based on rather crude assumptions on the overall proportion of cancer patients requiring RT at some point of their disease with the typical estimate being the almost mythical 50%. As the indication for RT varies considerably among cancer types, a more satisfactory approach would be to base the estimate of RT requirements on clinical evidence of appropriate rates of radiotherapy (ARR) utilization.

Evidence-based medicine has been defined as 'the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients' [37]. At the heart of this new paradigm for clinical excellence is the production and critical appraisal of clinical data—ideally originating from randomized controlled trials—on the risks and benefits of specific procedures for a given clinical indication [4]. The principle of evidence-based medicine can logically be extended from individual patient care to health care policy making. In Britain, for example, the National Health Service has founded the National Institute for Clinical Excellence (NICE) with a remit of making recommendations on treatments and care for various clinical conditions using the best available evidence [28]. Also RT, in spite of its strong historical foundations, is increasingly becoming an evidence-based medical discipline [3] and this means that the data required for a more rational consideration of appropriate utilization of RT are gradually becoming available from a number of sources.

The aim of the ESTRO QUARTS project was to provide health care planners and policy makers with objective estimates of infrastructure and staffing needs for RT. As a first step an inventory of RT facilities and their geographic spread was compiled together with an overview of existing

national guidelines. In addition to this, quantitative estimates of adequate resources for appropriate delivery of RT to patients with evidence-based indications were derived for each of the 25 EU countries. In this paper, the term 'evidence-based estimates' will be used as a convenient shorthand to indicate estimates obtained using the best available evidence in the published literature. This does not necessarily imply that the indication for RT in each of the cancer sites considered is supported by the strongest, so-called Level I [4], evidence from randomized controlled trials.

QUARTS was funded in part by the 5th EU Framework Programme (FP5) as an 'accompanying measures' project, providing only limited funding. For this reason the study proposed had to be restricted to laying the basis for a more ambitious subsequent project. It was necessary largely to tap into existing resources and to use existing networks of people volunteering their time in support of QUARTS (see Appendix). The project started on 1 January 2003 and ended on 30 June 2004. QUARTS was organised into four main tasks or work packages (WP):

- WP1 Comparative analysis of guidelines for staffing and infrastructure for radiotherapy in Europe (Ben Slotman)
- WP2+3 A review and comparative quantitative analysis of the provision of radiotherapy services in Europe (Brian Cottier)
- WP4 Evidence-based estimates of radiotherapy needs in the EU: indications, epidemiology, health economics. (Søren M Bentzen, Bengt Glimelius, Katrien Kesteloot, Walter Van Den Bogaert, Yolande Lievens)

This report provides an overview of the QUARTS findings with an emphasis on the results of WP4. More detailed accounts of the inventories produced from WP1 to 3 will be published separately.

Despite the obvious resource constraints on the QUARTS study, we were determined not only to document national variations in the provision of RT but also to arrive at actual estimates of RT infrastructure needs in the EU countries based on the best available evidence in the literature. This was seen as a tangible and potentially useful outcome of the project. We also felt that this was the most concrete way of critically examining the methodological challenges involved in providing such estimates and the limitations to our current knowledge base.

Evidence-based estimation of appropriate RT provision levels

In order to arrive at a rational estimate of the required number of megavoltage treatment units in a country, one needs four basic estimates: the proportion of patients with a given type of cancer who presents with or develops an indication for RT, the incidence of these cancer types in the country, the RT re-treatment rate and the machine throughput in terms of number of treatment courses per year for a linear accelerator.

Evidence-based indication for RT

The pioneering study was conducted by the Swedish Council on Technology Assessment in Health Care (SBU) that published two very comprehensive literature overviews first in 1996 and in updated form in 2003 [18,36]. The SBU also conducted audits of the actual level of RT activity in Sweden, compiled health economics data and detailed data on staffing and infrastructure. The SBU reports have been a rich source of information for the QUARTS study and many of our findings are derived from, or compared with, data from the SBU. This is not the result of a deliberate bias, but simply because data with this level of detail are not available for any other country. One limitation of the SBU study in the present context is that the reviewed literature was not synthesised into detailed quantitative estimates of RT utilization rates.

Two further studies on evidence-based indications for RT are in progress in Canada and Australia and these use the methodology first presented by Tyldesley et al. [44]. The Canadian study is conducted by the Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute (QCRI), Kingston, Ontario [15-17,44] and the Australian study is undertaken by the Collaboration for Cancer Outcomes Research and Evaluation (CCORE), Liverpool BC, NSW [12]. A schematic comparison of these three sources of evidence-based indications for radiotherapy is presented in Table 1.

Both the CCORE and the QCRI studies present their findings as decision trees or utilization trees [44]: at each node, a branch of the tree splits according to a specific clinical criterion, for example stage of disease. For each

branch, in this case: for each stage, the relative proportion of cases, again derived from the literature, in the branch is given. If there is evidence that all patients in a given stage do (or do not) require radiotherapy, the tree stops here. If further characteristics within a stage decide whether RT is indicated, a new branching node is introduced and so forth. The tree will include patients where primary RT—with curative or palliative intent—is indicated. Following the QCRI group, the overall proportion of patients with a specific cancer site where radiotherapy is indicated is called the Appropriate Rate of Radiotherapy, ARR [44]. This is multiplied by 100 to produce a percentage of patients.

An important observation is that the CCORE and QCRI studies do not follow patient time lines beyond the primary therapy. In other words, there is no attempt to quantify the proportion of specific patient groups developing a secondary indication for radiotherapy, either as salvage therapy or for palliation. This is in contrast to the SBU audit, further discussed in Section 1.3 below, where the proportions of treatment courses per patient were estimated for various tumour sites. Following, Moller et al. [27] we also express this figure as a percentage. Note, however, that this can be larger than 100% in a group of patients, where primary and secondary indications sum to an average number of RT courses per incident case that exceeds 1.

The main source of evidence-based radiotherapy utilization rates for QUARTS was the CCORE report, mainly because of the accessibility of its findings, the methodology used and its comprehensive coverage. In the CCORE study

Table 1
Major overviews of evidence-based indications for radiotherapy

Source	Contents	Coverage	Strengths	Limitations	Publication
Swedish Council on Technology Assessment in Health Care (SBU) overviews (1996 and 2003)	Systematic review of the literature combined with a national audit of the use of RT in Sweden in 2000	All main cancer sites	Pioneering, comprehensive study of primary literature; National audit of actual activity; Includes health economics, biological and technical aspects; Includes follow-up on first report;	No quantitative synthesis of findings Narrative evaluation of sometimes conflicting reports in the literature	Published as two supplements (1995) [38,39] and a double issue (2003) of <i>Acta Oncologica</i> [36] and a separate paper on prostate cancer [30]
Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute (QCRI), Kingston, Ontario, Canada (2001–present)	Systematic review of national guidelines for utilization of RT	Colo-rectal, lung, breast and prostate cancer studies published at the time of writing	Very detailed decision trees allow streaming of patients with a specific histology into indications for RT; Clear summary of main findings; Sensitivity analysis;	Reviewing guidelines rather than primary studies Limited coverage to date	Published as a series of papers [15-17,44]
Collaboration for Cancer Outcomes Research and Evaluation (CCORE), Liverpool BC, NSW, Australia (2003)	Systematic review of national guidelines for utilization of RT	All main cancer sites	Very detailed decision trees allow streaming of patients with a specific histology into indications for RT; Clear summary of main findings; Sensitivity analysis;	Reviewing guidelines rather than primary studies	Published as a report available on the internet. In addition published in a series of review papers [12]

[12], indications for radiotherapy for each cancer site were derived from treatment guidelines ‘...issued by reputed national and international institutions’. Highest priority was understandably given to Australian evidence-based clinical practice guidelines. For cancer types where guidelines did not exist, other sources of evidence were used. These included randomized controlled trials, population-based studies of care, and single-institution studies. When required, CCORE conducted a systematic review of published English-language literature for a specific cancer site.

Delaney et al. [12] from the Australian group compared the ARR for lung cancer estimated by CCORE and QCRI. The CCORE estimate was 76% as compared with 61% estimated by the QCRI [44]. Similar differences, with higher ARRs in the Australian study, were seen for small cell (SCLC), 79 versus 54%, and for non-small cell lung cancer (NSCLC), 75 versus 64%. Delaney et al. identify a number of differences between the two utilization trees that explain the overall difference in ARR: the QCRI study has lower proportions of patients with good performance status in limited-stage SCLC (84 versus 94%) and with good/fair performance status in early NSCLC (80 versus 90%); the QCRI study has a lower rate of surgically treated patients who develop symptomatic progressive disease for which palliative RT is indicated; the QCRI study only recommends RT in limited-stage SCLC in patients responding to chemotherapy. Finally, the QCRI study includes a number of nodes where patients may opt-out of RT, whereas Delaney and colleagues from CCORE argue that patient preferences are in themselves affected by accessibility of RT and by the information given to the patient.

The SBU 2001 audit found an empirical 71% RT utilization rate in lung cancer but it should be noted that the Swedish figure includes lung cancer cases receiving re-treatment. If we assume that an overall re-treatment rate of 25% (see below) also applies for lung cancer, the SBU estimate would be closer to the QCRI estimate of 76% than the CCORE estimate of 95%. Similarly, the estimated proportion of breast cancer patients who develop one or more indications for RT at any time was $66.4 \pm 4.8\%$ in the QCRI study as compared with the CCORE estimate of 83%. The actual utilization in the 2001 SBU audit was 81%, but again the Swedish figure includes re-treatment courses.

The QUARTS estimates are derived using the CCORE evidence-based ARRs.

RT re-treatment

As mentioned above, the CCORE ARR estimates do not include re-treatment broken down according to cancer site. Instead, Delaney et al. [12] propose to use an overall factor of 1.25 when converting from number of cases with an indication for radiotherapy to the actual number of treatment courses per incident case. In other words, for each four patients receiving primary RT one patient will receive RT either as salvage therapy or for subsequent palliation. Note that the cases where palliative RT is indicated at presentation are already accounted for in the QCRI/CCORE utilization trees. Note also that the re-treated cases are not necessarily *re-irradiated* as they may have received primary surgery or chemotherapy. The 25% re-treatment estimate was accepted in the QUARTS study.

In the SBU audit [27], all treatment courses in the audit period were recorded. The total number of treatments was broken down according to the irradiated target: primary tumour, loco-regional relapse or distant metastasis. In 41% of the recorded RT courses the irradiated target was a loco-regional relapse or a distant metastasis. This, however, cannot directly be compared with the 25% re-treatment rate adopted here, the reason being that quite a substantial proportion of these treatment courses will be the first—and often the only—course of RT in these patients and these will have been accounted for in the base ARR value when using the QCRI/CCORE methodology.

The Royal College of Radiologists [7] assumed that the average number of RT courses per patient was 1.4, corresponding to a 40% re-treatment rate. Note, however, that the proportion of cancer patients receiving RT was as low as 40.5%. This means that even with a 40% re-treatment rate, the number of RT courses per incident case is only 56%, well below the 65% achieved by applying the factor of 1.25 to the 52.3% ARR estimated by CCORE. Thus, the high relative re-treatment rate in the UK report should be seen in the light of the low utilization of RT in the primary setting.

Linear accelerator throughput

Linear accelerator throughput was quantified as the number of treatment courses per year. Clearly, this will vary with a multitude of factors including the complexity of the treatments, number of fields, number of dose fractions, extent of quality assurance procedures, efficiency of equipment and staff. Most of these factors vary with tumour type, stage of disease and the performance status of the patient. The QUARTS review of national guidelines identified seven countries (Austria, Ireland, Italy, Netherlands, Czech Republic, Poland and Slovakia) with a defined benchmark for linear accelerator throughput (Slotman et al., 2005). Generally, these varied between 400 and 600 treatments per year, in some cases qualified according to the complexity of treatments delivered. The exception was Italy with a benchmark of 200-500 new treatments per year depending on patient category. The 1996 SBU report [18] used 300 treatments per unit per year as their standard benchmark. However, as discussed below this figure was at the low end of the range of actual throughputs per unit in the 2001 SBU audit. Finally, a recent Dutch study used a benchmark of 500 treatments per year [41], whereas figures in the same report suggest that the actual throughput was around 410 treatments per year.

A benchmark value of 450 treatment courses per year was used by CCORE based on the value proposed by the Australian Health Technology Advisory Committee in 1996 [1]. Benign diseases contribute to the demand for megavoltage radiotherapy and CCORE proposed to factor this in when estimating the required number of linear accelerators in a region. We decided NOT to include this contribution in the QUARTS estimates partly due to our focus on radiotherapy for cancer but also due to the large national and local variation in the acceptance of benign indications for radiotherapy.

Looking at the actual utilization of treatment units, interesting data originate again from the SBU audit:

the average annual throughput per unit in Sweden in 2001 was 338 treatment courses with a variation among centres ranging from 248 to 442 [27]. There was a strong correlation between the number of treatment units in a department and the actual patient throughput in that department [31]. This suggests that treatment units are more efficiently utilised in larger departments. Another noteworthy observation in the 2003 SBU report is that the number of treatment courses per unit increased from the 1992 to the 2001 audits. This was despite an increase in the average number of treatment fields per patient treated with curative intent from 2.6 to 3.2. However, as noted by Moller et al. [27] the increasing use of multi-leaf collimators and computerised set-up reduces the relevance of number of fields treated as a measure of workload.

Synthesizing the above information, the QUARTS group decided to use 450 treatments per megavoltage unit per year as a reasonable value both in view of the available national guidelines and the actual utilization data from the Netherlands, Sweden and Australia.

Cobalt machines still constitute a sizeable fraction of megavoltage treatment units in many countries. While the Royal College of Radiologists used a factor of 0.5 in converting from cobalt machines to linear accelerator equivalents [7], we applied a factor of 1 in the QUARTS study. We felt that especially in larger departments, appropriate streaming of patients would provide similar throughputs on cobalt machines and linacs. Predicted RT requirements are reported as number of linacs per 1 million people, whereas current provision is given as megavoltage units, i.e. the sum of linacs and cobalt machines.

There is currently no realistic way of adjusting for treatment complexity. However, the QUARTS group felt that it was unreasonable not to apply some kind of weighting to the different cancer types. As a pragmatic solution a weighting factor for each cancer site was calculated from the data available in the SBU audit [27]. The weighting factor was defined as the average number of dose fractions for that site divided by the average number of fractions for all RT courses. Examples of weights are: head and neck cancer: 1.54; colo-rectal cancer: 0.38 (reflecting the use of the 5 Gy \times 5 pre-operative schedule in rectal cancer); non-Hodgkin's lymphoma: 0.70 (reflecting the lower total dose and lower number of fractions typically used in this indication). It was felt, that these weighting factors also mirrored other aspects of complexity such as number of fields, immobilization requirements, etc.

Number of incident cases

As an introduction to the RT requirement estimates below, it is important to distinguish between the age-standardised rate often used in epidemiological studies and the crude incidence. Take lung cancer in males in selected European countries as an example. The crude incidence is the actual number of incident cases in a year divided by the number of people, in this case: males, in the country. Typically, this is expressed as the number of cases per 100,000 individuals. As the risk of developing cancer varies greatly with age, much of the variation in crude cancer incidence in different countries is explained by varying

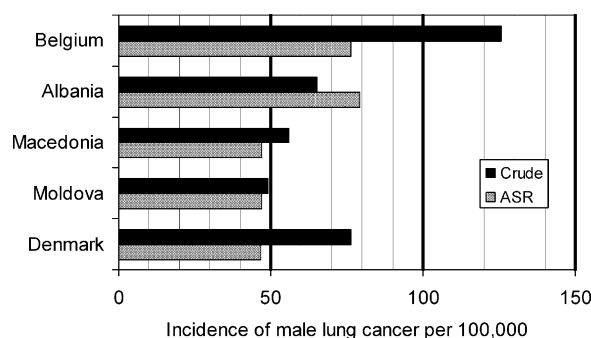


Fig. 1. Crude incidence compared with age standardised rate of lung cancer in males in five selected European countries. Data from EUCAN/GLOBOCAN.

population age structures. To adjust for this effect, the age-standardised rate is used: the crude cancer incidence as a function of age group in a given country is applied to a defined, hypothetical, population with a specified age structure. Fig. 1 shows two examples: Macedonia, Moldova and Denmark have very similar age-standardised rates for male lung cancer, but as the age distribution in Denmark is shifted towards older age groups compared with Macedonia and Moldova, the crude incidence of lung cancer in Denmark is substantially higher than that of the other two countries. Two other countries, Belgium and Albania have similar age-standardised rates both exceeding the Danish rate—suggesting larger exposure of these populations to etiological risk factors for lung cancer—but, whereas this result in a much higher crude incidence of lung cancer in Belgium than in Denmark this is not the case with Albania, again because of the difference in population age structure.

While age-standardised rates are relevant for discussions of cancer risk, it is the variations in crude cancer incidence that affect the appropriate number of RT facilities in various countries. The main aim of QUARTS WP4 was to apply evidence-based estimates of RT utilization rates to cancer epidemiological data and combine the resulting estimates with accelerator throughput benchmarks.

Comprehensive epidemiological data for the 15 European Union member countries prior to the latest enlargement are available in the EUCAN database [13]. Crude incidence data for 23 cancer sites for both genders are available for each country. Data for the 10 new member countries joining in 2004 were obtained from the GLOBOCAN database [19]. In GLOBOCAN, crude incidence data are presented for males and females separately and these were weighted in the QUARTS study by the male:female ratio for each country to produce a crude incidence per 100,000 people. The GLOBOCAN database also provides a more detailed breakdown of head and neck tumours according to the anatomical sub-site of origin, but in QUARTS these data were summed to produce a single figure as reported in EUCAN.

The QUARTS estimates of national treatment unit needs

The basis for the calculation was the evidence-based number of RT courses per one million people in each country and this was estimated as follows. Incidence data for each of

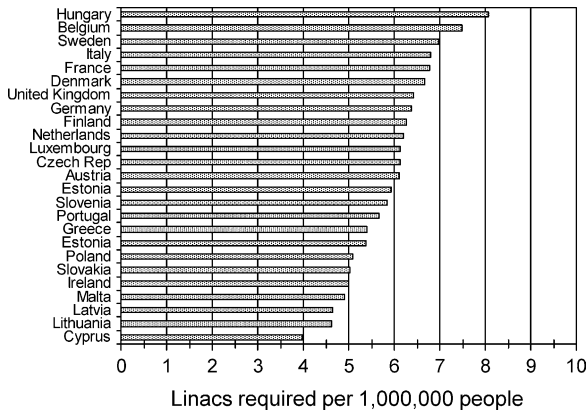


Fig. 2. QUARTS estimates of the number of linacs (megavoltage RT units) required per one million people in each of the 25 EU countries. See text for details.

the 23 sites in the EUCAN/GLOBOCAN databases were multiplied by the ARR for the same site as derived from the CCORE study. A re-treatment factor of 1.25 was applied uniformly for all sites. Finally, the fraction number weighting factor was applied for the specific site. The summed incidence over these 23 sites was compared with the incidence of all cancers (except non-melanoma skin cancer) also given in the databases. We found that these 23 sites accounted for between 89 and 94% of the total cancer incidence in the 25 EU countries. The difference is made up of a long list of relatively rare cancers, where there is often sparse evidence in the published literature concerning the indication for RT. In arriving at the QUARTS estimate of RT infrastructure requirements, we assumed that half of the remaining 6-11% of incident cancer cases would develop an indication for RT at some point in the course of their disease. The re-treatment and the fractionation factors were both assumed to be 1 for these less common cancer sites.

Fig. 2 displays the required number of linacs per million people in each of the 25 EU countries calculated by dividing the above estimate of the required number of treatment courses in each country by the benchmark accelerator throughput. The estimated adequate number of linacs per million people varied by a factor of two: from 4.0 in Cyprus to 8.1 in Hungary. The average for the 25 countries was 5.9 per million people. The lowest ranked countries on the list are characterised by having relatively young populations with a corresponding low overall incidence of cancer.

Theory and practice: ARRs and actual utilization in Sweden

How far are the CCORE ARR estimates from the current practice in the EU? Again, the SBU study provides a unique opportunity to look at the concordance—or discordance—between these estimates and the actual practice in Sweden. This of course cannot prove or disprove the validity of the CCORE estimates, for this to be the case one would have to assume that all of RT practice in Sweden in 2001 was in agreement with the best available evidence-based recommendations. However, the comparison highlights some

of the potential national issues that may lead to deviations from best practice and/or the overestimation of some indications.

The SBU 2001 audit of RT activity in Sweden

The SBU audit recorded the actual use of radiotherapy in all Swedish RT departments during 12 consecutive weeks, from 17 September to 9 December 2001 [27]. All patients starting a course of radiotherapy during this period were included; in other words, re-treatments as well as primary RT are included in the numbers. These numbers were scaled by a factor of 50/12 in order to arrive at estimates of annual activity. The use of a numerator of 50 rather than 52 was argued by the observation that the period audited did not include public holidays and that the '...activity at the departments was high' [27]. The empirical activity figures were compared with incidence data for 2000 from the national Swedish cancer registry to produce estimated ratios of RT courses per incident cancer case for the main tumour sites. Note, as mentioned above, that ratios exceeding 1 are truncated to become identical 1 in Table 1 in the paper by Moller et al. [27]. These ratios were re-calculated for the present comparison, the reason being that the average number of treatments per incident case can obviously exceed 1 and therefore these ratios should not be truncated. As these utility rates represent the quotient of two counts, we used Poisson statistics and standard propagation of error techniques to arrive at an approximate 95% confidence interval for the rates. A slightly different method was applied in the Swedish study [27], but the two methods will for the actual numbers concerned produce near-identical confidence intervals. The difference in utilization rates was calculated as an interval defined as the differences between the CCORE recommendation and the lower and upper bounds on the 95% confidence interval for the (scaled) empirical utilization rate from SBU. Following SBU, this was multiplied by 100 to produce a percentage scale.

Comparison with evidence-based utilization rates

Fig. 3 shows the differences between actual and evidence-based utilization rates in Sweden in 2001. Within the 95% confidence limits many sites show concordance

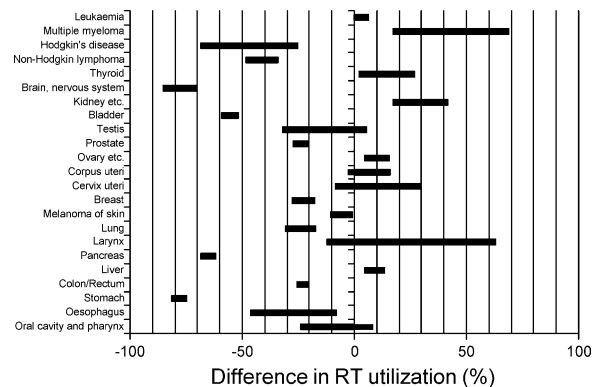


Fig. 3. Difference in RT utilization rate between the CCORE estimate and the actual utilization estimate from SBU. The horizontal black bars indicate the range from the lower to the upper 95% confidence limits of the Swedish estimate. See text for details.

between the CCORE estimates and current practice in Sweden. These include 'classical' indications for RT such as head and neck and gynaecological cancer. Few sites seem to be 'over-prescribed' RT, whereas RT utilization in Sweden is low relative to the CCORE recommendations in stomach, pancreas and bladder cancer, Hodgkin's disease, non-Hodgkin lymphomas, brain and CNS tumours. A detailed analysis of these differences is beyond the scope of the QUARTS project.

Estimating RT needs using Sweden as a model

As an alternative to the QUARTS estimates based on the CCORE evidence-based ARR, we can estimate the required number of treatment units in order to reproduce the Swedish utilisation pattern in other EU countries. It should be stressed again, that these are not evidence-based estimates but simply reflect the actual use of radiotherapy in Sweden in 2001 for various tumour sites. Across the EU countries, the estimated number of linear accelerators needed is on average 30% lower with the Swedish rates than with the QUARTS estimates. This number depends on the pattern of incident cases and ranges between 25% (in the Czech Republic) and 34% (in Portugal).

Projections and planning

How wide is the gap between the current provision of radiotherapy and the QUARTS estimates? Fig. 4 compares the actual number of megavoltage units per million people in 10 EU countries with our estimated evidence-based provision rate. Interestingly, three countries, the Czech Republic, England and France, all have national guidelines for adequate provision of RT. In all three countries, the actual provision is not far from the national guideline, which probably reflects a tendency for guidelines to be 'retrofitted' to actual provision levels! While the French guideline is remarkably close to the QUARTS estimate, the English and Czech guidelines set targets that are well below the evidence-based best estimate.

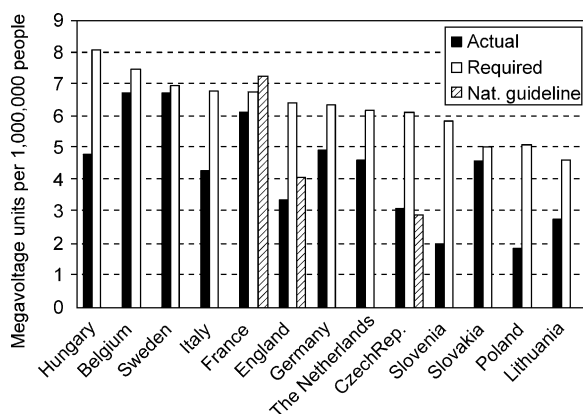


Fig. 4. Actual number of megavoltage therapy units (linacs and Cobalt units) in 13 European countries compared with the evidence-based required numbers derived in the QUARTS study and the national recommendation where available (Czech Republic, England and France).

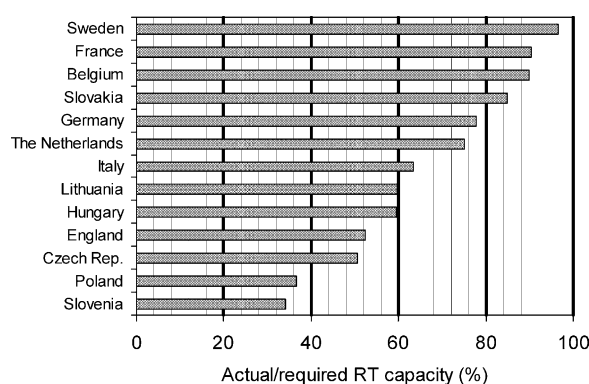


Fig. 5. The ratio of actual number of megavoltage therapy units (linacs and Cobalt units) to the evidence-based required numbers derived in the QUARTS study in 13 European countries where reliable data are available at the time of writing (October 2004).

Fig. 5 shows the actual provision as a percentage of the QUARTS estimates for the 13 countries analyzed above. The largest gap is seen for Slovenia and Poland followed by the Czech Republic and England. At the other end of the range, Sweden, France and Belgium are the only countries surveyed so far, where the availability of megavoltage therapy units reaches or exceeds 90% of the QUARTS estimate.

Governments and health authorities in several EU countries have identified under-provision of RT as a problem and are trying to improve the situation. Between the 1991 and 2001 SBU audits the proportion of Swedish cancer patients receiving radiotherapy increased from 32 to 47% [36]. An optimistic, but probably partly correct, interpretation would be that some of this increase was a consequence of the documented under-utilization of RT flagged up in the first SBU report. In the UK National Cancer Plan [42], under-provision of RT was acknowledged as a major cause for the relatively poor outcome in many cancers in the UK in comparison with other EU countries. The Cancer Plan also describes the 'postcode lottery', i.e. the large regional variability within the UK, in prescribing and getting access to RT. One of the specific proposed measures in the Cancer Plan was a major investment in RT facilities: from 3.5 megavoltage units per million in 2002 to 4.2 per million in 2004. Although this is a large relative improvement, the 2004 target is still far from the level that would allow delivery of the evidence-based RT utilization rates presented here. Other countries, e.g. the Netherlands and Denmark have also initiated an expansion of RT capacity in recent years.

Predicting future needs

Accurate forecasts of RT infrastructure needs are required for a consistent planning and investment policy assuring adequate access to optimal cancer care. Cancer incidence may change markedly over surprisingly short time spans. As an example, Fig. 6 shows the increasing annual incidence of breast cancer in the UK [9] from 1993 to 2000 and the estimated number of linear accelerators required for providing RT to these. The estimates are based on the actual RT utilization rate in breast cancer patients in Sweden in 2001 from the SBU audit [27]. Assuming an un-changed indication for RT, we estimate that over this relatively short

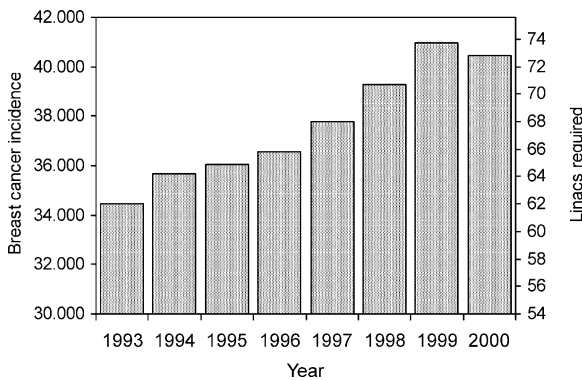


Fig. 6. Annual incidence of breast cancer in the UK from 1993 to 2000 and the corresponding number of linear accelerators required to treat these with RT based on the actual utilization rate in this indication in Sweden in 2001.

time span of seven years, the observed increase in the annual incidence of breast cancer in the UK has necessitated the addition of 11 new linear accelerators to provide the RT required in these cases.

Demographic studies show that the age distribution in the EU population will shift towards a higher proportion of elderly people in the coming years. This ageing of the population will not only increase the crude incidence of different cancers but will also affect the age distribution at presentation of the cancer patients. This in turn may affect the proportion of patients presenting with co-morbid conditions and the choice of treatment prescribed. Studies by Coebergh and colleagues have shown that age and co-morbid conditions affect the proportion of patients receiving RT [22,24] but that in those patients selected for RT there is no effect of age or co-morbidity on the prescribed dose-fractionation and no or only a limited effect on the incidence of RT side-effects. This is in concordance with other studies showing that chronological age is often not too important for the level of side-effects [35] although late functional endpoints may be influenced by a lower physiological reserved capacity in the elderly [5,6,20]. Thus, curative radiotherapy schedules are often well-tolerated in the elderly and RT may be used increasingly in this special population also because of its non-invasiveness and its potential for organ and function preservation.

The model developed by QUARTS can easily be applied with changed parameters either if indications for RT change or if the crude incidence of various cancer types changes. It is also straightforward to apply the model for a continuum of assumptions concerning future trends. In reality, of course, it is very difficult to predict major changes in the pattern of care that may depend on the exact outcome of a single or a few randomized trials. An example of this is the use of pre-operative RT for rectal cancer which was introduced in many centres based on the outcome of a single randomized controlled trial [25]. Also, major changes in the number of fractions used in a frequent indication could change the demand for RT units. This is reflected in the QUARTS model by inclusion of the fraction number weighting factor. A recent example is the change to single doses rather than multiple fractions for painful bone metastases [29]. Also, the outcome

of the UK START trial (Standardisation of breast Radiotherapy, principal investigator John Yarnold) comparing 13 versus 25 fractions in post-operative RT for breast cancer could have major implications for RT provision estimates as this indication alone accounts for 14% of the average QUARTS estimate of the need for RT in the 25 EU countries.

Despite all these potential confounding factors predictions of future RT needs have been shown to be of value. An RT infrastructure forecast for the Netherlands in 1993 [45] was revisited recently by Slotman and Leer [41] who concluded that from a 2003 perspective, the estimates produced in 1993 had been realistic albeit slightly conservative.

Sensitivity and limitations of the QUARTS study

A thorough sensitivity analysis was not attempted for the QUARTS estimates. However, if the somewhat lower QCRI ARR estimates were accepted for colo-rectal cancer [15], breast cancer [17], lung cancer [44] and prostate cancer [16] rather than the corresponding CCORE estimates, the average number of megavoltage treatment units required in the 25 EU countries decreased from 5.9 to 5.3 per million. The estimate for the top-ranked country, Hungary, decreased from 8.1 to 7.2 per million.

Hungary has a high incidence of head and neck cancer [19] and the fractionation weight factor described in Section 1.3 would give relatively high weight to these. Omitting the weight factor, i.e. assuming a weight of one irrespective of cancer type, and still keeping the lower QCRI estimates for the four common cancers listed above, reduced the average number of megavoltage units in the EU countries further from 5.3 to 5.2 per million. The estimate for Hungary decreased to 7.1, i.e. some 12% lower than the original QUARTS estimate. We conclude from this, that the QUARTS estimates are rather robust with respect to the difference between the QCRI and CCORE estimates and the application of the fractionation weighting factor.

Perhaps, the main information that could strengthen the QUARTS estimates would be information on the stage of disease at presentation in the various countries. Reliance on the CCORE ARR estimates implicitly assumes that stage distributions are similar in the EU and in the Australian systematic review. While this may be a reasonable assumption, it is not readily verifiable. One may speculate that patients in some EU countries tend to present with more advanced disease, where the curative potential of RT is less and therefore relatively simpler palliative techniques will dominate RT usage. This, however, is a somewhat short-sighted perspective: one would expect that with a more uniform access to health care and public education in all EU countries, these differences should diminish.

QUARTS did not attempt to produce estimates of the need for brachytherapy facilities in the EU countries. We feel that data are even scarcer for an evidence-based estimation of the appropriate use of brachytherapy.

The QUARTS study relied heavily on the SBU data and the evidence-based ARR estimates from the Australian CCORE group. Although we have no doubt about the quality of these data,

it would obviously have been a strength if the QUARTS estimates could have been cross-validated against other data sources. Especially, it would have been attractive if independent data sets of similar detail could be made available for central and southern Europe.

Cost and cost-effectiveness of radiotherapy in Europe

As mentioned above, the proportion of the global cancer care budget spent on RT is very modest, even in countries with optimal infrastructure. The latest cost calculations from the SBU, for example, estimated that RT consumes only 5.6% of the estimated total cost of oncology in Sweden [31]. Calculations performed in the 1990s on the cost of cancer care in the EU reported an average cost per RT course of €3000, whereas surgical procedures and chemotherapy were estimated to cost on average €7000 and €17,000, respectively [44]. Relating these figures to the clinical effect (RT contributes to some 40% of cures) suggests that RT is not only a relatively inexpensive cancer treatment, but a highly cost-effective one as well.

The estimation of infrastructure and staffing needs for RT within the EU, as accomplished in the QUARTS project, presents a unique starting point for a cost-calculation program for European radiotherapy. These data could be combined with demographical and epidemiological data on the different cancer types, with the evidence-based indications for RT and with data on the costs of the individual components of the RT process. Thus, all elements necessary to develop a comprehensive cost-accounting model for European RT would be available.

Activity-Based Costing (ABC) is an advanced cost-accounting technique that allocates indirect resource costs to the products using a multi-step allocation procedure based on activity consumption. ABC was developed with the aim to capture more accurately the economic consequences of product complexity (in terms of type and quantity of consumed resources and of production volume) and is of specific interest when overhead costs are considerable. Thus, the ABC-methodology is well suited for cost calculation of health care products [2,11].

In response to the need for reliable RT cost data, several RT departments have invested in the development of sophisticated systems (some of them based on the ABC methodology) for producing activity- or product-specific cost data at the institutional level [26,33]. As an example, the Leuven model demonstrated that even in this era of very sophisticated (and costly) RT equipment, personnel costs remain the most important cost component of a RT department, consuming about twice the budget of equipment (52 versus 28%). The fact that the daily RT delivery is very labour-intensive makes it the most costly of all RT activities. As a consequence, the cost of the final product is mainly determined by the length of the treatment (number of fractions) and by the daily treatment time. The widespread assumption that more sophisticated equipment will reduce personnel need (and the associated cost) was not confirmed in the Leuven study. As an example, although multi-leaf collimators allow more complex treatment

set-ups without a major increase in treatment time, they do not substantially shorten treatment time slots and consequently do not diminish the personnel cost. However, due to the indivisibility of these costly RT resources, one should aim for RT departments of sufficient size, if one wants to optimise cost-effectiveness. Within the Belgian context, a lower threshold for department size was found to be around 1000 patients treated annually [26].

Cost calculations performed at the department level are influenced by a variety of local aspects and are therefore not easily extrapolated to other departments, countries or health care systems. Ideally, when aiming to compare cost data amongst countries, a costing model should be developed at the supra-institutional, international level. As mentioned above, this could be accomplished using the QUARTS project data to develop an EU cost calculation model for RT. In a later stage of this project, a system can thus be designed to quantify the global costs of European RT departments, as well as their specific activity and product costs per treatment option and per cancer type. Benchmarking of the results from different countries within Europe may show inadequacies of certain national systems and yield strategies to move towards more cost-effective RT delivery. Together with the estimates of infrastructure and staffing needs, this can help decision-makers to make sound decisions about the investment of resources in terms of personnel, equipment and facilities.

In addition to its value in the cost-effective allocation of resources, such a cost-calculation model would yield the necessary cost data to perform economic evaluations of new treatment strategies and help to define correct reimbursement criteria.

Concluding remarks and the way ahead

Mainly due to limited funding, the QUARTS project has only been able to scratch the surface of defining the requirements for adequate and equitable access to RT in the 25 EU countries. In terms of the underlying knowledge-base, much has been accomplished in the last decade but there is still a long way to go before all RT is prescribed as evidence-based medicine [3]. Much of the current literature is of sub-optimal quality [4] and some indications for RT remain controversial. A major effort in clinical research is ongoing in an attempt to improve the evidence-base for prescription of RT and we strongly recommend that this be strengthened in the coming years.

One advantage of the QUARTS model is that it establishes RT requirements on the basis of a direct and transparent link between epidemiological data and the indications for RT derived from the best available evidence. With all its many strengths, the CCORE study still has a national, Australian starting point and we strongly recommend the creation of a similar resource covering a European perspective. As mentioned above, improved knowledge of the stage of disease at presentation of patients in each country would allow a more refined estimate of appropriate RT utilization rates at the national or regional level. This would require an EU-wide pattern-of-care study and we propose that such a study is undertaken.

QUARTS is just the beginning. We strongly encourage continuation of this study, with adequate support from the European Commission, as a way of improving RT provision on rational grounds throughout the European community and as a model for rational health care planning in the expanded EU.

Acknowledgements

The ESTRO project 'Radiation Therapy for Cancer: QUAntification of Radiation Therapy Infrastructure and Staffing Needs (QUARTS)' was supported by the EUROPEAN COMMISSION, Directorate General Research—Quality of Life and Management of Living Resources under contract: QLG4-CT-2002-30583.

QUARTS participants and supporting network

The QUARTS Study Group consisted of W. van den Bogaert (Project Lead), G. Heeren (Project Coordinator), B. Slotman (Lead WP1), B. Cottier (Lead WP2&3), S.M. Bentzen, B. Glimelius, K. Kesteloot and Y. Lievens (Leads WP4). Participants: J. Bernier, A. Bieta-Sola, B. Dubray, A. Kuten and M. Stuschke.

Active collaboration was also received from members of the Radiotherapy 2004 Committee: M. Coffey, M. Kinai, M. Krengli, E. Lartigau, P. Lukas, J. Malicky and E. Röttinger; from the International Atomic Energy Agency (P. Andreo, J. Izewska, B. Vikram) who provided access to the Dirac Directory; and from the European Commission: scientific officer J. Namorado.

Data were received from national contacts and representatives from the national radiotherapy and radiation physics societies: A. Kokobobo, Albania; S. Karamyan, Armenia; P. Lukas, Austria; M. Galina, Belarus; W. van den Bogaert, Belgium; N. Obralic, Bosnia-Herzegovina; T. Hadjieva, Bulgaria; E. Cepulic, Croatia; G. Christodoulides, Cyprus; H. Stankusova, Czech Republic; L. Specht, Denmark; M. Marjamagi, Estonia; T. Turpeenniemi-Hujanen, Finland; F. Eschwege, France; R. Gagaa, Georgia; E. Röttinger, Germany; D. Kardamakis & N. Throuvalas, Greece; J. Erfán, Hungary; D. Hollywood, Ireland; R. Pfeiffer, Israel; M. Krengli, Italy; D. Olina, Latvia; V. Atkocius, Lithuania; R. Untereiner, Luxembourg; S. Smickoska, Macedonia; M. Pirotta, Malta; B. Slotman, Netherlands; S. Levernes, Norway; J. Malicki, Poland; M. Pereira, Portugal; N. Ghilezan, Romania; Y. Pronin, Russia; N. Borojevic, Serbia-Montenegro; E. Boljesiková, Slovakia; P. Strojjan, Slovenia; A. Bieta Sola & L. Nuñez, Spain; B. Glimelius, Sweden; R. Greiner, Switzerland; M. Kinay, Turkey; D. Mechew, Ukraine; B. Cottier, United Kingdom.

Advice on specific aspects of the QUARTS study was received from: J. Borrás, J.W. Coebergh, E. van Eycken, T.R. Moller and S. Terpstra.

* **Corresponding author.** S.M. Bentzen, Department of Human Oncology, University of Wisconsin Medical School, K4/316 Clinical Sciences Center, 600 Highland Avenue, Madison, WI 53792-3684, USA. *E-mail address:* bentzen@humonc.wisc.edu

Received 22 November 2004; accepted 10 December 2004; available online 16 March 2005

References

- [1] Australian Health Technology Advisory Committee. Beam and isotope radiotherapy. Publication no. 2036. Australia: National Health and Medical Research Council; 1996.
- [2] Baker JJ. Activity-based costing and activity-based management for health care. Gaithersburg, MD: Aspen; 1988.
- [3] Bentzen SM. Towards evidence based radiation oncology: Improving the design, analysis, and reporting of clinical outcome studies in radiotherapy. *Radiother Oncol* 1998;46: 5-18.
- [4] Bentzen SM. A user's guide to evidence-based oncology. *Eur J Cancer Suppl* 2003;1:77-91.
- [5] Bentzen SM, Overgaard M, Thames HD. Fractionation sensitivity of a functional endpoint: Impaired shoulder movement after postmastectomy radiotherapy. *Int J Radiat Oncol Biol Phys* 1989;17:531-7.
- [6] Bentzen SM, Saunders MI, Dische S, Bond SJ. Radiotherapy-related early morbidity in head and neck cancer: quantitative clinical radiobiology as deduced from the CHART trial. *Radiother Oncol* 2001;60:123-35.
- [7] Board of the Faculty of Clinical Oncology. Equipment, workload and staffing for radiotherapy in the UK 1997-2002. London: The Royal College of Radiologists; 2003.
- [8] Boyle P, d'Onofrio A, Maisonneuve P, et al. Measuring progress against cancer in Europe: has the 15% decline targeted for 2000 come about? *Ann Oncol* 2003;14:1312-25.
- [9] Cancer Research UK. Cancer statistics. Internet website. Accessed 12 October; 2004. Available at <http://www.cancer-researchuk.org>.
- [10] Coles CE, Burgess L, Tan LT. An audit of delays before and during radical radiotherapy for cervical cancer—effect on tumour cure probability. *Clin Oncol (R Coll Radiol)* 2003;15: 47-54.
- [11] Cooper R. The rise of activity-based costing—Part one: what is an activity-based cost system? *J Cost Manage* 1988;Summer: 45-54.
- [12] Delaney GP, Jacob S, Featherstone C, Barton MB. Radiotherapy in cancer care: estimating optimal utilisation from a review of evidence-based clinical guidelines. Collaboration for Cancer Outcomes Research and Evaluation (CCORE). Sydney: Liverpool Hospital; 2003.
- [13] EUCAN. Cancer incidence, mortality and prevalence in the European union. Internet website. Accessed 4 August; 2004. Available at www-dep.iarc.fr/eucan/eucan.htm.
- [14] Falkmer U, Jarhult J, Wersall P, Cavallin-Stahl E. A systematic overview of radiation therapy effects in skeletal metastases. *Acta Oncol* 2003;42:620-33.
- [15] Foroudi F, Tyldesley S, Barbera L, Huang J, Mackillop WJ. An evidence-based estimate of the appropriate radiotherapy utilization rate for colorectal cancer. *Int J Radiat Oncol Biol Phys* 2003;56:1295-307.
- [16] Foroudi F, Tyldesley S, Barbera L, Huang J, Mackillop WJ. Evidence-based estimate of appropriate radiotherapy utilization rate for prostate cancer. *Int J Radiat Oncol Biol Phys* 2003;55:51-63.
- [17] Foroudi F, Tyldesley S, Walker H, Mackillop WJ. An evidence-based estimate of appropriate radiotherapy utilization rate for breast cancer. *Int J Radiat Oncol Biol Phys* 2002;53:1240-53.
- [18] Frodin JE, Jonsson E, Moller T, Werko L. Radiotherapy in Sweden—a study of present use in relation to the literature and an estimate of future trends. *Acta Oncol* 1996;35:967-79.
- [19] GLOBOCAN 2000. Cancer incidence, mortality and prevalence worldwide. Internet website. Accessed 4 August; 2004. Available at <http://www-dep.iarc.fr/globocan/globocan.html>.

- [20] Honore HB, Bentzen SM, Moller K, Grau C. Sensori-neural hearing loss after radiotherapy for nasopharyngeal carcinoma: individualised risk estimation. *Radiother Oncol* 2002; 65:9-16.
- [21] Hoskin PJ, Yarnold JR, Roos DR, Bentzen S. Radiotherapy for bone metastases. *Clin Oncol (R Coll Radiol)* 2001;13:88-90.
- [22] Houterman S, Janssen-Heijnen ML, Verheij CD, et al. Comorbidity has negligible impact on treatment and complications but influences survival in breast cancer patients. *Br J Cancer* 2004;90:2332-7.
- [23] James ND, Robertson G, Squire CJ, Forbes H, Jones K, Cottier B. A national audit of radiotherapy in head and neck cancer. *Clin Oncol (R Coll Radiol)* 2003;15:41-6.
- [24] Janssen-Heijnen ML, Smulders S, Lemmens VE, Smeenk FW, van Geffen HJ, Coebergh JW. Effect of comorbidity on the treatment and prognosis of elderly patients with non-small cell lung cancer. *Thorax* 2004;59:602-7.
- [25] Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* 2001;345:638-46.
- [26] Lievens Y, van den Bogaert W, Kesteloot K. Activity-based costing: a practical model for cost calculation in radiotherapy. *Int J Radiat Oncol Biol Phys* 2003;57:522-35.
- [27] Moller TR, Brorsson B, Ceberg J, et al. A prospective survey of radiotherapy practice 2001 in Sweden. *Acta Oncol* 2003;42: 387-410.
- [28] NICE. National Institute of Clinical Excellence. Internet website. Accessed 8 August; 2004. Available at <http://www.nice.org.uk/>.
- [29] Nielsen OS. Palliative radiotherapy of bone metastases: there is now evidence for the use of single fractions. *Radiother Oncol* 1999;52:95-6.
- [30] Nilsson S, Norlen BJ, Widmark A. A systematic overview of radiation therapy effects in prostate cancer. *Acta Oncol* 2004; 43:316-81.
- [31] Norlund A. Costs of radiotherapy. *Acta Oncol* 2003;42:411-5.
- [32] O'Rourke N, Edwards R. Lung cancer treatment waiting times and tumour growth. *Clin Oncol (R Coll Radiol)* 2000; 12:141-4.
- [33] Perez CA, Kobeissi B, Smith BD, et al. Cost accounting in radiation oncology: a computer-based model for reimbursement. *Int J Radiat Oncol Biol Phys* 1993;25:895-906.
- [34] Peto R, Boreham J, Clarke M, Davies C, Beral V. UK and USA breast cancer deaths down 25% in year 2000 at ages 20-69 years. *Lancet* 2000;355:1822.
- [35] Pignon T, Gregor A, Schaake KC, Roussel A, van Glabbeke M, Scalliet P. Age has no impact on acute and late toxicity of curative thoracic radiotherapy [see comments]. *Radiother Oncol* 1998;46:239-48.
- [36] Ringborg U, Bergqvist D, Brorsson B, et al. The Swedish Council on Technology Assessment in Health Care (SBU) systematic overview of radiotherapy for cancer including a prospective survey of radiotherapy practice in Sweden 2001—summary and conclusions. *Acta Oncol* 2003;42:357-65.
- [37] Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *Br Med J* 1996;312:71-2.
- [38] SBU. The Swedish council on technology assessment in health care: radiotherapy for cancer. Volume 1. *Acta Oncol* 1996;35.
- [39] SBU. The Swedish council on technology assessment in health care: radiotherapy for cancer. Volume 2: a critical review of the literature. *Acta Oncol* 1996;35.
- [40] Slotman BJ, Cottier B, Bentzen SM, Heeren G, Lievens Y, van den Bogaert W. Overview of national guidelines for infrastructure and staffing of radiotherapy. ESTRO-QUARTS: Work package 1. *Radiother Oncol* 2005;75:360-9.
- [41] Slotman BJ, Leer JW. Infrastructure of radiotherapy in the Netherlands: evaluation of prognoses and introduction of a new model for determining the needs. *Radiother Oncol* 2003;66: 345-9.
- [42] Talback M, Stenbeck M, Rosen M, Barlow L, Glimelius B. Cancer survival in Sweden 1960-1998—developments across four decades. *Acta Oncol* 2003;42:637-59.
- [43] The National Health Service. The NHS cancer plan. London: Department of Health; 2000.
- [44] Tyldesley S, Boyd C, Schulze K, Walker H, Mackillop WJ. Estimating the need for radiotherapy for lung cancer: an evidence-based, epidemiologic approach. *Int J Radiat Oncol Biol Phys* 2001;49:973-85.
- [45] van Daal WA, Bos MA. Infrastructure for radiotherapy in The Netherlands: development from 1970 to 2010. *Int J Radiat Oncol Biol Phys* 1997;37:411-5.
- [46] Waaijer A, Terhaard CH, Dehnad H, et al. Waiting times for radiotherapy: consequences of volume increase for the TCP in oropharyngeal carcinoma. *Radiother Oncol* 2003;66:271-6.