

# Modern cancer trials still lack information about QoL impacts on patients

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The majority of the initial seminal cancer treatment trials during the 1970s and later on focused on clinical efficacy and clinician-assessed harms. Patient-reported outcome measures (PROMs) including health-related quality of life (QoL) were rarely collected. Even once they started to be incorporated into clinical trials more routinely, PROMs were not often taken seriously. This was at a time when many cancer types had poor prognoses, so the primary goal was to find effective therapies that significantly improved survival, even when many interventions (chemotherapies and radiotherapy) had serious toxicities.

However, several cancer types are now practically curable, for example, early stage breast cancer, and well-differentiated thyroid cancer; and modern anticancer therapies including targeted agents and focused radiotherapy techniques (such as intensity modulated radiotherapy and proton beam therapy) can be associated with fewer toxicities and are more tolerable for patients. Clinical efficacy and harms are still essential outcomes but so is the quality of survival as patients live longer. Even for advanced cancers, where life expectancy might only be 6 months, it matters whether this short time is spent with some level of comfort or with adverse treatment-related QoL symptoms.

The article by Marandino *et al*<sup>1</sup> shows an overview of QoL reporting among cancer trials in 11 major medical journals between 2017 and 2021; updating a similar analysis they had performed for 2012–2016.<sup>2</sup> Despite many experts and decision-makers requesting that QoL be included, this new analysis showed that in the latest time period 32% of drug trials for solid tumours in adults did not collect such data. Unsurprisingly, commercial-sponsored trials (pharma companies) were more likely to collect QoL data than academic-sponsored studies (OR 1.48), because regulators and especially

health technology assessment (HTA) agencies expect this outcome measure. But the commercial-sponsored trials were then more likely to not publish in journals (51.6% vs 39%). This could partly be due to the companies only including QoL in their regulatory or HTA submissions; better than not reporting these data at all.

Perhaps the most disappointing finding in the study was that 70% of trials had still not reported the QoL results as long as 2 years after the primary efficacy publication. There does not seem to be many reasonable excuses for this. Similarly of note is that journals with high impact factors are less likely than those with low-impact factors to include QoL within the primary efficacy publication.

Limitations of this article<sup>1</sup> are exclusion of trials of haematological malignancies and non-drug interventions such as surgery.<sup>3</sup> It would also be useful to see how QoL data are collected and reported in several paediatric cancers where the goal is to reduce treatment exposure (fewer drugs or lower doses) to reduce toxicities and maintain/improve QoL, without materially affecting efficacy.

Appropriate QoL/PROMs instruments need to be selected carefully to reflect the particular cancer type, treatments and associated symptoms.<sup>4</sup> Also, QoL reporting in journals should be detailed enough to see whether trial treatments influence specific symptoms. 'Overall' or 'global' scores are often insensitive, and may give the false impression of minimal/no adverse impact of a new treatment. For example, in a trial of pazopanib versus placebo for metastatic soft tissue sarcoma, there was hardly any difference in global QoL score between the trial arms, but there were clear negative effects on nausea, loss of appetite and fatigue.<sup>5</sup>

There should be four main areas of trial results reported together as standard: efficacy, adverse events, adherence and QoL/



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PROMs.<sup>6</sup> Journal editors and peer reviewers should encourage this, and it would maximise the report's appeal to readers. In doing so, the message that all trials should include QoL as a major outcome measure in the design will spread. Nearly all journals now have online supplementary appendices that do not have a limit to the word count or number of tables/figures, so there is no justification for distributing trial results across different publications and over time. Having the main trial findings in a single journal article allows a fuller and upfront assessment of benefits and harms.<sup>7 8</sup>

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