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Original Research

Publication status of contemporary oncology randomised controlled trials worldwide

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Abstract ***Background:*** Little is known about the extent of selective publication in contemporary oncology randomised controlled trials (RCTs) worldwide. This study aimed to evaluate the rates of publication and timely publication (within 24 months) for contemporary oncology RCTs from all over the world. We also investigated the trial characteristics associated with publication and timely publication.

Patients and methods: We identified all phase III oncology RCTs registered on ClinicalTrials.gov with a primary completion date between January 2008 and December 2012. We searched PubMed and EMBASE to identify publications. The final search date was 31 December 2015. Our primary outcome measure was the time to publication from the primary completion date to the date of primary publication in a peer-reviewed journal.

Results: We identified 598 completed oncology RCTs; overall, 398 (66.6%) had been published. For published trials, the median time to publication was 25 months (interquartile range, 16–37 months). Only 192 trials (32.1%) were published within 24 months. Timely publication was independently associated with trials completed late in 2012. Trials conducted in Asia and other regions were less likely to have timely publication, but trials conducted in different locations were all equally likely to be published. Industry- and NIH-funded trials

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were equally likely to be published timely or at any time after trial completion. Among 391 published trials with clear primary outcomes, there was a trend for timely publication of positive trials compared with negative trials.
Conclusions: Despite the ethical obligations and societal expectations of disclosing findings promptly, oncology RCTs performed poorly.

1. Introduction

Randomised controlled trials (RCTs) are the gold standard for evidence-based practice in medicine. Physicians and policy-makers generally depend on publications in peer-reviewed biomedical journals, an important and direct means of disseminating trial results, to learn about RCT findings [1–3]. The timely trial results publication is widely recognised as a prerequisite for ensuring that clinical decisions by physicians and other stakeholders reflect the best scientific evidence and yield maximal benefits for public health and scientific progress [3–6]. However, trial results are often not shared publicly in a timely fashion; about 25–50% of the clinical trials remain unpublished, sometimes even years after completion [3–10]. Most of these studies are for trials conducted in the United States, and a recent study found poor performance and noticeable variation in clinical trial result publication across leading US academic medical centres, with the overall publication rate ranging 35–67% and the timely publication rate, i.e. within 24 months, ranging 11–40% [6]. This selective publication of clinical trials could limit the evidence available in the medical literature, impairing evidence-based clinical practice.

Cancer is a major public health problem worldwide and is the leading and second leading cause of death in China and the United States, respectively [11,12]; it remains the condition most commonly studied in clinical trials [6]. The interpretation of trials, especially phase III RCTs, is of great significance for treatment decisions in medical oncology. However, little is known of the extent of selective publication of oncology RCTs in other regions over the world. An early study simply described that only 18% of the US cancer drug RCTs completed before 2010 were published within 2 years, and the publication rate of RCTs were relatively lower than other clinical trials [13]. This is of particular concern because RCTs have more important implications for evidence-based practice, and it remains unclear the publication status of trials conducted in other areas. Accordingly, we extensively evaluated the publication and timely publication (within 24 months) rates for contemporary oncology RCTs from all over the world, and investigated the trial characteristics associated with publication and timely publication.

2. Methods

2.1. Data source and study sample

ClinicalTrials.gov is a publicly available trial registry and results database developed and maintained by the National Library of Medicine (NLM) for the National Institutes of Health (NIH). We used ClinicalTrials.gov data through the Aggregate Analysis of ClinicalTrials.gov database, reflecting data downloaded as of 27 September 2015 under the Clinical Trials Transformation Initiative. Among approximately 200,000 studies registered on ClinicalTrials.gov on 27 September 2015, we identified 633 phase III oncology RCTs (Fig. 1). We excluded phase II or II/III RCTs to avoid potential bias, as phase II trials often require additional studies to provide conclusive evidence [14]. The details of data source and study sample were presented in the Supplementary Methods.

2.2. Publication status and time to publication

To determine the publication status for the 633 trials, 2 reviewers (XL, JWL) independently searched the biomedical literature between October and December 2015, identifying the earliest primary publication date of the main results of the trial which reported the primary outcome. If there were multiple primary end-points, we used the earliest publication that reported the results of at least one primary outcome. A systematic 4-step search strategy was used to identify publications. The details of search strategy and methods to ensure manual review quality and consistency were presented in the Supplementary Methods.

For all published trials, we determined the time to publication (in months) from the primary completion date to the date of primary publication. For publications available online ahead of print, we adopted the earlier online access date. The follow-up time (in months) for trials not yet published was calculated from the primary completion date to the date of our final search (December 2015). As dates are reported by the month and year only, we defined the day of trial completion and publication as day 15 of the corresponding month for calculation. Given our interest in examining timely publication, we selected a publication