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Overview

Estimating the Population Benefit of Radiotherapy: Using Demand Models to Estimate Achievable Cancer Outcomes

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Abstract

The measurement of population benefits is important for priority setting, economic evaluation and quality improvement. It also informs advocacy. In this article, the use of demand models to estimate the achievable benefit of cancer therapy is reviewed. Achievable benefit refers to the treatment benefit achievable under optimal conditions. The population benefit of radiotherapy has been used as an example. Demand models provide a means of estimating the optimal proportion of patients with treatment indications when guidelines are followed. They may be used to estimate achievable benefit. The choice of end point should reflect the range of benefits associated with the treatment of interest. In some cases, further model development is needed if a pre-existing demand model is used. The benefit of treatment for each indication is estimated using a systematic review process. The highest level of evidence is used to define the benefit for each indication. In cases where multiple sources of the same level and quality of evidence exist, a meta-analysis is carried out. Population-based effectiveness data sources are considered, but three major challenges to their use are: (i) generalisability of the observed outcomes, (ii) data resolution and (iii) confounding and bias. The population benefit determined from this process describes the population proportion achieving a benefit due to the use of guideline-based treatment, compared with no use of that treatment. Sensitivity analysis provides a means for modelling the effect of model uncertainties. The predominant uncertainty is most often due to uncertainty in indication proportion. Preference-sensitive treatment decisions are a common example. The described approach to estimating the achievable benefit of cancer therapy is robust to model uncertainties, rapidly adaptable and is transparent. However, estimates rely on the quality of model data sources and may be affected by model assumptions. Models should be developed for a broader range of modalities of cancer therapy and relevant end points.

Key words: Demand model; population benefit; radiotherapy; effectiveness; systematic review; population outcomes; benchmarking

Statement of Search Strategies Used and Sources of Information

A sample search strategy for sources estimating population benefits of radiotherapy is provided in Table 1. For the overview, additional literature searches with combinations of keywords were performed. Key search terms were: 'radiotherapy', 'population', 'population based', 'groups', 'pragmatic', 'trial', 'benefit', 'efficacy', 'effectiveness', 'benchmark'. PubMed and Google Scholar were utilized. Reference lists from key publications were hand searched. Abstracts were reviewed and relevant manuscripts obtained.

Introduction

Measuring the population-level benefit of cancer treatment is important for a number of reasons. It provides necessary data for economic analysis. It can assist in priority setting for cancer services, inform advocacy and can also provide information on health system performance for quality improvement. Estimating the achievable benefit of cancer therapy in the 'real world' is the focus of this overview, using radiotherapy as an example. A brief background is first given, before elaborating on the

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Table 1
Example of an Ovid search strategy identifying articles on radiotherapy survival and local control benefit for cervical cancer

Ovid database inclusion: Medline, EMBase, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register, ACP Journal Club, Health Technology Assessment, NHS Economic Evaluation Database.	
1	((cancer$ or tumour$ or tumor$ or neoplas$ or malignan$ or carcinoma$) adj1 (cervi$)).mp. [mp = ti, ab, tx, kw, ct, ot, sh, hw, nm, ui, tn, dm, mf]
2	(radiation or radiotherapy or irradiation).mp. [mp = ti, ab, tx, kw, ct, ot, nm, hw, ui, sh, tn, dm, mf]
3	(adjuvant or “local control” or mortality or recurrence or survival or outcome or benefit).mp. [mp = ti, ot, ab, tx, kw, ct, sh, hw, nm, an, ui, tn, dm, mf]
4	1 and 2 and 3
5	limit 4 to human [Limit not valid in CDSR, ACP Journal Club, DARE, CCTR, CLCMR; records were retained]

demand model method of estimating the achievable benefit of a cancer therapy used according to guidelines.

Efficacy versus Effectiveness

Clinical trials investigating novel cancer therapies describe treatment efficacy in a carefully defined population. If a therapy shows efficacy, it will often be adopted for use in the general population. Given that this population is often different from the patient mix in clinical trials, the observed benefit may differ. The degree of treatment benefits when applied in the general population or ‘real world’ is defined as its effectiveness [1]. The measured effectiveness of a given therapy may be influenced by tumour-related, patient-related, treatment-related and health system-related factors. For example, in a population-based study of bladder cancer in the province of Ontario, age, socioeconomic status and comorbidity score (patient-related factors) were associated with cancer-specific survival, as was histology (a tumour-related factor) [2]. In Ontario, the adoption of synchronous chemotherapy with radical radiotherapy (a treatment-related factor) for cervical cancer was associated with improved population survival, as found in randomised trials [3]. Some health system-related factors can result in gaps between the achieved benefit of a given therapy and the achievable benefit by affecting either access to treatment or the quality of treatment [4]. For instance, longer waiting times for radiotherapy are associated with worse local control and survival of head and neck cancer [5].

Early Measures of Radiotherapy Population Benefit

Over 20 years ago, Glazebrook [6] estimated the population benefit of radiotherapy in a Canadian setting. All years of survival after radiation treatment were attributed to the effects of radiotherapy [6]. Although an attractive first-order approximation, this approach ignored the contribution of other modalities to cancer outcomes. Attributing all survival benefit after radiotherapy to the effects of radiotherapy also ignores the situation where untreated cancer is not immediately life-threatening. Early prostate cancer is an important example.

In 1995, Barton *et al.* [7] accounted for the variable contribution of radiotherapy to survival through literature-informed estimation. Overall, 21.4% of the survival after radiotherapy was attributed to the effects of radiotherapy. Adjusting for the proportional contribution of radiotherapy, the estimated average survival benefit for patients treated with radiotherapy was one year.

Although a more evidence-based approach, this method had some limitations. The study did not involve a clearly described systematic review when estimating the proportional contribution of radiotherapy to overall survival. Also, overall survival estimation relied on a single Australian institution’s cancer outcomes, limiting generalisability. It was also unknown if patients were referred and selected for radiation according to guidelines, or whether treatments were according to accepted technical standards and protocols. It was hence unclear if the reported treatment effectiveness represented what was achievable with radiotherapy in the general population under optimal conditions.

Estimation of the Population-based Demand for Radiotherapy

A substantial amount of work has now gone into estimating the demand for radiotherapy when utilised according to best practice. This is fundamental to measuring the benefits of radiotherapy under optimal conditions. The two established approaches to estimating demand for radiotherapy are evidence-based estimation and criterion-based benchmarking.

The criterion-based benchmarking approach assumes that radiotherapy would be practiced appropriately if the factors that would allow for optimum decision making and treatment accessibility are present in the community [8]. The criteria under which optimal delivery of radiotherapy may occur are first investigated, and then the radiotherapy rates in the ‘real world’ are measured in settings meeting the criteria. Use of a criterion-based benchmark approach has not been investigated as a basis for estimating radiotherapy population benefit under optimal conditions.

Evidence-based estimation uses evidence-based guidelines to determine what the indications for radiotherapy should be, and estimates their population incidence using the highest level of epidemiological evidence available [9]. These methods have been described in detail by others as part of this special issue on evidence-based demand for cancer therapy. In the following sections the use of evidence-based demand models as a framework for population benefit estimation is described.