

Summary



Chapter 1 provides background information on supportive care targeting head and neck cancer (HNC) patients. Head and neck cancer encompasses cancers originating from the oral cavity, oropharynx, hypopharynx and larynx, and is respectively the seventh and ninth most common cancer diagnosis in men and women. Due to HNC and its treatment, HNC patients often experience general and HNC-specific symptoms (e.g., fatigue, difficulty swallowing, and psychological symptoms), which can have a major influence on a patient's health-related quality of life. Supportive care can be offered in order to prevent and manage these symptoms and its influence on health-related quality of life. It encompasses information and care related to, for example, physical functioning, daily living, psychological functioning, sexuality, and lifestyle. Optimal supportive care is tailored to the needs of the individual patient, is effective, and provides good value for money (i.e., is cost-effective). The aim of this thesis was to obtain insight into supportive care needs in HNC patients using psychometrically tested patient-reported outcome measures, and to provide an economic perspective on supportive care in HNC patients.

MEASURING SUPPORTIVE CARE NEEDS IN HEAD AND NECK CANCER PATIENTS

The first part of this thesis (chapter 2, 3 and 4) focused on measuring the need for supportive care in HNC patients. *Chapter 2* aimed to identify cutoff scores on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-questions (EORTC QLQ-C30) and the HNC-specific module (EORTC QLQ-H&N35) that can discriminate between HNC patients with and without perceived unmet supportive care needs. On 12 of the 28 EORTC domains candidate cutoff scores (sensitivity ≥ 0.80 and specificity ≥ 0.60) or borderline candidate cutoff scores (sensitivity ≥ 0.70 and specificity ≥ 0.60 or sensitivity ≥ 0.80 and specificity ≥ 0.50) could be identified. Candidate cutoff scores of 90 were found for the EORTC QLQ-C30 domains physical functioning, role functioning, emotional functioning and social functioning. Cutoffs of 5 or 10 were found for the EORTC QLQ-H&N35 domains on swallowing (5), sexuality (10) and sticky saliva (10). Borderline candidate cutoff scores of 80 were found on global quality of life and of 5 - 30 on fatigue (20), oral pain (10), speech (10, 20, 30) and social eating (5). These cutoff scores may facilitate the interpretation of a patient's individual outcomes on the EORTC QLQ-C30 and QLQ-H&N35 in clinical practice.

Chapter 3 evaluated the psychometric characteristics of the Dutch translation of the Supportive Care Needs Survey Short-Form 34 (SCNS-SF34) and the newly developed HNC-specific module (SCNS-HNC) for measuring supportive care needs in HNC patients. First, the content validity of the newly developed SCNS-HNC was investigated. The content validity was overall considered to be good, although some frequently discussed HNC topics were missing. Second, the factor structure of both the SCNS-SF34 and SCNS-HNC was investigated. For the SCNS-SF34, four underlying factors with good internal consistency were identified, namely physical and daily living (Cronbach's alpha = 0.89), psychological (Cronbach's alpha = 0.95), sexuality (Cronbach's alpha = 0.79), and health system and information and patient support needs (Cronbach's alpha = 0.95). For the SCNS-HNC two underlying factors were identified: HNC-specific functioning (Cronbach's alpha = 0.89) and lifestyle (Cronbach's alpha = 0.60), and one single item on care of your stoma and/or voice prosthesis. Third, the construct validity was investigated. Construct validity of the SCNS-SF34 and the SCNS-HNC was good; 96% and 89% of the hypothesized correlations with other patient-reported outcome measures were found, and 57% and 67% also showed the hypothesized magnitude of correlation. Regarding expected differences in supportive care needs among groups with different age, sex, treatment procedures, or time since last treatment, three of the ten hypothesis were confirmed. The SCNS-SF34 domains discriminated between treatment procedure (physical and daily living and psychological needs) and time since treatment (health system, information, and patient support needs). Finally, test-retest reliability was studied. Test-retest reliability was in general good (intraclass correlation coefficients (ICC) ranged 0.67 - 0.83), although slightly too low for the domain on lifestyle (ICC = 0.67). Based on the findings of this study it was concluded that the SCNS-SF34 and the SCNS-HNC are valid and reliable instruments to evaluate the need for supportive care among (Dutch) HNC patients.

In *chapter 4*, the SCNS-SF34 and SCNS-HNC were used to measure (unmet) needs for supportive care in a specific group of HNC patients, namely patients treated with total laryngectomy (TL). Results showed that the need for supportive care was highest for HNC-specific functioning needs (76%), followed by health system, information & patient support (69%), psychological (66%), physical and daily living (62%), sexuality (38%) and lifestyle needs (19%). In total 71% reported at least one low, moderate or high unmet need, especially regarding HNC-specific functioning (53%), psychological (39%), physical & daily living (37%), and health system, information & patient support needs (35%). Female gender, living alone, and having a voice prosthesis were significantly positively associated with unmet needs on at least one supportive care domain. A worse health-related quality

of life was associated with unmet needs on all domains. As the total explained variance is with 10% – 29% rather low, further research is, however, recommended on explanatory factors in more detail. Also more research is needed on the course of (unmet) supportive care needs over time.

AN ECONOMIC PERSPECTIVE ON SUPPORTIVE CARE IN HEAD AND NECK CANCER PATIENTS

The second part of this thesis (chapter 5, 6 and 7) provided an economic perspective on supportive care. *Chapter 5* provided insight into the association between patient activation for self-management and total costs from a healthcare and societal perspective among TL patients. Patient activation was measured using the patient activation measure. A patient's total score was categorized into one of four levels of patient activation (low to high patient activation). Total costs were measured by patient self-report using the medical consumption and productivity cost questionnaire. Total costs from a healthcare perspective included healthcare costs, such as costs of visiting the medical specialist or costs of admission to the medical center. Total costs from a societal perspective included, besides healthcare costs, also costs relevant from a societal perspective, such as productivity losses and informal care costs. Results of this study showed that the total costs from a healthcare perspective in the three months prior to the study ranged from €1,346 (standard deviation (SD) = 2,597) in the group with the highest (best) patient activation level to €2,282 (SD = 3,798) in the group with the lowest (worst) patient activation level. Total cost from a societal perspective ranged from €1,909 (SD = 3,855) in the group with the highest (best) patient activation level to €2,627 (SD = 4,147) in the group with the lowest (worst) patient activation level. It was found that patients with a better patient activation for self-management are likely to report lower total costs from both a healthcare as a societal perspective, even after adjusting for socio-demographic and clinical characteristics. However, after adjustment for HRQOL, no such association seemed to be present anymore. More research is needed on the causality of the association between patient activation, HRQOL and total costs from both a healthcare and a societal perspective.

Chapter 6 reviewed the literature on the cost-effectiveness and cost-utility of psychosocial supportive care in cancer patients in general. A systematic search in PubMed and Web of Science resulted in 539 unique records, of which 11 studies were included that assessed

the cost-effectiveness or cost-utility of psychosocial care in cancer patients. Most studies were recently performed (2014 or 2015) and included breast cancer or mixed cancer populations. The studied interventions included collaborative care interventions (4 studies), group interventions (4 studies), individual psychological support (2 studies) and individual psycho-education (1 study). In general, results indicated that psychosocial care is likely to be cost-effective at different, potentially acceptable willingness-to-pay thresholds.

In *chapter 7* the cost-utility of a stepped-care program targeting anxiety and depression among HNC and lung cancer patients (published after the conduction of the review in chapter 6) was evaluated by means of a randomized controlled trial. This stepped care program consisted of four steps: 1) watchful waiting, 2) guided self-help, 3) face-to-face problem-solving therapy, and 4) specialized psychological interventions and/or medication. Patients stepped-up to the next step only when symptoms of anxiety and/or depression did not resolve. In total 156 patients were randomly assigned to stepped care or care-as-usual. Total costs from a societal perspective were calculated from start of study to 12 months after the end of the stepped care or care-as-usual period. For the total effects quality-adjusted life years were calculated. Total mean cumulative costs were €-3,950 (95% confidence interval (CI) ranged €-8,158 to €-190) lower and mean number of quality-adjusted life years were 0.116 (95%CI ranged 0.005 to 0.227) higher in the stepped care group compared to the care-as-usual group. The probability that quality-adjusted life years were higher and total costs were lower in the stepped care group was 96%. Four additional analyses which were conducted to assess the robustness of this findings showed a probability of 84% - 98% that quality-adjusted life years were higher and a probability of 91% – 99% that total costs were lower. In combination with previous findings on the efficacy of this stepped care program (as published by Krebber et al. (2016)), it was concluded that stepped care is expected to be beneficial in routine HNC and lung cancer practice. Further research is needed on optimal implementation of this stepped care intervention.

DISCUSSION AND CONCLUSION

Chapter 8 discussed the main findings presented in this thesis. Also, strengths and limitations, implications for clinical practice and recommendations for further research were outlined. To facilitate this discussion the supportive care framework of Fitch (2008) was used. This framework distinguishes among four different levels of supportive care, namely screening and monitoring, low-intensive, moderate-intensive and high-intensive supportive care. The framework conceptualizes that screening and monitoring should be offered to everyone, while each increasing level of supportive care (and often more expensive) is needed by a decreasing group of patients. This thesis specifically focused on supportive care targeting HNC patient. Findings of this thesis showed that the need for supportive care can potentially be screened using the EORTC QLQ-C30 and QLQ-H&N35 (level 1 of the supportive care framework), and that unmet supportive care needs are relatively high and varied among HNC and TL patients. Low, moderate and high-intensive supportive care interventions (level 2, 3 and 4 of the supportive care framework) aiming to target these needs were in this thesis shown to have the potential to be effective at acceptable costs. An integrated stepped care intervention targeting anxiety and depression combining different levels of the supportive care framework into one interventions was even found to be potentially effective at lower total costs. Although this thesis had several strengths, such as its broad focus and the usage of up-to-date methodology and statistical analyses, some potential limitations need to be taken into account. Sample sizes of the studies were relatively small, limiting the statistical power of the analyses. Also, the cross-sectional design of some of the studies, the impaired generalizability, and missing data are potentially important limitations. Despite these potential limitations, this thesis is expected to provide valuable information supporting implementation of supportive care interventions targeting HNC patients in clinical practice. Some specific requirements need, however, to be fulfilled to ensure optimal implementation, for example, the availability of a case manager. Also, continued monitoring and evaluation of implementation is warranted. To further enhance supportive care targeting HNC patients, more research is called for on cutoff scores to identify patients with a perceived unmet need, and the course of supportive care needs among groups of HNC patients over time. Also, more information is needed on healthcare utilization and other important societal costs among HNC patients, and the cost-effectiveness and cost-utility of supportive care approaches targeting HNC patients.