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Review

The level of patient-reported outcome reporting in randomised controlled trials of brain tumour patients: A systematic review

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Abstract ***Background:*** To determine the net clinical benefit of a new treatment strategy, information on both survival and patient-reported outcomes (PROs) is required. However, to make an adequately informed decision, PRO evidence should be of sufficiently high quality.
Objective: To investigate the methodological quality of PRO reporting in randomised controlled trials (RCTs) in patients with brain tumours, and to assess the proportion of studies that should impact clinical decision-making.
Methods: We conducted a systematic literature search in several databases covering January 2004 to March 2012. We selected relevant RCTs and retrieved the following data: (1) basic trial demographics and PRO characteristics, (2) quality of PRO reporting and (3) risk of bias.

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Studies that should impact clinical decision-making based on their methodological robustness were analysed systematically.

Results: We identified 14 RCTs, representing over 3000 glioma patients. Only two RCTs (14%) satisfied sufficiently many key methodological criteria to provide high-quality PRO evidence, and should therefore impact clinical decision-making. Important methodological limitations in other studies were lack of reporting of the extent (43%) and reasons (86%) of missing data and statistical approaches to handle this (71%). PRO results were not interpreted in 79% of the studies and clinical significance was not discussed in 86%. Studies with high-quality PRO evidence generally showed lower risk of bias.

Conclusions: Investigators involved in brain tumour research should pay special attention to methodological challenges identified in current work. The level of PRO reporting should continue to improve in order to facilitate a critical appraisal of study results.

1. Introduction

Although primary brain tumours constitute only 2% of all adult cancers [1], they result in a disproportionate share of cancer morbidity and mortality. Gliomas are the most frequent primary brain tumours in adults, and prognosis depends on histological tumour type, grade and tumour genetics [2]. Typically, patients with low-grade gliomas live longer than patients with higher grade gliomas. However, despite multimodal treatment with surgery, radiotherapy and chemotherapy, gliomas remain largely incurable [2,3].

Traditional outcome measures in randomised controlled trials (RCTs) are overall and progression-free survival. The incurable nature of gliomas has led to the recognition that palliation and maintenance or improvement of health-related quality of life (HRQoL) are just as important as prolonged survival. Consequently, HRQoL has become an important outcome measure in clinical brain tumour research [4–7]. HRQoL is a patient-reported outcome (PRO), reflecting the patient's perspective [8], and is a multidimensional concept covering physical, psychological and social domains as well as symptoms induced by the disease and its treatment [9]. Several PRO measures are available, ranging from one-dimensional (measuring a single aspect of HRQoL, such as fatigue) to multidimensional measures.

To determine the net clinical benefit of a new treatment strategy, information on both survival and HRQoL is required. The benefits of a new treatment strategy in terms of prolonged survival have to be carefully weighed against the side-effects of this treatment. HRQoL measurements should therefore be included in RCTs. In addition, it is important that PROs generate high-quality evidence to be of value. Inadequate or poorly designed RCTs including PRO measurements, or simply reporting insufficient PRO information, may limit their ability to inform clinical decision-making. In 2002, a systematic review showed that many RCTs in brain tumour patients which included PRO had methodological limitations, hampering the interpretation of the results [10].

The primary objective of this study was to investigate the methodological quality of PRO reporting in RCTs of primary brain tumours published since 2004. The secondary objective was to assess the proportion of studies that should impact clinical decision-making based on their methodological robustness.

2. Methods

2.1. Search strategy for identification of studies

We conducted a systematic literature search in the e-resources PubMed/Medline, the Cochrane Library, PsycINFO, and PsycARTICLES covering January 2004 to March 2012. The search strategy consisted of a combination of two strings, one related to PRO measures and one related to primary brain tumours (see supplementary file for full search string).

In PubMed/Medline, the search strategy was restricted to RCTs. Moreover, only English-language articles were considered. All retrieved titles and abstracts were screened, and full-texts of potential relevant articles were read and the reference lists of these articles were screened for additional studies. In addition, experts in the field were contacted to identify possible relevant articles that were not retrieved in the electronic search.

Preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines were followed to document details on the search strategy and selection processes [11].

2.2. Criteria for considering studies

2.2.1. Type of participants

Studies were considered to be eligible if adult ($\geqslant$18 years) patients were included with histologically confirmed primary brain tumours, or those with recurrence, regardless of the type and grade of the