CHAPTER 1
General introduction
The World Cancer Report 2014, published by the World Health Organization's International Agency of Research on Cancer, warns that the global burden of cancer is growing at high velocity: in 2012 approximately 14 million new cases of cancer were diagnosed worldwide and this number is expected to climb to an estimated 22 million annually within the next 20 years due to ageing and growth of the population\(^1\). In the Netherlands, the cancer incidence curves have flattened out or slightly dropped during the last 5 years\(^2\). Survival rates for cancer patients have increased in the past decennia\(^1\). Reasons for this increase are the earlier detection of cancer due to better screening techniques and more successful cancer treatments. Cancer patients encounter a number of difficulties that can deteriorate quality of life, including fatigue, insomnia, cognitive impairment, loss of appetite, pain and decreased sexual functioning. Also, psychological comorbidity is often present\(^3-5\).

This thesis addresses psychological comorbidity among cancer patients. This chapter provides background information on the principal matter of this thesis: improving access to high-quality and cost-effective psychosocial care for head and neck cancer (HNC) and lung cancer (LC) patients with psychological distress (symptoms of depression and/or anxiety).

**EPIDEMIOLOGY OF HNC AND LC**

HNC counts for 686,000 new cases worldwide every year\(^1\). LC is the most common diagnosed type of cancer with 1.8 million new cases every year, accounting for about 13% of total cancer diagnoses\(^1\).

HNC originates in the head and neck region, and includes malignancies of the lips, oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses or salivary glands. Around 85% of HNC tumors is of squamous cell histology. The primary causes of HNC are tobacco and alcohol use, and human papillomavirus (HPV), which occurs primarily in the oropharynx\(^6\). Around the world, three times as many men as women are affected\(^7\). This difference is probably associated with higher rates of substance abuse, in particular tobacco use among men than women\(^8,9\). The risk of HNC also grows with age: most tumors are diagnosed in the late fifth and seventh decades of life\(^10\). Prognosis for HNC is determined by the basis of tumor site, stage and HPV tumor status\(^6,11\). In the Netherlands, five-year survival rates range from 41% among patients with a tumor originating in the paranasal sinuses, 31-59% in the pharynx, 61% in the oral cavity, 67% in the salivary glands, 68% in the larynx, 69% in the nasal cavity and to 91% in the lips\(^2\).
LC refers to malignancies that originate in the airways or pulmonary parenchyma. Approximately 95% of all lung cancers are classified as either non-small cell lung cancer (NSCLC, 85%) or small cell lung cancer (SCLC, 10%). This distinction is essential for staging, treatment, and prognosis. Other cell types comprise about 5 percent of malignancies arising in the lung. The most important risk factor for LC is tobacco use, and consequently, similar to HNC, LC is twice as prevalent in men than in women\textsuperscript{7,9,12}. Other known risk factors for LC include exposure to occupational and environmental carcinogens (such as asbestos), and outdoor pollution\textsuperscript{13,14}. As it takes decades to develop LC after smoking initiation, diagnosis of LC before age 30 is rare and peaks in the elderly\textsuperscript{10,15}. LC is the most common cause of death from cancer worldwide, estimated to be responsible for nearly one in five\textsuperscript{10}.

**TREATMENT OF HNC AND LC**

Surgery, radiation and chemotherapy in varying combinations are administered in the management of HNC and LC, depending on TNM (classification of malignant tumors) stage, primary tumor site and physical performance status. In HNC, limited or early-stage disease (stage I and II) occurs in approximately 40% of patients and is usually well treated with surgery or radiation alone. Advanced disease (stage III and IV) is associated with a high risk of both local recurrence and distant metastases. Therefore, in advanced disease, combined modality treatment is required to optimize the chances for long-term disease control. These combined modality approaches include primary surgery followed by postoperative (chemo)radiation or concurrent chemoradiation with salvage surgery if needed. The role of induction chemotherapy is limited and still under investigation\textsuperscript{16,17}.

For patients with NSCLC, surgery offers the best opportunity for cure for early stage disease\textsuperscript{18}. In addition, stereotactic radiotherapy is nowadays considered as a good alternative\textsuperscript{19,20}. Survival rates in advanced disease remain low, despite developments in systemic therapies (e.g., chemotherapy, biologics, and targeted agents)\textsuperscript{21}. Because SCLC is disseminated at presentation in almost all patients, chemotherapy is an important component of treatment, with or without radiation\textsuperscript{22}. 
IMPACT OF HNC AND LC AND ITS TREATMENT ON QUALITY OF LIFE

Cancer has a tremendous impact on people’s life and is life disrupting at numerous levels. A diagnosis of cancer has significant psychological effects including uncertainty and fear. In addition, cancer treatment can have devastating acute and late consequences, negatively affecting health-related quality of life. Health-related quality of life is an important, multidimensional health outcome indicator, usually as perceived by the patient, and can be defined as “the extent to which one’s usual or expected physical, emotional and social well-being are affected by a medical condition or its treatment”23. Following treatment, many HNC or LC patients have to deal with deteriorating side effects, such as an altered appearance, respiratory, speech and swallowing problems, neuro- and nephrotoxicity, and high levels of symptomatology (fatigue, pain, hearing loss, dry mouth, shoulder dysfunction)24,25. Consequently, the implications of HNC and LC can give rise to psychological distress and social isolation25-27, with fear of recurrence and fear regarding secondary cancers adding to the burden. Comorbid symptoms of depression and anxiety are highly prevalent among HNC and LC patients28-31. Among a cohort of various cancer types Brintzenhofe-Szoc et al. found that HNC and LC are in the top four of cancer types with the highest rates of mixed anxiety/depression symptoms28.

PSYCHOLOGICAL COMORBIDITY IN CANCER PATIENTS

In literature on patients with somatic chronic diseases, the terms psychological distress and psychiatric disorder often appear under the heading “psychological comorbidity”32. In oncological settings the idiom distress is often applied, rather than psychiatric disorder as depression or anxiety, because it is thought to be less stigmatic33. Moreover, not every cancer patient who needs psychosocial care has a psychiatric disorder as diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM)34 or the International Classification of Diseases (ICD)35. Distress has been defined by the National Comprehensive Cancer Network (NCCN) as “a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears, to problems that can become disabling such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.”36. Psychological distress, by some referred to as the sixth vital sign in cancer care, can easily
be measured by self-report instruments, such as the Hospital Anxiety and Depression Scale\textsuperscript{37,38} (HADS) or the Distress Thermometer\textsuperscript{39}. Because self-report instruments do not allow case finding for anxiety and depressive disorders, screening for distress as a first step is recommendable, followed by proper diagnostic assessment.

As the cancer population is expanding, psychological comorbidity is expected to grow accordingly. A third or more of cancer patients suffer from a significant level of psychological distress following their diagnosis\textsuperscript{40}. Major depression is prevalent in 13\% of cancer patients and seems to be highest during treatment\textsuperscript{41}; anxiety is prevalent in 10\% of cancer patients\textsuperscript{42}. In long-term cancer survivors the prevalence is estimated to be 12\% and 18\% respectively\textsuperscript{43}. Depression and anxiety often occur concomitantly: more than half of cancer patients with depressive symptoms also suffer from anxiety symptoms\textsuperscript{38,44}. When depression and anxiety coexist symptoms of depression are more severe, psychological functioning is worse, compliance and response to anti-depressive therapy is lower\textsuperscript{44-46} and costs of health care utilization are higher\textsuperscript{47}. Depression among cancer patients is associated with an elevated risk of mortality\textsuperscript{48-52}. In their meta-analysis Satin et al. estimated a 26\% greater mortality rate among cancer patients experiencing depressive symptoms and a 39\% higher mortality rate among those diagnosed with major depression compared with non-depressed cancer patients\textsuperscript{48}.

PSYCHOLOGICAL TREATMENT OPTIONS IN CANCER CARE

In general, psychosocial intervention has shown to be effective in cancer patients with psychological distress\textsuperscript{53,54}. In their review Fawzy et al. speak of four covering types of psychosocial interventions in cancer care: psycho-education, psychotherapy (individual), cognitive behavioral training and group interventions\textsuperscript{55}. Cognitive behavioral therapy (CBT), problem-solving therapy (PST) and pharmacologic interventions appear to be superior in reducing depressive symptoms relative to control conditions for adults diagnosed with cancer\textsuperscript{53}. Despite proven efficacy of psychosocial interventions in cancer patients, many distressed cancer patients do not make use of mental health care and as a result psychological comorbidity is often undertreated in cancer patients\textsuperscript{56-60}. Barriers to referral to psychosocial care are insufficient screening for anxiety and depression at the often busy clinics, non-compliance, costs, and lacking knowledge about available psychosocial services on the part of both oncologists and patients\textsuperscript{39,57,58,61-63}. These bottlenecks are in contradiction with the high prevalence of psychological distress and
the high intensity of psychosocial care needs among cancer patients\textsuperscript{64-66}. The hiatus between the amount of patients experiencing distress and those getting psychological help has led to recommendations for implementing routine screening for psychological distress. In his review Mitchell stated that screening for distress and quality of life in cancer care is likely to benefit communication and referral for psychosocial help, and that it has the potential to influence patient well-being but only if barriers are addressed\textsuperscript{67}.

**CURRENT ORGANIZATION OF PSYCHOSOCIAL SUPPORT IN CANCER CARE**

The Dutch knowledge and quality institute for professionals and managers in oncological and palliative care, Netherlands Comprehensive Cancer Organisation (IKNL), recommends systematic screening of every adult cancer patient at the ambulant care department of a hospital for psychological distress using the so-called Lastmeter\textsuperscript{39}. The Lastmeter consists of the Distress Thermometer, a problem list, and the question “Would you like to talk to an expert about your problems?”. Internationally, other tools have emerged as well, such as Viewpoint, SupportScreen, ESRA-C, CHES, and OncoQuest\textsuperscript{58,68}. After filling out the Lastmeter, the IKNL advises immediate review of the results by a care professional (attending physician or nurse), who is trained to interpret the outcome of the Lastmeter and to discuss the results with the patient. If needed the trained care professional can offer basic psychosocial care focused on strengthening the patient’s ability to cope with and reducing the experienced burden, or refer to specialized psychosocial care for further assessment and help\textsuperscript{69}. The presence of a professional “care navigator” has shown to lead to higher patient satisfaction, shorter hospital stays, fewer cancer-related problems, better mental health, and greater patient empowerment\textsuperscript{69}.

**INNOVATION OF PSYCHOSOCIAL CARE**

Facilitators to improve psychosocial care are organizing supportive cancer care according to efficient care models, incorporating self-management and eHealth in these care models, and implementing systems to monitor health related quality of life and psychological distress in clinical practice. Several meta-analyses have suggested that minimal contact therapies, such as web-based and self-help interventions, can be effective treatments for psychological distress with comparable effect sizes to face-to-face treatments\textsuperscript{70-74}. In their meta-analysis on computerized CBT for anxiety and depressive disorders, Andrews et al.\textsuperscript{70}
concluded that patients adhered and were satisfied with computerized CBT, especially when offered via the Internet. And thus, by increasing convenience and reducing clinician time that would otherwise be required by face-to-face treatment, web-based CBT has the capacity to increase access to mental health care.

A comprehensive and integrated organization of psychosocial care, such as stepped care, might be an effective method to tackle undertreatment of distress in cancer patients. Stepped care is advocated in the National Institute for Health and Clinical Excellence (NICE) guidelines for common mental health problems, such as depression and anxiety. Usually stepped care includes watchful waiting, (guided) self-help, brief face-to-face counselling, and specialized interventions. Patients start with the least intensive treatment that is most likely to work. Treatment response is systematically monitored and patients who do not benefit from current treatment step up to a subsequent treatment of higher intensity and costs. Stepped care aims at effective and cost-efficient provision of therapeutic resources. There is evidence that, in primary care, stepped care is as effective as care as usual.

**OBJECTIVES AND OUTLINE OF THIS THESIS**

The main objective of this thesis is to investigate innovative psychosocial cancer care: screening for distress, stepped care, and self-management and eHealth. The focus is on HNC and LC patients.

The general outline of this thesis is as follows:

Chapter 2 describes a meta-analysis on the prevalence of depression and depressive symptoms in cancer patients during and after treatment. Chapter 3 outlines the added value of screening for psychological distress in follow-up care to identify HNC patients with untreated distress. Chapter 4 presents the study protocol of the randomized controlled trial on the (cost-)effectiveness of stepped care targeting head and neck cancer and lung cancer patients with psychological distress. In Chapter 5 the results of the randomized controlled trial testing the effectiveness of stepped care targeting psychological distress in HNC and LC patients are presented. Chapter 6 reveals the experiences with and perceived outcomes of step 2 of the stepped care program, the guided self-help intervention “Headlines”, targeting psychological distress in head and neck cancer patients. Finally, Chapter 7 provides the conclusions of this thesis, their clinical implications and suggestions for future research.
REFERENCES

Chapter 1


