European Journal of Cancer 56 (2016) 144–161

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Review

Patient-reported outcomes in head and neck and thyroid cancer randomised controlled trials: A systematic review of completeness of reporting and impact on interpretation☆

Rebecca L. Mercieca-Bebber [a,b,*], Alessandro Perreca [c], Madeleine King [a,b], Andrew Macann [d], Katie Whale [e], Salvatore Soldati [c], Marc Jacobs [f,g], Fabio Efficace [c]

[a] *Central Clinical School, Sydney Medical School, University of Sydney, NSW 2006, Australia*
[b] *Psycho-oncology Co-operative Research Group, School of Psychology, University of Sydney. Level 6 North, Chris O'Brien Lifehouse C39Z, University of Sydney, NSW 2006, Australia*
[c] *Data Center and Health Outcomes Research Unit, Italian Group for Adult Hematologic Diseases (GIMEMA), Via Benevento, 6, 00161 Rome, Italy*
[d] *Department of Radiation Oncology, Auckland Regional Cancer and Blood Service, Auckland City Hospital, 1023, New Zealand*
[e] *School of Social and Community Medicine, University of Bristol, Bristol, UK*
[f] *Academic Medical Center, University of Amsterdam, Department of Medical Psychology, Amsterdam, The Netherlands*
[g] *Pharmerit International. Marten Meesweg 107, 3068 AV, Rotterdam, The Netherlands*

Received 13 November 2015; received in revised form 22 December 2015; accepted 23 December 2015
Available online xxx

KEYWORDS
Quality of Life [I01.800];
Patient-reported outcome;
Data Reporting;
Systematic Review;
Head and Neck

Abstract ***Aim:*** To determine the completeness of reporting of patient-reported outcomes (PROs) of head and neck cancer (HNC) and thyroid cancer randomised-controlled trials (RCTs) and identify PRO measures used.
Methods: A systematic literature search was conducted for HNC and thyroid cancer RCTs with PRO end-points (January 2004–June 2015). Two investigators independently extracted data, assessed adherence to the International Society for Quality of Life Research (ISOQOL) PRO reporting standards and concordance between hypotheses and PRO measures used. Data were entered into the Patient-Reported Outcomes Measurements Over Time in Oncology (PROMOTION) Registry.

☆ This work was presented at the International Society for Quality of Life Research (ISOQOL) Scientific Meeting in Vancouver, BC, Canada in October 2015, Abstract number: 2007.

* *Corresponding author*: Quality of Life Office, Level 6 North, Chris O'Brien Lifehouse C39Z, University of Sydney, NSW 2006, Australia. Tel.: +61 2 9114 1365.
E-mail address: Rebecca.Mercieca@sydney.edu.au (R.L. Mercieca-Bebber).

http://dx.doi.org/10.1016/j.ejca.2015.12.025

Neoplasms;
Thyroid Neoplasms

Results: Sixty-six RCTs were included, 56 (85%) HNC and 10 (15%) thyroid cancer. Twenty-two (33%) included a primary and 44 (67%) included a secondary PRO end-point. A total of 40 unique PRO measures were used. Adherence to the ISOQOL PRO reporting standards was higher for RCTs with primary PRO end-points than for secondary PRO end-points: (mean adherence of 43% and 29% respectively). Completeness of PRO reporting did not improve with time: $r = .13$, $p = .31$. ISOQOL checklist items poorly reported included: PRO hypothesis (reported for eight RCTs, 12%), justification chosen of PRO measures (n = 16, 24%), rates of missing PRO data (n = 19, 29%), and generalisability of results (n = 12, 18%). Encouragingly, PROs were identified in 55 RCT abstracts (83%) and PRO results interpreted for 30 RCTs (45%).

Conclusions: Reporting of PRO end-points was more comprehensive in RCTs with primary rather than secondary PRO end-points. Improvement is needed in the transparent reporting of PRO studies, particularly regarding data collection, analyses and generalisability of PRO results.

Head and neck cancers (HNC) include cancers of the nasopharynx, oral cavity, oropharynx, hypopharynx, larynx, nasal cavity, paranasal sinuses and salivary glands. Though usually not classified a HNC, cancer of the thyroid is often grouped with HNC due to its similar anatomic location. Thyroid cancer is the most common endocrine malignancy based on data from the United States of America (USA) [1] and the fifth most common cancer diagnosis in women [2]. In Europe, there were approximately 192,400 new cases of cancer of the oral cavity, pharynx, larynx, and thyroid in 2012, and approximately 69,800 deaths from these cancers in the same year [3]. In the USA, HNC incidence rates are increasing, particularly in men [2]. Overall 5-year survival rates are 62% and 98% for HNC and thyroid cancers respectively [2], thus patient quality of life (QOL) and functional outcomes are important considerations in long term patient care in addition to tumour control [4].

The head and neck anatomy is associated with functional roles of breathing, vocalising, eating and swallowing. Treatment can lead to issues with these functions. Surgery is the most common treatment for thyroid cancer [5] and is used extensively as a primary treatment in HNC as well. Depending on the targeted site and degree of manipulation required, surgery can cause dysfunction or disfigurement, leading to issues with body image, social withdrawal, anxiety and poor QOL [6–8], issues which can persist into survivorship [9].

Radiotherapy is also used as a primary HNC treatment modality, delivered alone or in combination with surgery or chemotherapy. Approximately two-thirds of all HNC patients treated with radiotherapy will develop severe oral mucositis – a painful temporary ulceration and inflammation of the mucosa and submucosa [10], associated with pain and difficulty swallowing, copious oropharyngeal secretions, taste changes, vocal problems, sleep disturbance, psychosocial issues and poor QOL [11]. Also common is xerostomia, dryness of the mouth caused by damage to the salivary glands and reduced saliva production. Xerostomia causes difficulty swallowing (dysphagia), speaking and eating, weight loss, and increased risk of oral infection and dental caries [12].

High side-effect burden associated with HNC and thyroid cancer treatment can profoundly impact QOL. Thus patient-reported outcome (PRO) assessment is crucial in randomised-controlled trials (RCTs) of these cancers to provide effective, evidence-based supportive care, symptom management and rehabilitation [4,9,13]. The gap that has sometimes been observed between clinician- and patient- reports of symptom severity further highlights the importance of PROs in HNC and thyroid cancer research [14,15]. Indeed the need for PROs in oncology RCTs is being increasingly recognised, with an estimated 29% of oncology trials including a PRO end-point [16].

The quality and value of PRO data and resultant evidence about effects of treatments on PROs depends heavily on the quality of methodology and reporting [17,18]. Brundage and colleagues found that variation in the type, formats and quality of PRO data reported made translation of PRO findings difficult [19]. Additionally, there is growing evidence that reporting of PRO studies is often incomplete or suboptimal in cancer RCTs [20–22]. This is of concern as incomplete reports may be a barrier to research translation if PRO findings or their generalisability is not clearly communicated to clinical readers [19]. To date, the level of PRO reporting specifically in HNC and thyroid cancer trials is not known, thus it is unclear if reporting completeness has been a barrier to the translation of PRO findings into HNC or thyroid cancer care.

We undertook a systematic review of HNC and thyroid cancer RCTs with PRO end-points, aiming to: 1) systematically assess the completeness of reporting over time by status of the PRO end-point (primary