

## General discussion





This thesis focuses on supportive care in head and neck cancer (HNC) patients, especially on patients' need for supportive care and its cost-effectiveness and cost-utility. In this chapter, the main findings of this thesis are discussed in relation to current knowledge and practice of optimal supportive care targeting HNC patients. Both strengths and limitations of this thesis are presented. This chapter finishes with presenting the implications for clinical practice and by providing recommendations for further research.

## MAIN FINDINGS OF THIS THESIS

The first part of this thesis is aimed at obtaining insight into HNC patients' supportive care needs using psychometrically assessed patient-reported outcome measures. It was found that the widely-used European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-questions (EORTC QLQ-C30) and HNC-specific module (EORTC QLQ-H&N35) can be used in clinical practice for identifying patients with a perceived unmet supportive care need. Both sensitive and specific cutoff scores were identified (*chapter 2*). Also, the Supportive Care Needs Survey short-form (SCNS-SF34) and HNC-specific module (SCNS-HNC) were valid and reliable patient-reported outcome measures for measuring supportive care needs in HNC patients (*chapter 3*). Using these SCNS measures among HNC patients treated with total laryngectomy (TL), it was found that many TL patients have supportive care needs, especially regarding HNC-specific functioning (76%), health, system, information & patients support (e.g., written information on aspects of your care) (69%), psychological (66%), and physical and daily living needs (62%) (*chapter 4*). For many of these patients, their need for supportive was satisfactorily fulfilled, as unmet needs were respectively 53%, 35%, 39%, and 37%. Several supportive care interventions have been developed previously to target these unmet supportive care needs.

The second part of this thesis focused on the costs, cost-effectiveness and cost-utility of such interventions. As an increasing number of supportive care interventions encompass a self-management component, in *chapter 5* the association between patient activation for self-management and total costs was presented. This chapter showed that a better patient activation among TL patients is likely to be associated with lower total costs. In *chapter 6* the literature on the cost-effectiveness or cost-utility of psychosocial supportive care interventions was reviewed. Results showed that psychosocial care in general has the potential to be effective at acceptable costs in cancer patients (mainly breast cancer).

An additional study on a stepped-care program targeting anxiety and depression among HNC and lung cancer patients conducted at the VU University medical center, Amsterdam (published after the conduction of the review), was found to be more effective at lower costs as compared to care-as-usual (*chapter 7*).

## OPTIMAL SUPPORTIVE CARE TARGETING HEAD AND NECK CANCER PATIENTS

In the following paragraphs the findings of this thesis are discussed in relation to current knowledge and practice of optimal supportive care targeting HNC patients. To facilitate this discussion the supportive care framework of Fitch<sup>1</sup> (Figure 1) and a cost-effectiveness/cost-utility plane are used (Figure 2).

This thesis addressed three important aspects of optimal supportive care; 1) tailoring supportive care to the needs of the individual patient (patient-centered care), 2) offering effective supportive care (quality care), and 3) offering cost-effective supportive care (affordable care). Tailoring of supportive care should be based on a patient's individual needs and other personal factors (e.g., a patient's goals, skills and preferences). It is represented in Figure 1 by the four different levels of supportive care: 1) screening for supportive care needs and the provision of relevant information; 2) low-intensive supportive care such as additional information, education, self-help or self-management interventions; 3) moderate-intensive supportive care, such as nurse-led specialized interventions or group interventions; and 4) high-intensive supportive care, such as ongoing and complex specialized interventions<sup>1</sup>. It is conceptualized that each increasing level of supportive care is more expensive (i.e., the supportive care intervention itself) and is needed by a decreasing group of patients. In addition, offered care in each level should be effective and preferably also be cost-effective. The concept of cost-effectiveness or cost-utility is visualized in Figure 2. The four main outcomes of cost-effectiveness or cost-utility analyses are visualized by the four different quadrants. In case the supportive care intervention is more effective and more costly (north-east quadrant), the acceptability of the additional costs depends on the willingness-to-pay for an incremental unit of effect. Figure 2 presents two of such potential willingness-to-pay thresholds (i.e., the blue line and the dotted line), of which the dotted line represents the lower willingness-to-pay threshold.

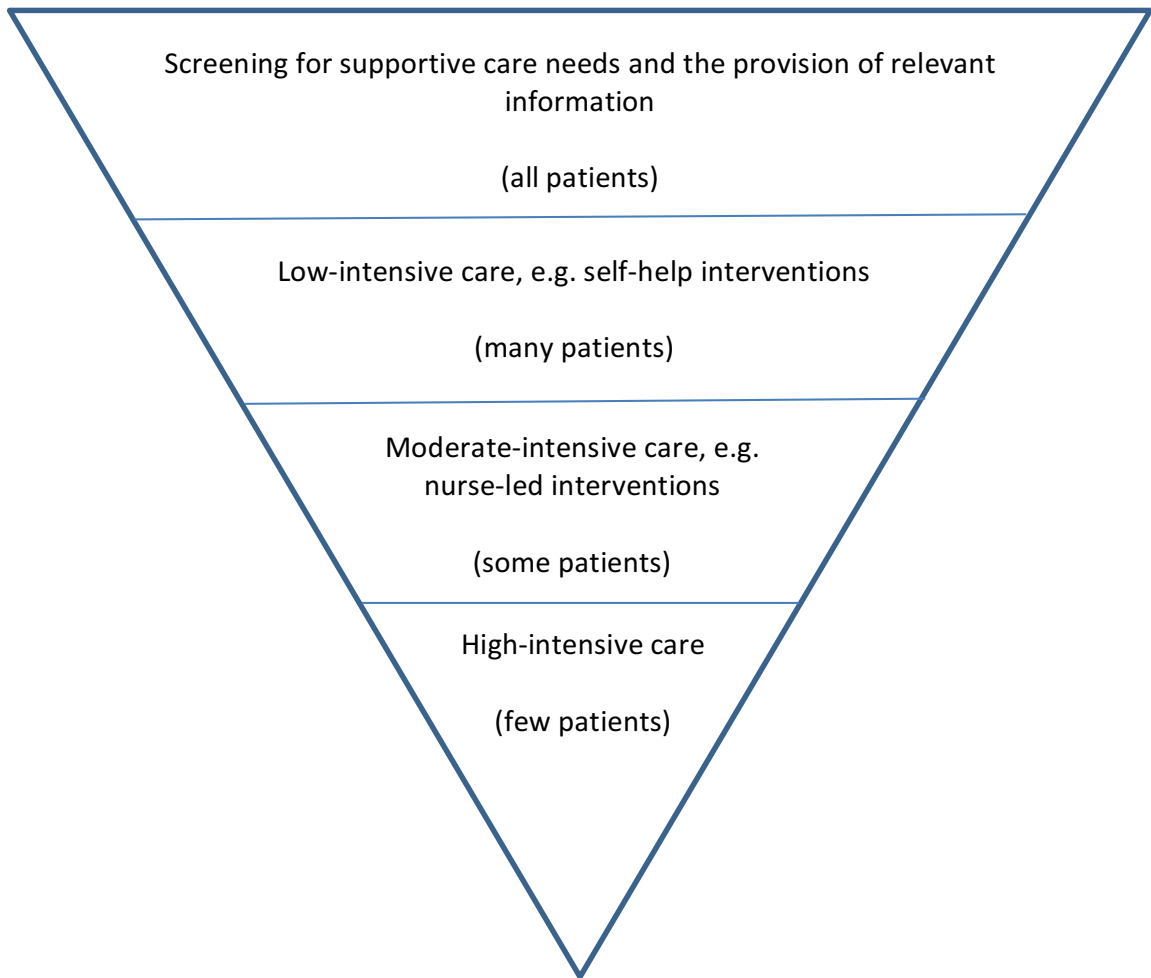


Figure 1. The (slightly-adjusted) supportive care framework of Fitch<sup>1</sup>

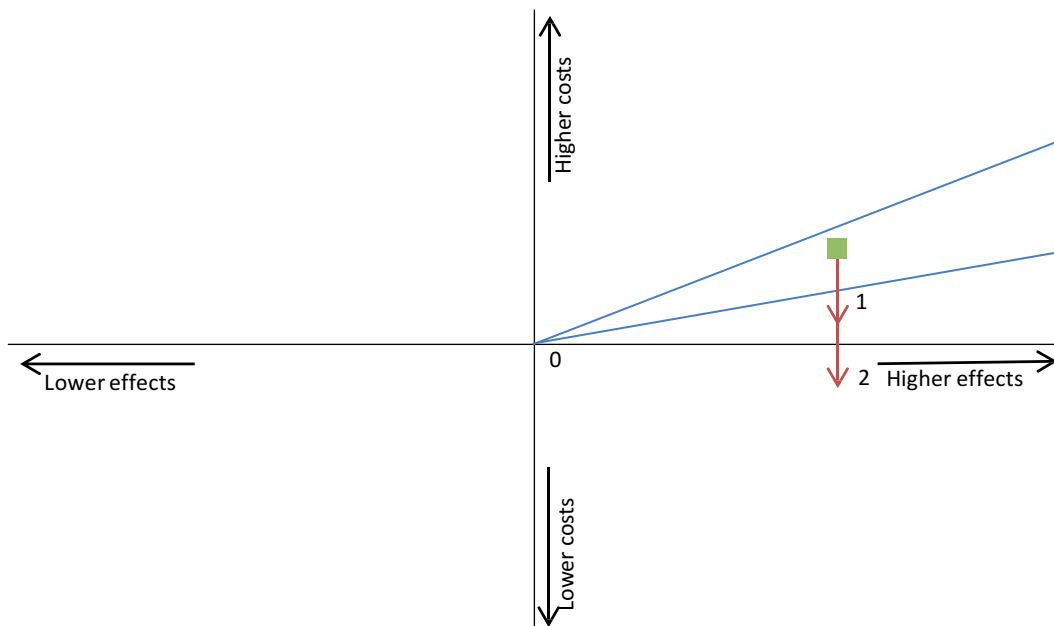


Figure 2. Visualization of a cost-effectiveness or cost-utility plane

In the following section supportive care targeting HNC patients will be discussed following the structure of the supportive care framework<sup>1</sup>. This section ends with a discussion on integrated supportive care approaches, such as stepped care. Also, its potential for improving the cost-effectiveness or cost-utility of supportive care will be discussed. Throughout this section, the added value of the findings presented in this thesis are emphasized.

#### Level 1: Screening for supportive care needs and the provision of relevant information

The first level of the supportive care framework conceptualizes that all cancer patients should be screened with respect to their need for supportive care and should be provided with relevant information. Screening and monitoring for symptoms and health-related quality of life (HRQOL) has recently also been recommended in the revised guideline on screening for psychosocial care<sup>2</sup>. Screening and monitoring has been found to improve communication between patients and healthcare professionals and to improve patient outcomes<sup>3</sup>. However, some concerns have also been reported<sup>4,5</sup>. One of these concerns is that screening or monitoring by itself does not improve a patient's outcomes<sup>5</sup>. To counteract this concern, screening and monitoring followed by the provision of individual feedback to both the patient and the care professional has been recommended<sup>5,6</sup>. At VU University medical center, Amsterdam, screening and monitoring for symptoms and HRQOL using a touch-screen computer system called OncoQuest in HNC patients is also followed by a consultation with a dedicated nurse<sup>7,8</sup>. As presented by Duman-Lubberding et al.<sup>9</sup>, HNC patients value such a nursing consultation. They especially value the time the nurse has to discuss the patient's individual feedback, the personal conversation and advice, and the answers provided on questions about their disease, HRQOL and symptoms.

This thesis adds some information to current knowledge and practice on screening and monitoring in HNC patients by providing cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 for identifying patients with a potential unmet need for supportive care (chapter 2). These cutoff scores might facilitate the nurse or other care professional with cues on the interpretation of a patient's individual outcomes. Some concerns have, however, been reported regarding the use of such cutoff scores, as cases may be missed, and those patients identified with a deviating outcome may not necessarily have a subjective need for supportive care<sup>4,5</sup>. To overcome this last concern, it is recommended that the cutoff scores are used as a signal for further evaluation of a potential problem or symptom (e.g., during a nursing consultation, as is the case in OncoQuest<sup>7,8</sup>), instead of immediate high-intensive follow-up care (e.g., referral to a psychologist).

### Level 2: Low-intensive supportive care targeting head and neck cancer patients

The second level of the supportive care framework conceptualizes that many patients identified with a need for additional supportive care may benefit from low-intensive supportive care. Low-intensive supportive care encompasses the provision of information, education, as well as self-help or self-management interventions. In current practice, there has been an increasing focus on self-help and self-management interventions, which are often offered in eHealth formats<sup>10-13</sup>. It is expected that such interventions may influence cancer patients' acquired skills (e.g., self-efficacy, problem-solving skills, and self-monitoring behavior), which in turn may influence patients' confidence in managing their disease. Patients' acquired skills as well as patients' confidence to manage (i.e., patient activation<sup>14</sup>) are hypothesized to influence patient outcomes, such as HRQOL or symptoms, and lower healthcare use and costs<sup>15</sup>. Previous studies have indeed found evidence for a potential effect of such interventions in terms of improved patient outcomes, such as perceived support, knowledge, and information competence<sup>11,16</sup>. This thesis investigated the potential association between patient activation for self-management and total costs (chapter 5). Patients with a better patient activation for self-management were likely to report lower costs than those patients with a lower patient activation. Further studies should be performed on the causality of this finding.

Low-intensive supportive care is also expected to be beneficial for HNC patients, as unmet supportive care needs among HNC patients and TL patients are high, especially regarding HNC-specific functioning (chapter 3 and 4). So far, several low-intensive supportive care interventions have been developed to target these needs<sup>17-20</sup>. An example is the guided self-help program 'In Tune without Cords' for TL patients. In Tune without Cords encompasses information and self-care skills education on stoma care, voice prosthesis care, speech, smelling, nutrition and mobility, and a guided self-help exercise program targeting speech, swallowing and shoulder problems<sup>18,21</sup>. A pilot study showed that this self-help intervention of In Tune without Cords was appreciated by patients<sup>18</sup>. Currently, a randomized controlled trial on the effectiveness and cost-utility of the guided self-help exercise program of In Tune without Cords is being conducted<sup>20</sup>.

### Level 3: Moderate-intensive supportive care targeting head and neck cancer patients

The third level encompass providing moderate-intensive supportive care, such as nurse-led specialized interventions or group interventions, to those patients for whom low-intensive care is not sufficient. Examples of moderate-intensive interventions developed for HNC patients are a group exercise program targeting physical fitness<sup>22</sup> and a nurse-led

intervention for depressive symptoms and HNC-related physical symptoms<sup>23,24</sup>. Beneficial results have been reported regarding feasibility and effectiveness on fitness outcomes, symptom management, HRQOL, and symptoms of depression<sup>22-24</sup>. None of these studies have, however, investigated its cost-effectiveness or cost-utility so far. Previous psychosocial nurse-led interventions or psychosocial group interventions targeting cancer patients (non-HNC) have, however, in general, found that such interventions have the potential to be effective at additional costs (see Arving et al.<sup>25</sup>, Lemieux et al.<sup>26</sup>, Lengacher et al.<sup>27</sup>, Mewes et al.<sup>28</sup> and Sabariego et al.<sup>29</sup> as reviewed in chapter 6). The acceptability of these additional costs depends on the willingness-to-pay for an incremental unit of effect (as visualized in Figure 2). For quality adjusted life years (QALYs), the National Institute of Health and Clinical Excellence has proposed a willingness-to-pay threshold of £20,000 – 30,000 per QALY<sup>30,31</sup>. When using this threshold, several of the psychosocial care interventions are likely to be cost-effective. This may warrant implementation of these interventions in clinical practice. In the Netherlands, however, no such willingness-to-pay threshold exists (although higher thresholds have been proposed for more serious diseases<sup>32</sup>). Therefore, such a willingness-to-pay threshold with respect to supportive care is called for.

#### Level 4: High-intensive supportive care targeting head and neck cancer patients

Finally, the last level includes high-intensive supportive care targeting a small subgroup of all patients. High-intensive supportive care interventions are, for example, intensive and ongoing consultations with a speech therapist to target speech or swallowing problems or individual psychological interventions (e.g., cognitive behavioral therapy). Previous studies found that such individual psychological interventions are likely to be effective, especially when the study preselects patients regarding their level of symptoms<sup>33</sup>. This is also the idea underlying this supportive care framework (i.e., saving the high-intensive interventions for those patients for whom interventions with lower intensity are not sufficient). So far, two studies evaluated the cost-utility of such high-intensive psychological care in respectively breast cancer and mixed cancer populations (see Arving et al.<sup>25</sup> and Chatterton et al.<sup>26</sup> as reviewed in chapter 6). Both studies reported that the total costs in the intervention group were lower, while the effects were higher (south-east quadrant of Figure 2), implicating dominance of the intervention.

#### Innovative approaches combining different levels into one intervention

Several supportive care interventions have been developed for HNC patients previously aiming to target patients' unmet supportive care needs. This thesis provided some



evidence that such interventions have the potential to be effective at acceptable costs (chapter 5 and 6). However, more innovative approaches are called for<sup>34,35</sup>. Innovative interventions integrating different levels of the supportive care framework into one intervention are expected to improve cost-effectiveness or cost-utility or to be even cost saving (as visualized by respectively arrow 1 and 2 in Figure 2)<sup>36,37</sup>.

An example of an integrated approach is the eHealth self-management application OncoKompas<sup>38-40</sup>. Using OncoKompas, cancer patients can monitor their symptoms and HRQOL at home, which is followed by automatically generated tailored information and support to find and obtain the supportive care they need. The advice for supportive care is tailored to a patient's individual needs as well as patient's preferences (e.g., individual or group interventions). Previous studies among HNC patients<sup>39</sup> and breast cancer patients<sup>40</sup> have shown beneficial results regarding feasibility and patient satisfaction and, possibly, also effectiveness in improving patient activation. Until now cost-utility of such an integrated eHealth self-management application targeting (HNC) cancer patients is unclear. Therefore, currently a multicenter randomized controlled trial is conducted coordinated from the Vrije Universiteit, Amsterdam, with the aim to find these answers<sup>38</sup>.

Other examples of integrated approaches are collaborative care or stepped care interventions targeting anxiety and depression. Collaborative care is a multidisciplinary care model in which different healthcare providers (e.g., a psychologist or psychiatrist) actively collaborate in the treatment of a patient, assisted by a case manager (e.g., a nurse), and typically combines psychological and pharmacological treatments<sup>41</sup>. Stepped care is an approach in which effective, yet low-intensive treatment is delivered to the patient first (e.g., an intervention of level 2), followed by more intensive treatments if symptoms do not resolve (e.g., an intervention of level 3 or 4). Both collaborative care and stepped care have been found to be effective in improving outcomes (e.g., HRQOL and symptoms of depression) of cancer patients<sup>41,42</sup>. To shed light on the potential of such interventions to improve cost-effectiveness or cost-utility of supportive care, this thesis investigated the cost-utility of a stepped care approach targeting psychological distress in HNC and lung cancer patients. It was found that stepped care was highly-likely to be more effective and less costly compared to care-as-usual (chapter 7). Collaborative care on the other hand has been shown to be effective in cancer patients, however, at additional costs (see Choi Yoo et al.<sup>43</sup>, Duarte et al.<sup>44</sup>, Strong et al.<sup>45</sup> and Walker et al.<sup>46</sup> reviewed in chapter 6).

One reason why the study on the stepped care intervention found lower total costs, in contrast to previous studies on collaborative care<sup>43-46</sup>, may be the societal perspective from which the analyses were performed. This perspective takes into account both healthcare costs and other costs from a societal perspective, such as productivity losses and informal care costs. Usage of a societal perspective is also recommended in current guidelines, including the Dutch guideline of the National Healthcare Institute<sup>31,47-49</sup>. Previous studies on collaborative care, however, were all performed from a healthcare perspective<sup>43-46</sup>. Another reason may be the stepped care design itself. This stepped care program started with two weeks of watchful waiting (step 1), after which 28% recovered from their symptoms (as presented by Krebber et al.<sup>42</sup>). After step 2 (guided self-help), 34% of the participants recovered. When still not recovered, more resource intensive care was offered, namely face-to-face problem-solving therapy (step 3), and specialized psychological interventions and antidepressant medication (step 4). High-intensive, resource-intensive treatments are thus only offered to a small sample of the study population, reducing costs of the supportive care intervention itself.

More research is, however, needed to investigate in more detail the potential of stepped care interventions to be less costly. Other studies in non-cancer populations often found evidence for beneficial effects of stepped care at higher costs<sup>50-58</sup>. Also, more knowledge into the cost-effectiveness of other integrated supportive care interventions is needed. To enhance comparability of findings, it is recommended that in line with the Dutch guideline<sup>47,49</sup>, the studies are performed from a societal perspective. In addition, it is recommended that QALYs are used as outcome measure, preferably measured using the EQ-5D, as this increases comparability of outcomes among types of interventions and different diseases. Besides the primary analysis, additional analyses can be conducted using a different outcome measure (e.g., the QLU-C10D based on the EORTC QLQ-C30<sup>59</sup>) or from a different perspective (e.g., a healthcare perspective). Although the societal perspective is the perspective of first choice, it is acknowledged that there is a need to specifically focus on healthcare costs. To bend the cost curve in healthcare, the concept of value based healthcare of Porter and Teisberg (2006) has been introduced in the last years, conceptualizing that shifting current perspective from volume-based to patient-centered care may improve patients' outcomes and lower healthcare costs at the same time<sup>60-62</sup>. Further insight is needed into how this concept may influence current supportive care targeting HNC patients.

## STRENGTHS AND LIMITATIONS

A strength of this thesis is the wide range of aspects taken into consideration with regard to optimal supportive care, i.e., from measuring the need for supportive care to the cost-effectiveness or cost-utility of supportive care. Cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 have been identified in this thesis, and a patient-reported outcome measure for measuring unmet supportive care needs has been psychometrically evaluated. This valid and reliable patient-reported outcome measure was used in chapter 4 to measure supportive care needs among TL patients, which is a strength of this thesis. Another strength is the societal perspective used in chapter 5 and 7, which provides a thorough overview of costs that may be influenced by supportive care interventions. The conduction of cost-effectiveness or cost-utility analyses from a societal perspective has also been recommended in several guidelines<sup>31,47,48</sup>. Besides analyses from a societal perspective, additional analyses from a healthcare perspective may be performed. Finally, a strength of this thesis is the up-to-date methodology used to perform the analyses. In chapter 5 and 7, for example, missing data were imputed using multiple imputation. In addition, bootstrapping was performed to provide insight into the uncertainty surrounding the findings.

Some limitations should also be noted. The studies included in this thesis were conducted in relatively small sample sizes ranging from 96 to 288 patients, limiting the statistical power of the analyses. In addition, study participants may not have been representative for the entire group of HNC patients, limiting generalizability of findings to all patients. For example in chapter 2 and 3 only HNC patients were included who completed curative treatment, thereby hampering the generalizability of findings to HNC patients still under treatment or in palliative stage. However, one could also argue that results on the entire group of HNC patients are too broad to interpret in a meaningful way. From both a scientific and clinical point of view therefore a focus on subgroups of HNC patients may be favored.

Furthermore, a potential limitation is the cross-sectional design of some of the studies (e.g., chapter 4 and 5), which hampers the ability to draw conclusions regarding the causality of findings. Finally, a potential limitation of all studies is the missing data. In chapter 5, for instance, missing data on patient activation resulted in the selection of patients that were somewhat younger and that presented within a shorter timespan since TL surgery, hampering generalizability of findings. In chapter 7, patients with missing

data were not excluded, however, some assumptions were made regarding the missing data (e.g., multiple imputation and linear interpolation). These assumptions may not necessarily reflect reality.

## IMPLICATIONS FOR CLINICAL PRACTICE

An important finding of this thesis for clinical practice is that supportive care has the potential to be effective at acceptable costs. An integrated stepped care intervention may even be effective at lower total costs. These findings lend support for implementation of such supportive care interventions in current clinical practice. An important requirement for offering these types of interventions in clinical practice is, however, the availability of a case manager<sup>63</sup>. A case manager is needed to provide individual feedback to the patient after screening or monitoring for their symptoms and HRQOL (level 1 of the supportive care framework), and to discuss, if necessary, supportive care options with the patient. Also, a case manager is needed to arrange referral to appropriate supportive care tailored to the individual needs and preferences of the patient. In addition, a case manager is necessary to monitor progress of the patient and to refer a patient to a next level of the supportive care framework, in case symptoms do not resolve.

Besides a case manager, an important requirement for implementation is that reimbursement of costs needs to be arranged. Also, all stakeholders (e.g., patient, care provider and insurance companies) need to be informed on the available supportive care options. In addition, a network of care professionals or institutes that can offer the supportive care should be available. Finally, after implementation of supportive care interventions, continued monitoring and evaluation is warranted, for example using the RE-AIM model<sup>64</sup>. This model conceptualizes that attention should be paid to the Reach of the intervention, Efficacy of the intervention in clinical practice, Adoption of the intervention by care providers, Implementation of the intervention in clinical care, and Maintenance of the intervention in long-term clinical practice.

## RECOMMENDATIONS FOR FURTHER RESEARCH

Following the chapters of this thesis and the previous paragraphs, several recommendations can be formulated for further research. Firstly, more knowledge is needed on cutoff scores when screening and monitoring for supportive care needs (level 1 of the supportive care framework), and the prevalence of supportive care needs in HNC patients. Previously identified cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 need to be replicated in other HNC populations. Also, new cutoff scores for those EORTC QLQ-C30 and QLQ-H&N35 domains for which no cutoff scores have been proposed need to be identified. Besides, in the future, cutoff scores on the newly developed QLQ-H&N43 measure may be warranted<sup>65</sup>. In addition, detailed insight into a patient's individual changes in EORTC QLQ-C30 and QLQ-H&N35 scores over time that mandate clinical attention is recommended<sup>66</sup>. Moreover, more research on the course of supportive care needs among (groups of) HNC patients over time is called for. So far, only one study investigated the course of supportive care needs among HNC patients (in this case oral cavity cancer patients)<sup>67</sup>. Insight into the course of supportive care needs among groups of HNC patients over time will provide detailed knowledge on the specific needs patients encounter at specific points in time and may, consequently, facilitate better tailoring of supportive care provision to those specific needs. Currently, a longitudinal cohort study is ongoing in a large group of HNC patients (i.e., up to 739) in which supportive care needs are measured, using the SCNS-SF34 and SCNS-HNC, which is expected to provide valuable information to investigate supportive care needs over time<sup>68</sup>.

Secondly, future studies should shed light onto HNC from an economic point of view. Knowledge is needed on medical service utilization, non-medical service utilization and productivity losses among HNC patients at different points in time. This would provide insight in total costs involved in HNC patients as well as excess costs of HNC patients (i.e., how much higher are the costs in HNC patients compared to other comparable non-HNC persons). Also, more information on factors which may influence these costs is needed. Previous studies in cancer patients found that better health outcomes, such as lower levels of psychological distress<sup>69</sup>, depression<sup>70-72</sup>, and fear of recurrence<sup>73,74</sup> were associated with lower healthcare utilization or healthcare costs in cancer patients. In addition, associations between better health outcomes and other societal cost outcomes, such as between lower levels of anxiety and return to work<sup>75</sup> or lower levels of depression or distress and lower levels of unemployment<sup>76,77</sup>, were reported among cancer patients, including HNC patients<sup>75,77</sup>. However, other studies found no such results<sup>78,79</sup>. Further

(prospective) studies are needed into the causality of these potential associations. Unravelling these associations may provide knowledge necessary to provide HNC patients with the supportive care they need, while at the same time controlling the total economic burden of cancer.

Thirdly, more research specifically focusing on the cost-effectiveness or cost-utility of certain supportive care interventions is called for. It would be interesting to investigate whether a stepped care program in which effective, low resource-intensive care is offered to patients first, followed by more resource-intensive care in case symptoms do not resolve, will be cost-effective or even cost saving in other cancer populations or for other symptoms than psychological distress (e.g., head, neck and shoulder complaints or sleep problems). Further knowledge is also needed on the optimal order of supportive care interventions in such a stepped care approach, and other opportunities to further match the order of steps to the individual needs and preferences of a patient.

## **CONCLUSION**

This thesis presented evidence that the need for supportive care among HNC patients can potentially be measured using both the EORTC QLQ-C30 and QLQ-H&N35 as well as the SCNS-SF34 and SCNS-HNC. As unmet needs among HNC and TL patients have been reported to be relatively high and varied, tailoring of supportive care to a patient's individual needs is necessary. This thesis found that supportive care aiming to target these unmet needs, might possibly be effective at acceptable costs. An integrated stepped care approach was found to be potentially more effective at lower total costs in HNC and lung cancer patients compared to care-as-usual. More in depth research is, however, needed on the cost-effectiveness and cost-utility of supportive care approaches targeting HNC patients.

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