Physical and Psychosocial Correlates of Rehabilitation, Survival and Relapse in Head and Neck Cancer Patients

ISBN 90 5166 6519

Eburon Publishers
PO Box 2867
2601 CW Delft
E-Mail: info@eburon.nl

Physical and Psychosocial Correlates of Rehabilitation, Survival and Relapse in Head and Neck Cancer Patients

Lichamelijke en Psychosociale Factoren in relatie tot Rehabilitatie, Overleving en Recidief bij Patienten met een Hoofd-halstumor

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Erasmus Universiteit Rotterdam
op gezag van de rector magnificus
Prof. dr P.C.W. Akkermans M.A.
en volgens besluit van het College voor Promoties.
De openbare verdediging zal plaatsvinden op
woensdag 16 september 1998 om 15.45 uur

door

Maarten Ferdinand de Boer
geboren te Bergen op Zoom

Promotie-commissie:
Promotores: Prof. dr C.D.A. Verwoerd
Prof. dr H.W. van den Borne

Overige leden: Prof. dr S.E.R. Hovius
Prof. dr J. Passchier
Prof. dr G. Stoter

Co-promotor: Dr J.F.A. Pruyn

The work of this thesis was financially supported by:
The Dutch Cancer Society (NKB/KWF)
Entermed B.V.
MEDIPROF

Aan mijn moeder
Aan Carien
Aan Mariet en Annelot

CONTENTS

Chapter 1

GENERAL INTRODUCTION

INTRODUCTION

The number of new patients in the Netherlands each year diagnosed with head and neck cancer is about 2100.[1] This number will increase in the coming years because of progessive aging of the population and the particularly high birthrate post second world war, producing a cohort of children who are now at risk for developing head and neck cancer. Moreover, patients are currently 'in medical hands' for a longer time than before because of the introduction of treatment techniques for more advanced tumors and better palliative care. In 1995 the estimated number of patients alive with carcinoma of the most common sites of head and neck cancer was 9125.[2]

Traditionally, the medical treatment of head and neck tumors has been directed at irradicating the disease and aiming for a longer survival of the patient. Therefore, the main focus has been on clinical data such as localization, type and staging of the tumor and the effect of treatment, demonstrated by loco-regional control and survival.

As Bailar and Gornick stated recently, the effect on mortality of new treatments, in the period 1970 through 1994, has been disappointing for most cancer sites.[3] Also, the survival rate for head and neck cancer in 1994 was found largely unchanged since 1973. In the Netherlands, the 5-year overall relative survival for oral cavity cancer improved from 52 to 58%, for oropharynx cancer decreased from 38 to 30% and remained unchanged (70%) in laryngeal cancer.[2] For the patients both quantity and quality of life are important.

Today head and neck cancer patients and their healthcare providers are confronted with the effects of more aggressive treatment modalities introduced since the 70's. Fundamental life functions, like breathing, eating and speaking, and the bodily appearance of the patient, are often largely affected by tumor and treatment, often with severe consequences for daily life and social interaction.

Contrary to the emphasis on "clinical" data, less attention has been payed to the analysis of psychosocial and physical functions in head and neck cancer patients.[4] In 1993 Hassan[5] may have noticed an increased interest in psychosocial rehabilitation outcomes, Morris[6] concluded in the same year that little had been reported on these issues in comparison with other types of cancer, such as breast cancer or Hodgkins' disease.

Psychosocial and physical rehabilitation outcomes are important indicators of the *quality of life*. These aspects of the quality of life are now recognized as significant measures of treatment effectiveness in addition to the more traditional outcome measures as tumor recurrence and survival time.

The question underlying this thesis is whether and how care and cure in head and neck cancer patients can be improved. This thesis will mainly deal with the outcome of rehabilitation and with the prediction of survival by reviewing literature and reporting the results of a descriptive and prospective study.

REHABILITATION

In 1986 our group published a review of studies on physical and psychosocial correlates of head and neck cancer between 1966 and 1984.[7] The majority of these studies concerned the rehabilitation of laryngectomy patients. Most of them emphasized the side effects and complications of treatment following radiotherapy or surgery, which are known to require special care.[8] We further observed great variation in the reported results of rehabilitation and poor understanding of the factors, which could influence rehabilitation outcomes of *long-term* survivors.[7] It was a remarkable finding that at that time no studies on physical and psychosocial rehabilitation outcomes of T1 glottic larynx carcinoma were available, despite the fact that these tumors form the majority of head and neck cancer sites.

Since 1984 quality of life research in head and neck cancer has increased manifold.[9] An update of literature is presented in chapter 2.

For patients, the time around the diagnostic procedure and treatment of the disease is a short but burdening period of their life. Most remember it as a horrible episode that they would rather forget. After this period, patients must come to terms with the new handicaps caused by their illness and the necessary treatment. Contrary to what one would expect, the end of the period of active medical care (treatment and aftercare) is often associated with heightened uncertainty and anxiety.[10] Nearly all patients worry about the possibility of disease recurrence and need the reassurance that emanates from the specialist's examination. In order to respond adequately to worries of the patients, we need a better understanding of their physical and psychosocial functioning over a longer period of time. The available literature provides insufficient data in this respect.

DESCRIPTIVE STUDY

The first objective of the retrospective study (chapter 3) was to map the rehabilitation process and outcomes in three different treatment groups of long-term survivors: (1) T1 glottic cancer patients treated with irradiation (2) laryngectomy patients and (3) those who had surgery for cancer in the oral cavity and/or oropharynx.

The second objective was to find factors in the rehabilitation process that could be considered to be predictors of rehabilitation outcomes.

Included in the study were patients with head and neck cancer with a follow up period of two to six year after treatment. With the help of a special questionnaire, concerning medical and psychosocial issues, and data extracted from the medical records, information on the rehabilitation was obtained.

PREDICTORS OF SURVIVAL

The course of malignant disease is probably influenced by a complex interaction of medical, sociodemographic and psychosocial factors. In the first place we tried to review current data on medical prognostic factors in head and neck cancer. Secondly, information regarding the prognostic value of sociodemographic and psychosocial factors had to be obtained. As soon as it became clear that no information on psychosocial prognostic factors for head and neck cancer was available, the study of literature was extended to other cancer sites.

MEDICAL PROGNOSTIC FACTORS IN HEAD AND NECK CANCER

Patients treated for head and neck cancer have an overall five year survival of 50%.[11] The cause of death in the remaining 50% is related to the primary disease or to another cause. Traditional correlates of treatment outcomes such as tumor and treatment factors are extensively discussed in the literature. The gross morphologic extent of the tumor, characterized by the TNM (tumor, node, metastasis) classification system, at the beginning of the treatment, is described as an important prognostic factor.[12] Some histological tumor factors, such as histological grading, surgical margins, status of cervical nodes and micro-vascular invasion, have also been found to provide prognostic information with respect to tumor control and survival.[13] In the last few years there has been a growing number of biological tumor factors that might have an effect on prognosis. Apart from tumor factors, patient factors such as gender, age, social-class, nutritional state and general health status, are mentioned as having possible influences on prognosis.[14] A review of the literature which focused on identifying factors generally accepted as have a bearing on prognosis is presented in chapter 4.

PSYCHOSOCIAL PROGNOSTIC FACTORS

Today's knowledge of medical prognostic factors cannot explain why two patients, both in similar general condition, with the same tumor localization, the same tumor staging, with the same treatment regime, differ in their survival times. This may indicate that still unexplored medical prognostic factors play a role. On the other hand several publications suggested the possibility that psychosocial functioning is not only an outcome measure of tumor treatment but can also have an effect on the risk of cancer incidence, the course of the illness, and even the survival of the patient.[15]

A study of the literature (chapter 5) on the interaction between psychosocial factors and prognosis in cancer revealed contradictory conclusions and methodological shortcomings. Therefore, no definite conclusions could be drawn.

PROSPECTIVE STUDY

Until now the relation between psychosocial factors and prognosis in patients with head and neck cancer was not yet studied. Moreover, very little is known about the *interaction* of medical, sociodemographic and psychosocial factors in relation to the quantity of life of these patients.

With these caveats in mind a prospective study was conducted. In this study described in chapter 6, medical, socio-demographic and psychosocial data were collected just before treatment. Six years after the treatment the tumor status and survival were scored from the medical dossier. The objective of the study was to analyze the relation between psychosocial, medical, physical and sociodemographic factors, and survival and tumor relapse.

MODEL OF COPING WITH CANCER

The basis of studying physical and psychosocial functioning within the framework of this thesis is the theoretical model of coping with cancer introduced by Van den Borne and Pruyn.[16] This model is based on the assumption that uncertainty, negative feelings (eg, feelings of depression, loneliness and psychosocial complaints), loss of control, and threatened self-esteem are the four most important psychosocial problems experienced by cancer patients. Coping strategies of patients are directed at preventing or reducing these problems as much as possible. The environment of the patient (eg, his/her family, medical specialist) can also help by offering information and support. In this process of coping with cancer, person-related factors and illness-related factors may influence outcomes of rehabilitation and prognosis.

CONCLUSIONS

The final chapter (7) comprises the summary, as well as recommendations for future research and suggestions for improving daily care.

REFERENCES

1 Visser O, Coebergh JWW, Schouten LJ. (eds): *Incidence of Cancer in the Netherlans 1992: fourth report of the Netherlands Cancer Registry* Utrecht, 1995, 23-43.

2 Coebergh JWW, Van der Heijden LH, Janssen-Heijnen MLG. Cancer incidence and survival in the Southeast of the Netherlands 1955-1994: a report from the Eindhoven Cancer Registry. Eindhoven, the Netherlands: IKZ, 1995:101,117.

3 Bailar JC, Gornick HL. Cancer undefeated. *N Engl J Med* 1997;22:1569-74.

4 Barofsky I. Response on quality of life in cancer patients. *Cancer* 1984;53:2299-302.

5 Hassan SJ, Weymuller EA. Assessment of quality of life in head and neck cancer patients. *Head Neck* 1993;15 485-96.

6 Morris J. Widening perspectives: Quality of life as a measure of outcome in the treatment of patients with cancers of the head and neck. *Eur J Cancer B Oral Oncol* 1994;30:29-31.

7 Pruyn JFA, Jong PC de, Borne HW van den, Bosman LJ, Poppel JWMJ van, Rijckman RM, Mey K de. Psychosocial aspects of head and neck cancer: a review study. *Clin Otolaryngol* 1986;11:469-74.

8 Ganz P.A. Current issues in cancer rehabilitation *Cancer* 1990;65:742-51.

9 Morton RP. Evolution of quality of life assessment in head and neck cancer. *J Laryngol Otol* 1995;109:1029-35.

10 Shernan AC, Simonton-Atchley S. Psychological aspects of treating oncology patients In *Cancer of the Head and Neck, Third Edition.* Edited by Meyers EN, Suen JY. Philadelphia: WB Saunders, Co.;1996.

11 Muir C, Weiland l. Upper aerodigestive tract cancers. *Cancer* 1995;75:147-53.

12 Deleyiannis FWB, Weymuller EA. Outcomes research in head and neck oncology. *Cur Opin Otolaryngol Head Neck Surg* 1996:4:73-7.

13 Weymuller EA, Ahmad K, Casiano RR, Schuller D, Scott CB, Laramore G, Al-Sarraf M, Jacobs JR. Surgical reporting instrument designed to improve outcome data in head and neck cancer trials. *Ann Otol Rhinol Laryngol* 1994:103:499-509.

14 Stell PM. Prognosis in mouth cancer: host factors. *J Laryngol Otol* 1992;106:399-402.

15 Holland JC. Behavioral and psychosocial risk factors in cancer: human studies. In: Holland JC, Rowland JH. *Handbook of psycho-oncology.* New York, Oxford: University Press, 1989: 705-26.

16 Borne HW van den, Pruyn JFA. Lotgenotencontact bij kankerpatiënten.

(*Contacts between fellow cancer patients*). Thesis, Van Gorcum, Assen/Maastricht, 1985.

1

Chapter 2

PHYSICAL AND PSYCHOSOCIAL CORRELATES OF HEAD AND NECK CANCER: A REVIEW OF THE LITERATURE

ABSTRACT

This chapter reviews recent literature on the physical and psychosocial correlates of head and neck cancer, with a focus on quality of life issues, rehabilitation outcomes and changes in the literature from the previous decade. These studies have shown that head and neck cancer has an enormous impact on the quality of life of patients. The most important physical complaints are speech problems, dry mouth and throat, and swallowing problems. Pain is also frequently reported. Disturbances in psychosocial functioning and psychological distress are reported by a considerable number of patients: worry, anxiety, mood disorder, fatigue and depression are the main symptoms. Cancer of the head and neck has a negative effect on social, recreational and sexual functioning. Despite of a growing number of longitudinal studies, little is still known about the rehabilitation outcomes over a longer period of time. Future research is necessary to form a consensus about the further development and use of specific instruments to study patients with cancer of the head and neck, to conduct more prospective studies, and to develop programs that are aimed at maximizing rehabilitation outcomes and evaluate these programs with randomized designs.

INTRODUCTION

The diagnosis and treatment of any cancer is frightening for patients and their families. Cancers of the head and neck account for 5% of all malignant tumors.[1,2] Surgery and radiotherapy, alone or in combination are still the treatment modalities of choice, depending on several factors such as tumor stage, accessibility and the expected post-treatment function; however, in more advanced cancers, chemotherapy is being used more frequently in combination with radiotherapy with the goal of organ preservation, in the so-called "neoadjuvant* setting."[3] Many vital functions, such as mastication, swallowing, speaking, taste, smell and appearance can be affected, both before and after treatment. Even minor disturbances of the anatomy by surgery may lead to significant dysfunction and disfigurement, and hence to psychosocial complaints. For this reason, head and neck cancer has been described as a psychologically highly traumatic cancer type. Although improvement in surgical skills with refinement of reconstructive techniques and more sophisticated radiotherapy have made treatment of more advanced tumors possible with an acceptable functional and cosmetic outcome, these improvements only have a positive influence on loco-regional tumor control. Unfortunately, this does not result in a better survival; since in the past decade the 5-year survival-rate has stabilized at about 50%.[4]

Given the visible deformities caused by head and neck cancer, several studies have been conducted to identify the psychosocial impact of the disease. Morris[5] concluded that despite the importance of the impact of this disease, the studies that have been conducted are, compared with other types of malignancies, relatively few, and the results are often conflicting.Nevertheless, there is a steadily increasing body of clinical research in this field, which has been the subject of recent reviews from different aspects.[6,7,8,9,10,11]

In 1986, a review of the literature on the psychosocial aspects of head and neck cancer patients was conducted by our group.[6] The review included 117 reports of studies conducted between 1966 and March 1984 that related to factors influencing the rehabilitation processes. It appeared that the majority of studies had focused on the rehabilitation of patients who had undergone laryngectomy. Few investigations described the physical and psychosocial consequences of surgical treatment for cancer of the oral cavity and/or oropharynx. It was concluded that there was great variability in the reported results of rehabilitation and that there was little insight available about which

---

* Chemotheraphy as a substitute for surgery in treatment of advanced resectable head and neck cancer.

factors influenced rehabilitation. Very little was known about the nature of the problems experienced and the factors which influenced these problems during the course of the illness. Contradictory results and limited insight into the rehabilitation process were found to be the result of methodological shortcomings and a lack of theoretical basis of most of the studies (hypotheses have been tested in only seven studies). The majority of the studies used a descriptive, retrospective methodology. Only 13 studies chose a longitudinal approach. It was also mentioned that retrospective studies have a number of drawbacks, including overrepresentation of patients with positive treatment outcomes.

A decade has passed since the aforementioned literature review was conducted, and progress has been made in this area. The purpose of this article is to update the literature and to assess the extent of progress in the past 10 years.

DEFINITION REHABILITATION OUTCOMES: QUALITY OF LIFE

The term *rehabilitation* is used in different ways. We defined rehabilitation as: the intentional and unintentional behavior of the patient, professional and significant others, aimed at reduction or solving as many problems for the patient as possible or aimed at the preventing of problems. Rehabilitation has physical, psychological and social aspects. Rehabilitation outcomes can be considered as an equivalent of quality of life and the terms are often used interchangeably.

Although the term *quality of life* has been used as both a concept and an instrument of measurement, it has rarely been defined explicitly.[9,12.13] At its most fundamental level, quality of life is both subjective, including patients view, and multidimensional, covering a broad range of areas of patients life. Quality of life also is dynamic, because it often changes across time and situations.[14,15] Some authors mentioned quality of life as representing the gap between the perceived reality of what one has, and what one wants or expects.[10,16,17] We were able to find only one manuscript in which a theoretical model of quality of life after laryngectomy was developed.[18] Assessment of health related quality of life has been advocated as a means for translating how a patients' response to treatment is experienced by the patient. Thus quality of life has become an important outcome measure in oncology.

METHODS

The search procedure was similar to that conducted in 1984; the computer databases MedLine and Psychlit were archived beginning with the keywords *head and neck tumor* or *head and neck cancer*. This lengthy data set was reduced by limiting the search with the keywords *rehabilitation* and *psychology*. To be certain that all applicable articles were included, the next step in the procedure involved including the phrases *quality of life*, *psychosocial functioning*, and *laryngectomy*. The search encompassed the years 1984 through 1995. References from identified manuscripts were traced for potential additions to the database. We also retrieved references in recent relevant articles. Only studies published since 1984 in English were included in our data set. Abstracts and manuscripts of identified articles were reviewed and a final set of 50 studies was used for inclusion in this review.

Most studies were presented in 1990 through 1996 (n=37), indicating that there is a growing interest in psychosocial and functional correlates of head and neck cancer (Table 1). Nearly half of the studies dealt with all sites of head and neck tumors (n=21). Nine studies were concerned with the larynx (surgery, partial or total, and radiotherapy, n=8 and n=l, respectively). Patients who were treated for a tumor located in the oral cavity or oropharynx were the subject of study in 8 articles. The remaining 12 studies dealt with both larynx and oral cavity/oropharynx.

Most studies have a cross-sectional study design (n=34) whereas one third are prospective, using at least two measures over time. In the majority of studies the statistical analyses were limited to univariate techniques. Multivariate analyses were used in only eight studies.

INSTRUMENTATION

The most frequently used instruments in assessing quality of life have each been critiqued in the literature as nonspecific to head and neck cancer patients, thus rendering their reliability somewhat questionable. For example, the Karnofsky scale, although specific to cancer, does not include items on facial disfigurement, difficulty in speaking or eating concerns.

Although the bulk of the research relating to psychosocial correlates of head and neck cancer that has been conducted in the past 10 years has focused on quality of life measures, there is a general lack of consistency across studies. A number of potential correlates of head and neck cancer survival and the quality of life after diagnosis have been mentioned in the literature.

Table 1 Properties of Quality of Life studies in head and neck cancer patients

Author	Study design	Sample Size	Type of analisys	Variation in time since treatment	Sample sites	Valid instrument
1. Ackerstaff, 1994 [26]	Cross-sectional	63	Univariate	3 mo-24 yr	Total laryngectomy	Yes
2. Albertini, 1993 [53]	Cross-sectional	43	Univariate	Long-term survivors	Total laryngectomy	Unknown
3. Baile, 1993 [39]	Prospective	63	Univariate	Pretreatment	All sites	Yes
4. Baker, 1992 [62]	Cross-sectional	51	Univariate	7 mo -5 yr	All sites (≥ stage II)	Yes
5. Beeken, 1994 [71]	Cross-sectional	25	Univariate	1-8 yr	Oral cavity, pharynx, salivary glands	Some
6. Bjordal, 1992 [13]	Cross-sectional	126	Univariate	Used for analysis	All sites	Validation
7. Bjordal, 1994a [55]	Cross-sectional	204	Multivariate	7-11 yr	All sites	Yes
8. Bjordal, 1994b [19]	Cross-sectional, pre-test	60	Univariate	Pretreatment -> 6 mo	Oral cavity, larynx, other sites (12)	Development
9. Bjordal, 1995a [36]	Cross-sectional	204	Multivariatie	7-11 yr	All sites	Yes
10. Bjordal, 1995b [72]	Cross-sectional	50	Univariate	1-6 yr	Oral cavity, pharynx, parotic glands and carcinoma unknown primary	Yes
11. Browman, 1993 [73]	Longitudinal	175	Univariate	Weekly (6½ wk of treament and 4 wk posttreatment)	Oral cavity, oro/ hypoparynx, larynx	Some
12. Chaturvedi, 1996 [34]	Cross-sectional	50	Univariate	Perioperative	Oral cavity, oropharynx and larynx	Yes
13. Davies, 1986 [40]	Prospective	38 and 44	Multivariate	Preteratment	All sites	Yes
14. D'Antonio, 1996 [14]	Cross-sectional	50	Univariate	3 mo-6 yr	Larynx, oral cavity, pharynx, other (4)	Yes
15. De Boer, 1995 [25]	Cross-sectional	118	Multivariate	2-6 yr	Larynx, oral cavity, oropharynx	Yes
16. Espie, 1989 [35]	Cross-sectional	39	Univariate	Used for analyses	Oral cavity, oropharynx (major surgery)	Some

Table 1 Continued

Author	Study design	Sample Size	Type of analisys	Variation in time since treatment	Sample sites	Valid instrument
17. Gamba, 1992 [30]	Cross-sectional	66	Univariate	6 mo-8 yr	All sites (surgically treated)	No
18. Giardi, 1992 [74]	Longitudinal	104 and 514 healthy controls	Univariate	Pretreatment - 1 yr (max 5 measures)	All sites	Yes
19. Gritz, 1991 [68]	Longitudinal, randomised, intervention	186	Univariate	Pretreatment - 1 yr (max 5 measures)	Oral cavity, pharynx, larynx	Yes
20. Gritz, 1993 [69]	Longitudinal, randomised, intervention	186	Multivariate	Pretreatment - 12 mo (4 measures)	Oral cavity, pharynx, larynx	Yes
21. Hassan, 1993 [20]	Longitudinal	75	Univariate	Pretreatment - 3 mo (3 measures)	All sites	Yes
22. Hilgers, 1990 [28]	Cross-sectional	59	Univariate	6 mo - 19 yr	Total laryngectomy	Yes
23. Jay, 1991 [49]	Cross-sectional	65	Univariate	6 mo - 36 yr	Total laryngectomy	No
24. Jensen, 1994 [27]	Cross-sectional	43	Univariate	5.4-12.2 yr	Larynx, pharynx	No
25. Jones, 1992 [48]	Cross-sectional	48	Univariate	4-26 mo	All sites (surgically treated)	Some
26. Keefe, 1985 [31]	Longitudinal	30	Univariate	Pretreatment to 2-3 mo (3 measures)	All sites (≥ stage II)	Some
27. Kornblith, 1996 [75]	Cross-sectional	47	Multivariate	7 mo - 9.7 yr	Upper alveolar ridge, palate, maxilla	Yes
28. Kreitler, 1993 [15]	Cross-sectional (also orthopedic patients and healthy individuals)	55 (head and neck)	Univariate	6 mo - 21 yr	All sites	Some
29. Kreitler, 1995 [63]	Cross-sectional	55	Univariate	6 mo - 21 yr	All sites	Some

Table 1 Continued

Author	Study design	Sample Size	Type of analisys	Variation in time since treatment	Sample sites	Valid instrument
30. Krouse, 1989 [29]	Longitudinal	33	Univariate	Preoperative & 3, 9, 12 mo after discharge	Larynx, oral cavity, oropharynx, other sites (4)	Yes
31. Langius, 1993 [33]	Cross-sectional	29	Univariate	Pretreatment, (1 measure)	Oral cavity, pharynx (surgically treated)	1
32. Langius, 1994 [64]	Cross-sectional/ longitudinal	27/15	Univariate	12 mo / before & 2-4 mo after treatment	Oral cavity, pharynx (surgically treated)	Yes
33. Langius, 1995 [23]	Cross-sectional	42	Univariate	12 mo	Oral cavity, pharynx (surgically treated)	Some
34. Lansky, 1989 [76]	Cross-sectional	150	Univariate	Varying intervals from diagnosis, >5yr	Oral cavity, parynx, larynx, other (10)	No
35. List, 1990 [54]	Cross-sectional (comparison with breast cancer group)	181	Univariate	3 wk - 38 yr	Oral cavity, parynx, larynx, other (12)	Development
36. List, 1990 [54]	Longitudinal	21	Univariate	2, 6, 12 wk & 6 mo	Larynx (different surgical procedures)	Yes
37. Llewellyn, 1984 [78]	Longitudinal	30/29	Univariate	4-times during treatment/ 2-times posttreatment, 6 wk apart	Larynx, radiotherapy only	Yes
38. Manuel, 1987 [37]	Longitudinal	35	Multivariate	Pretreatment and 2 times during/after treatment	All sites (≥ stage II)	Yes

Table 1 Continued

Author	Study design	Sample Size	Type of analisys	Variation in time since treatment	Sample sites	Valid instrument
39. Mathias, 1988 [61]	Longitudinal	14	Univariate	At 8 wk intervals	All sites (stage III/IV)	No
40. Mathieson, 1991 [32]	Cross-sectional	51	Univariate	1-128 mo (9 with pain)	Total laryngectomy	Yes
41. Morton, 1984 [41]	Cross-sectional	48	Univariate	6 mo - 3 yr	Oral cavity, pharynx, larynx	Yes, uncommon
42. Morton, 1995 [56]	Longitudinal	130	Univariate	Before & 3, 12 and 24 mo	All sites	Development
43. Mohide, 1992 [24]	Cross-sectional	20	Univariate	1-10 yr	Total laryngectomy	No
44. Padilla, 1991 [79]	Longitudinal	129	Univariate	During wk 1& 3, at the end, & 1st follow-up	All sites (receiving radiotherapy)	No
45. Rathmell, 1991 [51]	Cross-sectional	96	Univariate	6 m -> 5 yr used for analysis	All sites (advanced stages)	No
46. Rapoport, 1993 [50]	Cross-sectional	55	Univariate	6 mo - 21 yr used for analysis	All sites, all stages	Yes
47. Stam, 1991 [59]	Cross-sectional	51	Multivariate	Unknown (after larngectomy)	Total laryngectomy	Yes
48. Strauss, 1989 [38]	Cross-sectional	28	Univariate	2-5 yr	All sites (major surgery)	No
49. Teichgraeber, 1985 [52]	Cross-sectional	51	Univariate	> 6 mo	Oral cavity	Development
50. Westlin, 1988 [42]	Cross-sectional	53	Univariate	Unknown	All sites	Some

Table 2 Head and neck specific quality of life measures

Module no.	Author	Domains (no. of items, assessment)	Module
1	Bjordal [19]	Physical functioning, role functioning, pain, fatigue, emesis, scales measering QoL, disease- and treatment-related symptoms (37-items, patient rated)	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck (EORTC QLQ-H&N37)
2	Browman [72]	Acute morbidity caused by radiotherapy (22-items, patient rated)	Head and Neck Radiotherapy Questionnaire (HNRQ)
3	Cella [21]	Functional assessment of food intake, quality of voice, appearance (9-items, patient rated)	Functional Assessment of Cancer Therapy-Head and Neck Scale (FACT-HNS)
4	Skeel [79]	Physical complaints, functional ability, emotional well-being, treatment satisfaction, social and occupational functioning (34-items, patient rated)	Function, Symptoms and Perception of Wellness Evaluation (FSPE)
5	Hassan [20]	Pain, disfigurement, activity, recreation/entertainment, employment, eating, swallowing, speech, shoulder disability (40-item, patient rated)	University of Washington Quality of Life Questionnaire (UW-QOL)
6	De Boer [25] De Haes [80]	Uncertainty, physical and psychosocial complaints, self-efficacy, information and support (21-50-31-items, patient rated)	Rotterdam Symptom Check List-Head and Neck (RSCL-H&N), Head and Neck specific Self-Efficacy - and Uncertainty Scale (H&N-SES&US)
7	Jones [48]	Food-intake, weigt loss, physical and psychosocial complaints, stoma care (14-items, patient rated)	EORTC Head and Neck-module
8	Kornblith [74]	Obturator functioning (15-item, patient rated)	Obturator Functioning Scale (OFS)
9	Jensen [27]	Side effects of treatment, speech function, eating function, xerostomia, pain, social relations, employment situation, overall opinion of treatment (27-items, patient rated)	Late Side effects on daily life scale
10	Langius [23]	Surgery-, radiotherapy-, psychosocial-related conditions (29-items, patient rated)	Oral and Pharyngeal Nursing Care Questionnaire (OPNCQ)

Table 2 Continued

Module no.	Author	Domains (no. of items, assessment)	Module
11	Lansky [76] List [54]	Understandebility of speech, normalicy of diet, eating in public (unstructured interview, clinician rated)	Performance Status Scale-Head and Neck (PSS-HN)
12	Llewellyn [77]	Voice quality (16-items, patient rated)	Linear Analogue Self Assessment of voice quality
13	Mathias [60]	Social support, faith, self-concept, perception of health related to illness (21-items, patient rated)	QOL instrument pertinent to HNSCC patients
14	Teichgraeber [52]	Intelligibility of speech, swallowing ability, employment status, pain levels, weight, salivation, status of mandible and teeth, taste (clinician rated)	Test series for functional evaluation of oral cavity cancer

A recent review of quality of life measures in head and neck cancer identified over 20 parameters that have been used to study quality of life.[10]

During the past decade several head and neck-specific modules have been developed (Table 2). In reviewing the literature we found 14 different modules. In analyzing the domains of specific head and neck measures, we concluded that there has been no systematic approach to the drawing up of the majority of the modules. The parameters that have been used to gather the specific information pertaining to head and neck cancer, are categorized in Table 3. It appears that most of the specific head and neck instruments have been developed in the area of physical and psychosocial functioning and complaints.

None of the tumor specific modules for head and neck cancer patients are in general use. However, a few are being tested across cultures and languages, and/or in a large patient population, such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Head and Neck-37,[19] the University of Washington Quality of Life Questionnaire,[20] and the Functional Assessment of Cancer Therapy-Head and Neck Scale.[22]

There is a general consensus that the equivalence of clinician ratings and patient ratings is questionable.[22] Several investigators agree that the responses of health care professionals do not fully correlate with head and neck cancer patients priorities.[9,13,23,24] Therefore it is concluded that patients should be

Table 3 Domains of the Specific Head and neck modules

Domain	Module no. from Table 2
Physical functioning and complaints	1,3,4,5,6,8,9,11,12,14
Pain	1,5,9,14
Psychosocial functioning and complaints	4,6,7,10,13
Body and self image	6
Social and recreational functioning	1,4,5,9,14
Treatment-related factors	1,2,9,10
Information and support	6,12
Other factors that influence rehabilitation outcomes	7,8
Global ratings of quality of life	1,13

the primary source of data collection and thus minimize the opportunity for health worker bias.[13,20]

REHABILITATION OUTCOMES

Physical Functioning The findings on physical functioning outcomes were varied. Some studies reported a considerable number of physical complaints following treatment[25], and others reported physical complaints among a small percentage of the study population.[26] In irradiated T1-larynx carcinoma patients, these complaints were hoarseness in 58%, choking in 41 %, and phlegm in mouth and throat in 57%.[25]

Patients who had undergone laryngectomy tended to report more problems with speech and eating than patients receiving composite resections.[25,27] Hilgers et al. found that of 59 patients who had undergone laryngectomy, 98% reported daily sputum production as their principal symptom.[40] Krouse et al.[29] found in patients with different tumor sites that those who underwent radiation therapy after surgery had the most physical difficulties, which remained even at 1-year follow-up.

Appearance is often a concern of patients with head and neck cancer. One in five patients, disease free 6 months to 8 years after both minor and extensive disfiguring surgery, perceived themselves as changed physically.[30] More than half of of the patients with larygectomy and composite resection believed their appearance was damaged by their treatment.[25]

Many head and neck cancer patients report pain as a negative outcome of their disease and subsequent treatment.[29,31,32] Shoulder and back pain were perceived as the frequent general symptoms of oral and pharyngeal cancer patients.[33] In a study involving patients with oral cancer and patients with laryngeal cancer in India, it was found that the latter group experienced significantly more pain that those of the former group.[34]

Other physical complaints such as a reduced sense of taste and smell, stiff neck, drooping shoulder, and an ill-fitting dental prosthesis as a result of the tumor and its treatment were mentioned as more or less serious outcomes.

Psychosocial Functioning Although several studies have examined factors such as psychological distress, a standard anxiety assessment was not available. Espie et al.[35] compared anxiety levels between patients who had received different types of treatment (pedicle flap vs. radial free flap reconstruction) and between patients with different tumor sites (anterior floor of the mouth, tongue, retromolar trigone, buccal mucosa). They found no significant differences between groups on any measure of psychological distress. Bjordal and Kaasa[36]. reported that a high prevalence of psychological distress was found in patients treated with different radiotherapy regimen. In patients with oral and pharyngeal cancer feelings of worry and anxiety were perceived as frequent general symptoms.[33]

The experience of stress associated with head and neck cancer was greatest at the point of diagnosis and receded as the patient progressed through treatment.[37] In a descriptive study among 28 patients who had disfiguring oral and maxillofacial treatment, all patients reported considerable presurgical anxiety.[51] Anxiety and depression were significant problems in patients before the biopsy was taken, regardless whether the lesion was malignant or benign.[39]

Reports of the prevalence of depression associated with head and neck cancer are inconsistent. Some studies have found high levels of depression in their patients,[25,29,39,40] whereas others point out that it is an uncommon feature of the disease.[37,41] Although one study found that depression among head and neck cancer patients was related to age, this finding has not been validated.[35] The relationship between gender and depression among patients with head and neck cancer is also inconsistent. Espie et al.[35] found that depression was significantly higher among women than among men, and Westin et al.[42] found no reported depression among women in their sample. The Westin et al. study suggested that mental depression may be linked with malnutrition rather than the malignant condition. However, in this study the relatively small sample contained many tumor sites and stages in the head and neck region, at different points in therapy, after several types of treatments, and with various levels of treatment success.

One outcome of depression is suicide, and although suicide in connection to cancer is rare, the odds of suicide have been found to be much higher among cancer patients than among controls.[43-45] In an 8-year survey of hospital suicides, it was discovered that cancer patients were involved in one-fourth.[46] Twenty different cancer sites were studied, and in 19%, the tumor was located in the in the larynx and oral cavity. In the group of male Swedish cancer patients who had commited suicide, Bolund[44] found that nine patients witin a 3-year period, had oral and pharyngeal cancer, which was the largest group in the study.

Fatigue is now acknowledged to be the most common symptom that occurs in cancer patients.[47] Jones et al.[48] found that symptoms of fatigue were common among who had undergone laryngectomy and other operations. A longitudinal study of post-surgery patients with cancer of the head and neck found that fatigue and weakness were major concerns, as long as 9 to 12 months after surgery.[29] Another study found a correlation between fatigue and voice quality in patients who had undergone laryngectomy.[28]

One of the major concerns reported by patients with head and neck cancer is the disfigurement associated with their disease and subsequent treatment. In a study by Gamba et al.,[30] 45% of the patients with head and neck cancer reported that self-image was the most important change following their surgeries. The negative comments of a group with extensive disfigurement nearly doubled those of a second group with minor disfigurement. Many patients with cancer of the head and neck cancer who are concerned about their appearance will isolate themselves from their family and friends.[45] Intensive interviews with patients with cancer of the head and neck revealed that 57% of the patients interviewed experienced being stigmatized or discounted because of their appearance.[38] With the passage of time, patients generally came to accept the change in their physical appearance and no patients reported taking steps to hide their appearance.

Because of the cancer and subsequent treatment, some patients have to discontinue their usual activities in job, household and other activities. Studies of patients who had undergone laryngectomy and patients who had undergone radiotherapy indicated a reduction in social activities following treatment.[34,49] As a result, patients often become socially isolated.[30] Consequences of mutilation seemed to be the greatest outside the primary environment.[7] Problem domains that are the most pervasive include communication with a partner, functioning in the family, and social and interpersonal relationships.[35,50] A study of long-term side effects on daily life following radiotherapy for larynx and pharynx cancer found few reported social concerns. About 10% reported having less contact with other people than before their treatment and only a few reported increased contacts with others.[55] Rathmell et al.[51] found decreased social contacts in 78% of the patients interviewed immediately after radiotherapy was completed.

In a study by Jensen et al.[27] 10% of the patients who had undergone irradiation for larynx/pharynx carcinoma had retired due to cancer, or therapy-related side effects. Most of the patients with an oral cavity carcinoma who were employed before their surgery were working again by three months after surgery.

Although the extent of sexual functioning has been included in several studies, it has not yet been the major focus of any study. Patients with extensive disfigurement after surgery reported significantly greater reduced sexuality than patients with minor disfigurement.[30] Studies have reported decreases in sexual contact ranging from 17% to 48%.[25,49,53] However, another study concluded that sexuality was not a significant problem domain for patients with cancer of the head and neck.[50] Given the concern that patients have for their physical appearance, it is not surprising that patients with cancer of the head and neck have reported some decline in sexual functioning after surgery.

Factors Related to Rehabilitation Outcomes The type of treatment and perception of care received can have a significant effect on recovery, in terms of speed of recovery, pain associated with recovery, and extent of disfigurement.

List et al.[54] found that patients receiving total laryngectomy scored lower on understandability of speech and normalcy in diet, compared to a flap reconstruction group, which scored lower on eating in public. Teichgraeber et al.[52] studied the oral cavity function and general health of patients treated for oral cavity cancer. In this study patients with intraoral skin grafts had the best speech results and those with primary closure had the best swallowing performance. Three studies comparing radiotherapy to other treatments found that patients treated with radiotherapy reported greater difficulty adjusting, higher psychological distress and physical problems such as bad taste, mouth dryness, chewing problems, and mouth pain.[29,36,55] In a study involving patients with buccopharyngeal cancer, it was found that functional disability was lower and performance status higher in those treated with radiotherapy alone.[41] It was concluded that radiotherapy seemed to be a well-tolerated treatment with relatively little impairment of the daily life in patients with laryngeal cancer. No differences were found between treatment groups for depression, pain, psychological well-being, or life satisfaction. A later study involving 130 patients with head and neck cancer reported that treatment modality was not a significant determinant of life satisfaction.[56]

The importance of social support in recovery and rehabilitation from cancer has been widely reported.[57-60] Mathias et al.[60] found in patients with head and neck cancer that social support contributed to a patient's well being independent of tumor status. It has been suggested that negative outcomes associated with physical and psychological disorders are modified by the availability of social support.

Family, friends, professional care givers, and fellow patients have been identified as potential sources of social support. De Boer et al.[25] found that open discussion of illness in the family, social support from others and adequate information from specialists were predictors of positive rehabilitation outcomes in head and neck cancer patients. Other studies have confirmed the significant contribution of social support to positive rehabilitation outcomes, particularly when the support comes from family and close friends.[62] One of the strongest predictors of distress in a study involving patients who received a laryngectomy was whether a fellow laryngectomy patient had visited the patient before surgery.[10] Patients who were highly informed reported better adjustments in interpersonal relations and had more intimacy with family, but had more fears, anxiety, worries about health, and concern with physical symptoms.[63] The levels of support and information have not been found to be correlated to successful coping.[64]

Patient-related factors, such as locus of control, and the strategies of coping are likely to have influence on rehabilitation outcomes. Patients with high internal locus of control have more self-confidence in speech and physical functioning and greater feelings of self-esteem with regard to their achievements.[25] In a longitudinal study examining coping strategies in patients with head and neck cancer, patients who used either approach or avoidance coping strategies showed lower initial levels of emotional distress than patients who did not use either strategy.[37] Symptoms of distress decreased in patients using these coping strategies.

Espie et al.[35] found that women and younger people were more at risk to psychological distress than men and older people. Women scored significantly higher than men with respect to state anxiety, psychosocial complaints, and head and neck-specific complaints and reported more often the feeling that their appearance was damaged.[25]

Little is known about rehabilitation outcomes over time. In general, the longer the time since treatment, the fewer psychosocial complaints the patients had and the better the quality of life.[25,28,51] Patients had a considerable number of physical and psychosocial problems between 2 and 4 years after surgery and radiotherapy.[30,51] Most physical problems related to the disease decreased with time, but psychological problems got worse. The authors ascribe this unexpected deterioration in quality of life to "patient burnout", which could be decreased by acquiring adequate coping skills.[50] Espie et al.[35] could not find any effects on psychological distress based of time elapsed since operation.

Continued smoking among patients with cancer of the head and neck has been shown to lead to as much as a fourfold increased relative risk of cancer recurrence compared with the risk in nonsmokers, and a doubled risk compared with that in patients who quit smoking.[65] Early studies reported little success with physician led smoking cessation interventions for patients with head and neck cancer, although more recent studies have reported greater success.[66,67] A physician-based smoking cessation intervention with patients with head and neck cancer yielded no significant effects.[68,69] In several studies involving laryngectomies 9 to 13% of patients continue smoking after surgery.[25,26,49] Stam et al.[59] found that the amount smoked before the onset of cancer was strongly associated with the patients' length of stay in the hospital after laryngectomy. Little is known about the smoking habits of patients after irradiation of their larynxes. In one study, more than one quarter of the 66 Tl-larynx carcinoma patients continued to smoke following radiotherapy.[25]

Alcohol is less generally understood as a cause of increased risk for cancer of the head and neck.[70] Strauss et al.[38] found that 71% of the patients interviewed felt that they had significant habit-related risk factors that had increased their chance of having cancer, and about one third continued to smoke or drink in spite of their disease. Two to six years after surgery 67% of the patients who had undergone laryngectomy and 70% of patients cavum oris/oropharynx cancer appeared to have increased their alcohol intake.[25] Fifty-six percent of these patients used alcohol every day.

CONCLUSIONS

Head and neck cancer has an enormous impact on the quality of life of patients. Quality of life encompasses several domains of rehabilitation outcomes. The most important physical complaints are speech problems, dry mouth and throat, and swallowing problems. Pain is also frequently reported. Disturbances in psychosocial functioning and psychological distress are reported by a considerable number of patients; worry, anxiety, mood disorders, fatigue and depression are the main symptoms. These psychological disorders might be responsible for the higher suicide rate in patients with head and neck cancer than patients with other types of cancer. Another problem domain specific to head and neck cancer is the damage to body image and self-esteem as a result of the illness and/or disfiguring treatment. It can be concluded that cancer of the head and neck has a negative effect on social, recreational and sexual functioning. With respect to addictive behaviors the review reveals that there is a general decline in smoking habits after treatment, but in patients receiving laryngectomy, there is an increase in alcohol use. It can be concluded that most of the rehabilitation outcomes are related to the type of treatment. The extent of surgery or the target site of irradiation are responsible for the kind of physical problems; Patients treated with radiotherapy alone seem to be better off with respect to the level of quality of life impairment. The combination of treatment modalities influences the seriousness of their physical and psychosocial complaints. Despite of a growing amount of longitudinal studies, little is still known about the rehabilitation outcomes over a longer period of time.

There are indications that certain factors, such as coping strategies, patient sex, and use of well-functioning prostheses have a positive effect on rehabilitation outcomes. Factors that clearly have a positive influence on the rehabilitation results are information and support. The latter was also an important finding in our previous review from 1986.

When we make further comparisons between the results of this study and the review from ten 10 years ago, we see three positive developments. (1) more studies describe medical and psychosocial aspects in an integrated way; (2) there is an increasing balance between the number of articles addressing patients having cancer of the larynx and patients with cancer of the oral cavity and the oropharynx; and (3) there is a considerable growth in the development of specific head and neck instruments. We also come to the same four conclusions: (1) there is still a great variability and contradiction in results, probably because of the small sample sizes and varying instruments; (2) most studies are still retrospective in design; (3) many studies still use only descriptive or correlational analyses (multivariate analyses were performed much less often); and (4) there is still a lack of theoretical basis.

On basis of the above results, for future research it is necessary to:

1. Come to a consensus about the further development and use of specific instruments to study patients with cancer of the head and neck.
2. Conduct more prospective studies to identify the quality of life domains that are most affected by the treatment, with large enough sample sizes and multivariate analyses.

3. Further develop and use theoretical models from the view of integrated care and coping models.
4. Develop programs that are aimed at maximizing rehabilitation outcomes and that evaluate these programs with randomized designs. At least the aim of programs should be directed at optimizing information and social support.

REFERENCES

1 Million RR, Cassisi NJ, Clark JR. Cancer of head and neck, In: *Cancer: principles and practices*, Devita V, Hellman S, Rosenberg SA, eds, 3rd ed. Philadelphia: Lippincott Co., 1989:488-90.

2 Visser O, Coebergh JWW, Schouten LJ. (eds): *Incidence of Cancer in the Netherlands 1992: fourth report of the Netherlands Cancer Registry* Vereniging van Integrale Kankercentra, Utrecht, 1995. p.23-43.

3 Ganz P. Current issues in cancer rehabilitation. *Cancer* 1990;65:742-51.

4 Coebergh JWW, Van denHeijden LH, Janssen-Heijnen (eds.): *Cancer Incidence and Survival in the Southeast of the Netherlands 1955-1994: a report from the Eindhoven Cancer Registry* Eindhoven: Integraal Kankercentrum Zuid, 1995. p.20-7.

5 Morris J. Widening perspectives: Quality of life as a measure of outcome in the treatment of patients with cancers of the head and neck. *Eur J Cancer B Oral Oncol* 1994;30b(1):29-31.

6 Pruyn JFA, Jong PC de, Borne HW van den, Bosman LJ, Poppel JWMJ van, Rijckman RM, Mey K de. Psychosocial aspects of head and neck cancer: a review study. *Clin Otolaryngol* 1986;11:469-74.

7 Koster META, Bergsma J. Problems and coping behaviour of facial cancer patients. *Soc Sci Med* 1990;30(5):569-56.

8 Mathieson CM, Stam HJ, Scott JP. Psychosocial adjustment after laryngectomy: a review of the literature. *J Otolaryngol* 1990;19(5):331-6.

9 Gotay CC, Moore TD. Assessing quality of life in head and neck cancer *Qual Life Res* 1992;1:5-17.

10 Morton RP. Evolution of quality of life assessment in head and neck cancer. *J Laryngol Otol* 1995a;109:1029-35.

11 Morton RP. Quality of life measures in head and neck cancer: capabilities and caveats. *Cur Oncol* 1995b;2(2):77-83.

12 Calman KC. Definitions and dimensions of quality of life. In: *The Quality of life of cancer patients.* Aaronson NK, Beckmann J. eds. New York: Raven Press, 1987:1-10.

13 Bjordal K, Kaasa S. Psychometric validation of the EORTC core quality of life questionnaire, 30-item version and diagnostic-specific module for head and neck cancer patients. *Acta Oncol* 1992;31:311-21.

14 D'Antonio LL, Zimmerman GJ, Cella DF, Long SA. Quality of life and functional status measures in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg* 1996;122:482-7.

15 Kreitler S, Chaitchik S, Rapoport Y, Kreitler H, Algor R. Life satisfaction and

health in cancer patients, orthopedic patients and healthy individuals. *Soc Sci Med* 1993;4:547-56.

16 Cella DF. Quality of life: the concept. *J Palliat Care* 1992;8:8-13.

17 Calman KC. Quality of life in cancer patients: an hypothesis. *J Med Ethics* 1984;10:124-7.

18 Maas A. A model for quality of life after laryngectomy. *Soc Sci Med* 1991;33(12):1373-7.

19 Bjordal K, Ahlner-Elmqvist M, Tollesson E, Jensen AB, Razavi D, Maher EJ, Kaasa S. Development of an European Organization for Research and Treatment of Cancer (EORTC) questionnaire module to be used in quality of life assessments in head and neck cancer patients. *Acta Oncol* 1994;33(8):879-885.

20 Hassan SJ, Weymuller EA. Assessment of quality of life in head and neck cancer patients. *Head Neck* 1993;15:485-96.

21 Cella DF, Tulski DS, Bonomi A. The functional assessment of cancer therapy (FACT) scales: incorporating disease-specificity and subjectivity into quality of life assessment. *Proc Annu Meet Am Soc Oncol* 1990;9:325-30.

22 Aaronson NK. Quality of life assessment in clinical trials: methodologic issues. *Control Clin Trials* 1989;10:195S-208S.

23 Langius A, Lind MG. Well-being and coping in oral and pharyngeal cancer patients. *Eur J Cancer B Oral Oncol* 1995;31B(4):242-9.

24 Mohide EA, Archibald SD, Tew M, Young JE, Haines T. Postlaryngectomy quality-of-life dimensions identified by patients and health care professionals. *Am J Surg* 1992;164:619-22.

25 De Boer MF, Pruyn JFA, Borne B vd, Knegt PP, Ryckman RM, Verwoerd CDA. Rehabilitation outcomes of long-term survivors treated for head and neck cancer. *Head Neck* 1995;17:503-15.

26 Ackerstaff AH, Hilgers FJM, Aaronson NK, Balm AJM. Communication, functional disorders and lifestyle changes after total laryngectomy *Clin Otolaryngol* 1994;19:295-300.

27 Jensen AB, Hansen O, Jørgensen K, Bastholt L. Influence of late side-effects upon daily life after radiotherapy for laryngeal cancer. *Acta Oncol* 1994;33(5):487-91.

28 Hilgers FJM, Ackerstaff AH, Aaronson NK, Schouwenburg PF, Zandwijk N van. Physical and psychosocial consequences of total laryngectomy. *Clin Otolaryngol* 1990;15:421-5.

29 Krouse JH, Krouse HJ, Fabian L. Adaptation to surgery for head and neck cancer. *Laryngoscope* 1989;99:789-94.

30 Gamba A, Romano M, Grosso IM, Tamburini M, Cantú G, Molinari R,

Ventafridda V. Psychosocial adjustment of patients surgically treated for head and neck cancer. *Head Neck* 1992;14:218-23.

31 Keefe FJ, Brantley A, Manue GL, Crisson JE. Behavioral assessment of head and neck cancer pain. *Pain* 1985;23:327-36.

32 Mathieson CM, Stam HJ, Koopmans JP. Pain following laryngectomy: psychosocial and medical correlates. *Pain Clinic* 1991;4(1):29-36.

33 Langius A, Björvell H, Lind MG. Oral and pharyngeal cancer patients perceived symptoms and health. *Cancer Nurs* 1993;16(3):214-21.

34 Chaturvedi SK, Shenoy A, Prasad KMR, Senthilnathan SM, Premlatha BS. Concerns, coping and quality of life in head and neck cancer patients. *Support Care Cancer* 1996;4:186-90.

35 Espie CA, Freedlander E, Campsie LM, Soutar DS, Robertson AG. Psychological distress at follow-up after major surgery for intra-oral cancer. *J Psychosom.* Research. 1989; 33(4):441-8.

36 Bjordal K, Kaasa S. Psychological distress in head and neck cancer patients 7-11 years after curative treatment. *Br J Cancer* 1995a;71:592-97.

37 Manuel GM, Roth S, Keefe FJ, Brantley AB. Coping with cancer. *J Human Stress* 1987;winter:149-58.

38 Strauss RP. Psychosocial responses to oral and maxillofacial surgery for head and neck cancer. *J Oral Maxillofac Surg* 1989;47:343-8.

39 Baile WF, Gibertini M, Scott L, Endicott J. Prebiopsy assessment of patients with suspected head and neck cancer. *J Psychosoc Oncol* 1993;10(4):79-90.

40 Davies ADM, Davies C, Delpo MC. Depression and anxiety in patients undergoing diagnostic investigations for head and neck cancer. *Br J Psychiatry* 1986;149:491-3.

41 Morton RP, Davies DM, Baker J, Baker GA, Stell PM. Quality of life in treated head and neck cancer patients: a preliminary report. *Clin Otolaryngol* 1984;9:181-5.

42 Westin T, Jansson A, Zenckert C, Hällström T, Edström S. Mental depression is associated with malnutrition in patients with head and neck cancer. *Arch Otolaryngol Head and Neck Surg* 1988;144:1449-53.

43 Allebeck P, Bolund C. Suicides and suicide attemps in cancer patients. *Psychol Med* 1991;21(4):979-84.

44 Bolund G. Suicide and cancer II; medical factors in suicide by cancer patients in Sweden, 1973-1976. *J. Psychosoc Oncol* 1985;3:31-52.

45 Dhooper SS. Social work with laryngectomees. *Health Soc Work* 1985;10(3):217-27.

46. Faberow NL, Ganzler S, Cutter N, Reynolds CV. An eight-year survey of hospital suicides. *Life-Treatening Behavior* 1971;1:184-201.

47 Piper BF. Fatigue In: Carrieri-Kohlman V, Lindsey A, West C. (Eds): *Pathophysiological phenomena in nursing* 2nd ed. Philadelphia: WB Saunders; 1993. pp. 279-302.

48 Jones E, Lund VJ, Howard DJ, Greenberg MP, McCarthy M. Quality of life of patients treated surgically for head and neck cancer. *J laryngol Otol* 1992;106:238-42.

49 Jay J, Ruddy J, Cullen RJ. Laryngectomy: the patient's view. *J Laryngol Otol* 1991;105:934-38.

50 Rapoport Y, Kreitler S, Chaitchik S, Algor R, Weissler K. Psychosocial problems in head and neck cancer patients and their change with time since diagnosis. *Ann Oncol* 1993;4:69-73.

51 Rathmell AJ, Ash DV, Howes M, Nichols J. Assessing quality of life in patients treated for advanced head and neck cancer. *Clin Oncol* 1991;3:10-16.

52 Teichgraeber J, Bowman J, Goepfert H. New test series for the functional evaluation of oral cavity cancer *Head Neck Surg* 1985;8:9-20.

53 Albertini D, Ferro G, Lombardo P, Maina G, Ravizza I, Bussi M. Total laryngectomy: evaluation of the psychosocial impact on a group of 43 patients. *Proceedings 5th International Congress on Surgical and Prosthetic Voice Restoration after total Laryngectomy* 1993:10-12 sept;p.131, abstract.

54 List MA, Ritter-Ster Ch, Lansky SB. A performance scale for head and neck cancer patients. *Cancer* 1990;66:564-9.

55 Bjordal K, Kaasa S, Mastekaasa A. Quality of life in patients treated for head and neck cancer: a follow-up study 7 to 11 years after radiotherapy. *Int J Radiat Oncol Biol Phys* 1994a;28:847-56.

56 Morton RP. Life-satisfaction in patients with head and neck cancer. *Clin Otolaryngol* 1995c;20:499-503.

57 Wortman CB. Social support and the cancer patient. Conceptual and methodoligic issues. *Cancer* 1984;53(10 Suppl):2339-62.

58 Cohen S. Psychosocial models of the role of social support in the etiology of physical disease. *Health Psychol* 1988;7:269-97.

59 Stam HJ, Koopmans JP, MathiesonCM. The psychosocial impact of a laryngectomy: a comprehensive assessment. *J Psychosoc Oncol* 1991;9(3) 37-58.

60 Richardson JL, Bourque LB. Communication after laryngectomy. *J Psychosoc Oncol* 1985;3(3):83-97.

61 Mathias E, Smith D, Gonzalez F. Quality of life in patients with head and neck squamous cell carcinoma: a preliminary report, abstract. *Proceedings Am Soc Clin Oncol* 1988;7:268.

62 Baker CA. Factors associated with rehabilitation in head and neck cancer.

Cancer Nurs 1992;15:395-400.

63 Kreitler S, Chaitchik S, Rapoport Y, Algor R. Psychosocial effects of level of information and severity of disease on head and neck cancer patients. *J Cancer Educ* 1995;10(3):144-54.

64 Langius A, Björvell H, Lind MG. Functional status and coping in patients with oral and pharyngeal cancer before and after surgery. *Head Neck* 1994;16:559-68.

65 Stevens MH, Gardner JW, Parkin JL, Johnson LP. Head and neck cancer survival and life style changes. *Arch Otolaryngol* 1983;109:746-9.

66 Silverman S, Gorsky M, Greenspan D. Tabacco usage in patients with head and neck carcinomas: a follow-up study on habit changes and second primary oral/oropharyngeal cancers. *J Am Dent Assoc* 1983;106:33-5.

67 Spitz MR, Sider JG, Newell GR. Salivary gland cancer and risk of subsequent skin cancer. *Head Neck* 1990;12(3):254-56.

68 Gritz ER, Carr Cr, Rapkin DA, Chang C, Beumer J, Ward PH. A smoking cessation intervention for head and neck cancer patients: trial design, patients accrual, and characteristics. *Cancer Epidemol Biomarkers Prev* 1991;1:67-73.

69 Gritz ER, Carr Cr, Rapkin DA, Abemayor E, Li-Jui C, Chang C, Wong WK, Belin TR, Calcaterra T, Robbins KT, Chonkick G, Beumer J, Ward PH. Predictors of longterm smoking cessation in head and neck cancer patients. *Cancer Epidemol Biomarkers Prev* 1993;2:261-70.

70 Breitbart W, Holland J. Psychosocial aspects of head and neck cancer *Semin Oncol* 1988;15:61-9.

71 Beeken L, Calman F. A return to "normal eating" after curatieve treatment for oral cancer. What are the long-term prospective? *Eur J Cancer B Oral Oncol* 1994;30B(6):387-92.

72 Bjordal K, Freng A, Thorvik J, Kaasa S. Patient self-reported and clinician-rated quality of life in head and neck cancer patients: a cross-sectional study. *Eur J Cancer B Oral Oncol* 1995b:31:235-41.

73 Browman GP, Levine MN, Hodson DI, Sathya J, Russell R, Skingley P, Cripps Ch, Eapen L, Girard A. The head and neck radiotherapy questionnaire: a morbidity/quality of life instrument for clinical trials of radiation therapy in locally advanced head and neck cancer. *J Clin Oncol* 1993;11:863-72

74 Girardi P, Pisa de E, Cianfriglia F, Perrino A, Tatarelle R. Compliance with treatment for head and neck cancer: the influence of psychologic and psychopathalogic variables. A longitudinal study. *Eur J Psychiatry* 1992;6:40-50.

75 Kornblith AB, Zlotolow IM, Gooen J, Huryn JM, Lerner T, Strong EW, Shah JP, Spiro RH, Holland JC. Quality of life of maxilectomy patients using an obturator prosthesis. *Head Neck* 1996;18:323-34.

76 Lansky SB, List MA, Ritter-Sterr C, Logeman J, Pecis K. Quality of life in head and neck cancer survivors, abstract. *Proc Am Soc Clin Oncol* 1989;8:169.

77 List MA, Ritter-Sterr CA, Baker TM, Colangelo LA, Matz G, Roa Pauloski B, Logemann JA. Longitudinal assessment of quality of life in laryngeal cancer patients. *Head Neck* 1996;18:1-10.

78 Llewellyn-Thomas HA, Sutherland HJ, Hogg SA, Campi A, Harwood AR, Keane TJ, Till J, Boyd NF. Linear analogue self assessment of voice quality in laryngeal cancer. *J Chronic Dis* 1984;37(12):917-24.

79 Padilla GV, Grant MM, Lipsett J. Health quality of life and colorectal cancer *Cancer* 1992;70:1450-56.

80 Skeel RT. Quality of life assessment in cancer clinical trials-it's time to catch up. *J Natl Cancer Inst* 1989;81:472-73.

81 De Haes JCMC, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *Br. J. Cancer* 1990;62:1034-8.

Chapter 3

REHABILITATION OUTCOMES OF LONG-TERM SURVIVORS TREATED FOR HEAD AND NECK CANCER

ABSTRACT

Background. Little is known about the rehabilitation outcomes of long-term survivors following treatment for head and neck cancer. There are, for example, no studies on physical and psychosocial rehabilitation outcomes of T1 glottic larynx carcinoma despite the fact that these form the majority of head and neck cancer sites. Thus, this investigation afforded a unique opportunity for examining similarities and differences among T1 glottic larynx patients, laryngectomy patients, and those who had surgery for cancer of the oral cavity and/or oropharynx along a variety of physical and psychosocial dimensions.

Methods. To describe the impact of these three types of head and neck cancer and their treatment on the physical and psychosocial functioning of long-term survivors, a self-report questionnaire was completed by 110 patients treated between 2 and 6 years previously in a major cancer center.

Results. Data indicate that a higher percentage of patients treated with laryngectomy or commando procedures still experience severe psychosocial distress between two and six years after their last treatment than do patients treated with radiotherapy for a T1 carcinoma of the glottic larynx. Psychosocial and physical complaints are still reported by many laryngectomy patients, apparently the result of problems in effective communication with others. Many commando procedure patients experience problems with respect to food intake, and with disfigurement and its consequences. T1 larynx patients mainly experience a considerable number of physical complaints. The greater the time that had elapsed since treatment, the fewer the psychosocial problems associated with head and neck tumors. Open discussion of the illness in the family, social support, and perceptions of adequate information from the specialist are the most important predictors of positive rehabilitation outcomes.

Conclusions. This study indicates that the T1 larynx patients report many physical complaints even though several years had elapsed since treatment. Also, laryngectomy patients may need psychosocial guidance for a longer posttreatment period and health care personnel must involve the partner as much as possible in all communications. Commando procedure patients in particular feel hindered by their disfigurement and its consequences. Future research with respect to validation of the specific head and neck modules is needed.

INTRODUCTION

From a review of the literature on the rehabilitation of patients with head and neck cancer,[1] it appeared that the majority of studies had focused on the rehabilitation of laryngectomy patients. Only a few investigations have described the physical and psychosocial consequences of surgical treatment for cancer of the oral cavity and/or oropharynx. The fact that relatively few studies have been conducted on lesions of the oral cavity and/or oropharynx is remarkable in view of the fact that many operations of this type are performed each year. Moreover, studies on this latter group indicate that many of these patients also experience severe problems related to speech, food intake, and physical appearance.

The need to conduct more research on patients who have had treatment for cancer of the oral cavity and/or oropharynx is supported by the fact that the results of studies on this subject are ambiguous with regard to the patients' physical and psychosocial functioning. In our review, contradictory results for these patients were noted, with respect to vocational problems, performance of everyday activities, stigmatization because of physical appearance, decrease in social contacts, and feelings of depression. In a recent literature review on psychosocial adjustment after laryngectomy[2] the conclusion is drawn that the largest group of studies focus primarily on acquiring esophageal speech, but that predictors of rehabilitaion outcomes are not confined to variables related to speech alone.

We found no studies on the physical and psychosocial rehabilitation outcomes of T1 glottic larynx carcinoma, although these form the majority of the head and neck cancer sites. An explanation of this fact may be that, unlike patients who had surgery for cancer of the oral cavity, oropharynx or a laryngectomy, T1 larynx carcinoma patients have fewer physical and psychosocial problems because there is little or no disfigurement and they have a good prognosis. However, the question arises whether these patients have problems coping with fear of recurrence.

Only a few studies deal with the psychosocial effects of cancer in long-term survivors.[3-7] These studies are characterized by one or more of the following limitations: a description of only one medical treatment, the employment of a limited number of psychosocial variables, a lack of distinction made between different medical treatments, the use of qualitative measurement, and limited patient sample size.

In a recent review on assessing quality of life (QOL) in head and neck cancer patients, Gotay and Moore[8] report 18 studies concerning specific patient populations. They conclude that there is still little consensus in defining or assessing QOL. Although the term quality of life is considered too vague, there is a consensus of opinion, at the very least, that QOL is multidimensional.[9] There is considerable agreement that a "module" approach[8,10] may be optimal, wherein scales designed specifically for head and neck cancer patients are used to supplement information about broader areas. In this article the concepts "rehabilitation process" and "rehabilitation outcomes" are used, where rehabilitation process variables refer to intentional and unintentional behavior of the patient, professionals, and significant others, aimed at preventing, reducing or solving problems as much as possible; rehabilitation outcomes are the experienced problems of the patient. In recent articles several modules are described.[11-17] However, these approaches are not specific or complete enough for our purposes.

The present exploratory study has two major goals: (1) to describe the rehabilitation outcomes of three different treatment groups of long-term survivors, along a variety of physical and psychosocial dimensions, to ascertain similarities and differences between them; and (2) to search for those factors in the rehabilitation process that are correlated with outcomes for all long-term suvivors of the three groups. To achieve these goals for some concepts, we had to develop new instruments to measure physical and psychosocial problems specific to head and neck patients.

MATERIALS AND METHODS

Participants Candidates for the study consisted of patients with head and neck cancer who had been treated between two and six years previously in the Rotterdam Academic Hospital, Dijkzigt and the Daniel den Hoed Cancer Center, who had undergone one of the following treatments:

Group 1 A full course of radiotherapy for a small carcinoma limited to the vocal cords (T1 larynx).

Group 2 Total laryngectomy without neck dissection for a laryngeal carcinoma (or a recurrence of a laryngeal carcinoma). Pre- or postoperative radiotherapy was part of the treatment.

Group 3 Surgery for carcinoma in the oral cavity and/or oropharynx (or a recurrence of a carcinoma in the oral cavity and/or oropharynx). The surgery consists of a radical surgical procedure which includes resection of the primary site, partial mandibulectomy (or trans mandibular "swing" resection), a radical neck dissection, reconstruction of the bone and soft tissue defect and temporally tracheotomy. This is the so-called "commando procedure" (composite resection). Pre- or postoperative radiotherapy was part of the treatment.

Patients were excluded from the study on basis of the following criteria: (1) the presence of a second primary tumor (n=23), and (2) not being able to fill in the questionnaire themselves, eg, mentally disabled patients and patients unable to read the Dutch language (n=7).

This procedure yielded 313 participants, of which 136 were deceased at the time of the study. One hundred seventy-seven patients were asked to complete a questionnaire, and 131 returned it, giving a response rate of 74%. Twenty-one of the participants were excluded because they returned only partially completed questionnaires. (Incidentally, 80% of the patients who returned incomplete forms were older than 70 years). The data of the remaining 110 patients were used in the study.

Assessment and Data Analysis It is important that the development of instruments used in rehabilitation studies fits a theoretical basis.[18] In this study, we used a theoretical model of coping with cancer.[19,20] This model is based on the assumption that uncertainty, negative feelings (eg, feelings of depression, loneliness and psychological complaints), loss of control, and threatened self-esteem are the four most important psychosocial problems experienced by cancer patients. These problems are the rehabilitation outcomes.

Efforts of the patients themselves are directed to prevent or reduce these problems as much as possible. These efforts are called coping strategies. Also the environment of the patient (eg, his/her family, medical specialist) can help by offering information and support. In this process of coping with cancer, person-related factors such as education, age, and locus of control, and illness-related factors (eg, type of treatment) can possibly influence rehabilitation outcomes. In this investigation, the physical and psychosocial problems experienced by patients are measured as well as interpersonal concepts, such as information and support they received from others, illness-related factors and person-related factors (eg, daily activities, smoking and drinking habits, and marital status and other sociodemographic variables).

As mentioned previously, the primary goal of the study is to describe rehabilitation outcomes and to gain insight into the rehabilitaion process in

Table 1 Review of scales

Scale	Mean	S.D.	No. items	Min. score	Max. score	α * (This study)	α * (Previous study †)
Uncertainty							
Prospects of disease and treatment	24.651	8.131	9	9	36	.94	.93
Access to help and to solve problems	18.441	6.463	8	8	32	.90	.87
How to handle practical consequences of the illness	23.143	9.272	11	11	44	.93	–
How to cope with one's own emotions	14.547	6.600	7	7	28	.93	–
State anxiety	34.034	11.017	18	18	72	.94	.95
Loneliness	7.307	1.493	5	5	10	.70	.69
Complaints							
General psychosocial complaints	12.082	4.355	8	8	32	.88	.91
General pysical complaints	11.041	3.323	7	7	28	.70	.76
Head and neck specific psychological and physical complaints	31.087	8.810	21	21	84	.89	–
Loss of control	2.059	2.109	8	0	8	.76	.77
Self-efficacy with head and neck tumors							
Self confidence in oral presentation	37.561	10.050	9	9	54	.84	–
Perceived speech abilities	22.534	5.096	4	4	24	.70	–
Perceived abilities in swallowing and food intake	37.329	7.122	8	8	48	.73	–
Locus of Control							
Cause of the illness	5.566	2.718	3	3	12	.82	–
Religious control	6.218	3.443	3	3	12	.88	–
Course of the illness	20.199	4.186	7	7	28	.66	–
Self-esteem							
– With respect to the ability to perform	14.713	3.000	6	6	18	.72	–
– With respect to social functioning	12.168	2.219	5	5	15	.65	–
Feelings of depression	16.913	5.159	10	10	40	.83	.83
Openness to discussion of the illness in the family	18.342	6.915	8	8	32	.71	.81
Appreciation of information from the specialist	5.477	0.875	3	3	6	.71	.72

* Cronbach's alpha
† van den Borne and Pruyn[20,21]

head and neck cancer patients. Partly we gave this description by using validated scales used from the van den Borne and Pruyn research[21] on psychosocial functioning of breast cancer patients and Hodgkin patients. In Table 1 the reliability coefficients[22] of their study as well as of the present study are presented. The scales used from the study of van den Borne and

Pruyn are uncertainty, loneliness, feelings of depression, loss of control, openness to discussion of the illness in the family, appreciation of the information by the specialist and state anxiety. In the present study also the cancer locus of control scale and a self-esteem scale were used. Finally, with respect to specific problems of head and neck cancer patients a number of new scales were developed: uncertainty (two subscales), complaints (two subscales) and a version of Ryckman's physical self efficacy scale[23] (three subscales).

As can be seen in Table 1, the reliability indices of the scales vary between Cronbach's alpha .65 and .94, so it can be concluded that the internal reliability of the scales is satisfactory. The cancer locus of control scale, the self-esteem scale and the new, specially developed scales are described below. In the results section the rehabilitation outcomes will be presented on basis of results of scales as well as items. With regard to the outcome variables differences between sex were tested with a Student's *t* test. To examine the relation between process and outcome variables, a multiple regression analysis was performed.

Cancer Locus of Control The perception that the cause of specific events may be attributed to personal (internal control) or situational (external control) elements is called "locus of control". To measure this perceived cause-and-effect relation (attribution) in cancer patients, a three-factor scale was developed that represented (1) cancer patients' internal locus of control with respect to the cause of the illness, (2) cancer patients' internal locus of control with respect to the course of the illness, and (3) patients' religious control. The development of this scale has been reported elsewhere.[24,25] Sample items of the three-item "cause-of-illness scale" are: "That I am ill has to do with my life-style" and "That I have become ill is entirely my fault". Sample items for the seven-item "course of illness scale" are "I have a strong influence on the course of my illness" and "By fighting against my illness I can influence its course". Two items of the three-item "religious scale" are "That I have become ill is partly because it is the will of God" and "My faith influences the course of my illness".

Self-Esteem To measure self-esteem, a seven-item scale that was primarily based on the self-esteem dimension of the Dutch Personality Questionnaire[26], which is a translation of the California Psychological Inventory, was used. This scale was extended with four new items about the patients' evaluation of their competence in social situations. A factor analysis of all the items revealed two self-esteem subscales: (1) self-esteem with respect to performance, and (2) self-esteem in regard to social functioning. Sample items for the six-item performance scale are "I can handle my problems" and "I can cope with a set-back only with great difficulty". Sample items for the five-item social functioning scale are "Other people do not perceive me as attractive" and "I am pleasant to associate with".

Uncertainty Scale Specifically for Head and Neck Tumors Twenty-one items with respect to speech, food intake, and physical appearance were selected on the basis of their apparent relevance from a review study[1], and on the basis of consultation with experts in the fields of head and neck oncology, oncological nursing and counseling. Items were included that might contribute to the "uncertainty" concept. Patients were asked to report on their needs for information in these areas, using a four-point scale, ranging from (1) "Not at all", (2) "A little", (3) "Rather much", and (4) "Very much". A factor analysis of the items resulted in two subscales: (1) uncertainty about how to handle the practical consequences of the illness and (2) uncertainty about how to cope with one's emotions. Sample items for the eleven-item "handling illness" scale are "How to learn to talk better" and "How to dress better so that you minimize the chances that others will notice your handicap". For the seven-item "coping with emotion" scale sample items are "How to learn to control yourself" and "How to do relaxation exercises" (eg, yoga, respiratory exercises).

Assessment of Physical and Psychosocial Complaints To assess the patients' complaints, the Rotterdam Symptom Checklist was used.[27,28] Patients reported the extent to which they were suffering from a variety of physical and psychosocial problems. In the checklist there are two basic scales: general physical complaints and general psychosocial complaints. Fifty items were added to the checklist as a means of assessing complaints which might be more specific to head and neck cancer patients. These items were measured on a four-point scale, including (1) "Not at all", (2) "A little", (3) "Rather much", and (4) "Very much". A principal-components analysis of these items yielded a 21-item scale, labelled here as "specific physical and psychosocial head and neck complaints". Sample items on this list are: tickling in the throat, hoarseness, difficulty in breathing, coughing, phlegm formation, having frequent colds, feelings of shame during eating, and feelings of not being able to make oneself intelligible.

Head and Neck Self-Efficacy Scale It was considered highly important to assess patients' perceived physical abilities and confidence that are related to their head and neck problems. For this purpose, a list of thirty-one statements on feelings of personal competence related functions and activities in the head and neck area were constructed. All subjects responded to the statements which were measured on a six-point scale, including (1) "strongly disagree", (2) "somewhat disagree", (3) "slightly disagree", (4) "slightly agree", (5) "somewhat agree", (6) "strongly agree". They were subjected to a principal-components analysis, revealing three factors: (1) perceived speech ability, (2) perceived speech self-presentation confidence and (3) perceived swallowing ability. Sample items for the nine-item speech ability scale are "People usually cannot hear me when I speak" and "When I speak, there are many other sounds". Sample items for the four-item speech confidence scale are "I am relaxed when speaking to others" and "People can understand my speech". Sample items for the seven-item swallowing scale are "I can swallow well" and "I have troubles with eating and drinking".

RESULTS

The number of patients in the three treatment groups, demographic data, working status, time elapsed since treatment, and smoking and drinking habits are presented in Table 2. The patients varied in age from 31 to 86 years, with an average age of 63.5 years. Ninety-nine patients were men, 11 were women. All participants were clinically disease-free at the time of completing the questionnaire.

DESCRIPTION OF REHABILITATION OUTCOMES

Physical Complaints A high percentage of the laryngectomy (78%) and of the commando procedure patients (58%) reported experiencing a loss of control because they cannot make themselves well understood (Figure 1). In contrast with 26% of the laryngectomees, 69% of the commando procedure patients and 68% of the T1 larynx patients perceived themselves as having good speech abilities. Fifty-eight percent of the T1 larynx patients were still bothered by hoarseness at the time of filling in the questionnaire.

Half of all commando procedure patients have problems with eating and drinking as a result of the treatment; 22% of the laryngectomy patients report these problems. Sixty-seven percent of these commando procedure patients experience feelings of shame while eating. Thirty-three percent of the laryn-

Table 2 Descriptive data

	T1 larynx	Laryngectomy	Commando procedure	Total
Number of respondents	66	32	12	110
Gender (male/female)	64/2	29/3	6/6	99/11
Median age	64.2	62.9	60.5	63.5
Marital status (living together/ single)	57/9	26/6	9/3	92/18
Educational level (elementary school/ vocational school/high school or university)	40/18/8	25/1/3	8/2/2	73/21/13
Working status (working/retired/unemloyed)	21/36/7	5/10/12	2/3/6	28/49/25
Time since treatment (2 yr/3 yr/4 yr/ 5-6 yr)	5/26/13/22	1/4/6/21	0/3/6/3	6/33/25/46
Smoking (no/moderate/much)	49/13/4	28/3/1	9/2/1	86/18/6
Alcohol (no/moderate/much)	12/36/18	4/8/20	3/7/2	19/51/40

gectomy patients and commando procedure patients have difficulties in swallowing. Problems with choking are reported by 41% of the T1 larynx patients and 58% of the commando procedure patients. Other food-intake complaints that are related to the treatment which they had undergone are: for T1 larynx patients the proportion who had (a little, some, or a great deal of) phlegm in the mouth/throat was 57%, while 44% had a dry mouth and 11% had difficulty with chewing. For the laryngectomy patients, these percentages were 63%, 27%, and 27%, respectively; and for the commando procedure group 92%, 83%, and 67%, respectively.

Just over half the laryngectomy patients (56%) and commando procedure patients (55%) felt that their appearance is "a good deal" or "very much" damaged by the treatment. For the laryngectomy group, the stoma constitutes the greater part of this damage. Perceived mutilation following a commando procedure consists of the change in appearance/facial form (42%), stiff neck (33%), a "drooping shoulder" (17%), and an ill-fitting dental prothesis (17%). Women reported more often ($t = 2.45$; $p<.016$) than men the feeling that their appearance is damaged.

Although laryngectomy patients in particular have physical complaints found specifically in head and neck cancer patients, such as respiratory-system complaints and difficulties in breathing, T1 larynx patients also appear to experience considerable physical complaints, such as frequent colds (54%), coughing (45%), and tickling in the throat (47%). This group of patients also experiences general physical complaints like sore muscles (62%) and tiredness (53%). Few of these "long-term survivors", however, complain of being

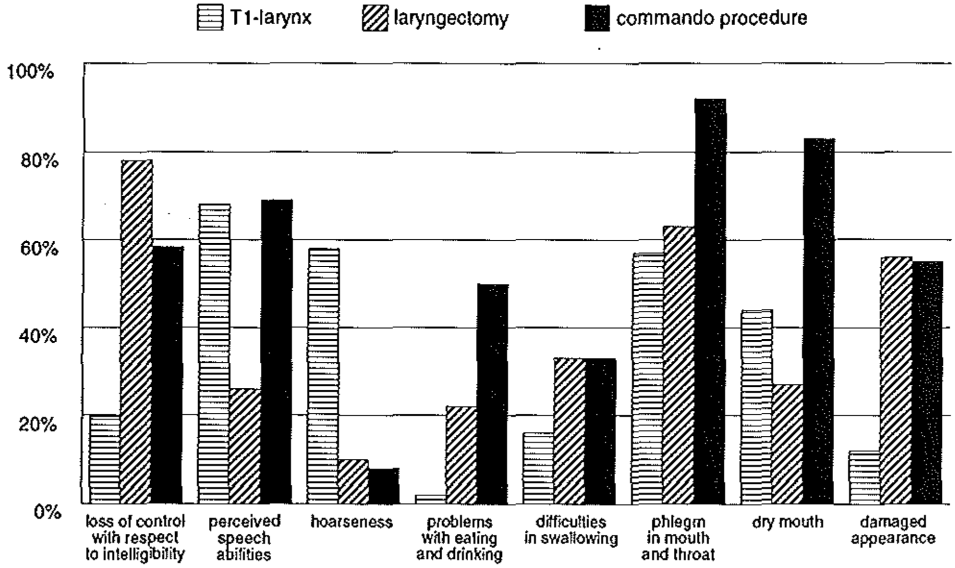

Figure 1. Physical poblems experienced by three treatment groups, radiotherapy for T1 larynx (N=66), laryngectomy (N=32) and commando procedure (N=12). Percentages of high scores are given.

hindered by carrying out their everyday physical activities.

Psychosocial Complaints Despite the fact that the treatment had taken place at least 2 years previously, more than half of all the patients are still troubled by feelings of uncertainty, particularly with regard to the disease and treatment prospect (Figure 2). Laryngectomy patients, in particular, feel uncertainty in coping with the negative consequences of the disease and treatment (56%) and in managing their own emotions (62%).

One in five patients feels a diminished self-esteem and indicates that this has troubled him/her. However, with respect to being able to deal with a considerable workload in a short time, more commando procedure patients and laryngectomy patients feel a diminished self-esteem (67% and 63%, respectively). Especially laryngectomy patients report threatened self-esteem with respect to social functioning (40%). This group of patients also exhibits feelings of loss of control more often than the rest of the patients. Negative feelings, such as loneliness, depression, and anxiety occur in a quarter of T1

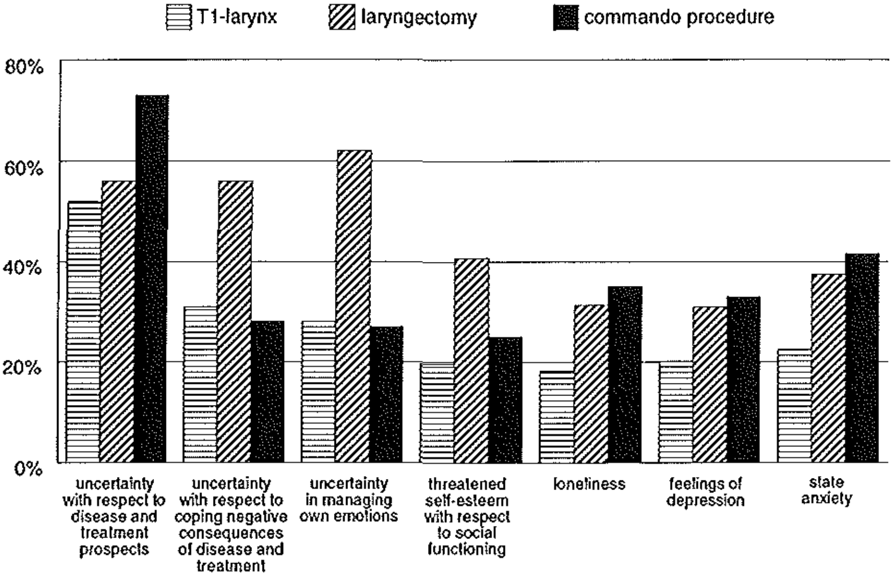

Figure 2. Psychosocial problems experienced by the three treatment groups (radiotherapy for T1 larynx, laryngectomy and commando procedure). Percentages of high scores are given.

larynx and half of the laryngectomy and commando procedure patients. We found that women scored significantly higher than men with respect to state anxiety, psychosocial complaints and head and neck cancer specific complaints ($t = 3.44$; $p<.001$, $t = 2.47$; $p<.015$, and $t = 2.14$; $p<.035$, respectively).

Social and Everyday Functioning As a consequence of the disease and the treatment, there are changes in the frequency of patients' contacts with others (Figure 3). It is particularly striking that in the three research groups personal contact with the partner has been improved since the diagnosis of the tumor and treatment. However, for just over a quarter of patients, personal contact with the family physician decreased. Thirty-eight percent of laryn-gectomy patients report a decrease in personal contacts with family and friends. Almost half of the patients in this group (47%) experience tensions and difficulties in the family as a result of the disease. Two of every three patients (67%) report that these problems were never or only partially solved. Less

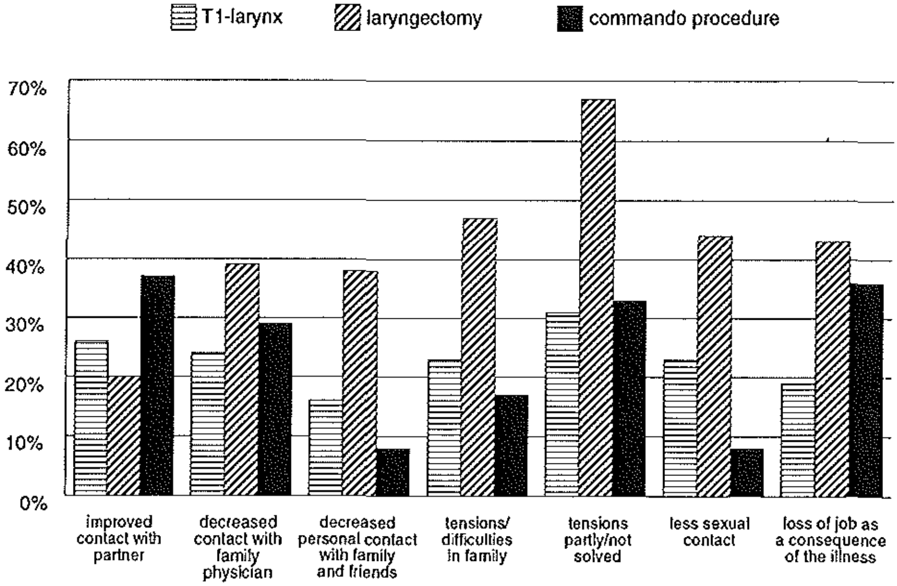

Figure 3. Social/everyday functioning of the three treatment groups (radiotherapy for T1 larynx, laryngectomy and commando procedure). Percentages of high scores are given.

than a quarter of the respondents in the other treatment groups have had these problems. Patients also report sexual problems: 23% of the T1 larynx, 44% of the laryngectomy and 10% of the commando procedure patients indicate having less sexual contact with their partner than before the disease was diagnosed.

Everyday life is more strongly influenced by the disease and treatment for laryngectomy and commando procedure patients than for the T1 larynx group. They restrict their activities more to the home environment or a close circle. It is notable that nearly two-thirds of the laryngectomy patients go walking or cycling more often than before. Of the T1 larynx group, 19% have lost their job as a consequence of the illness. For the laryngectomy and commando procedure group these pecentages are 43% and 36%, respectively.

Smoking and Drinking A high percentage of the patients have a past history of extensive tobacco and/or alcohol use. It appears that 27% of patients with a T1 -larynx tumor and 13% of patients who have undergone a laryngectomy

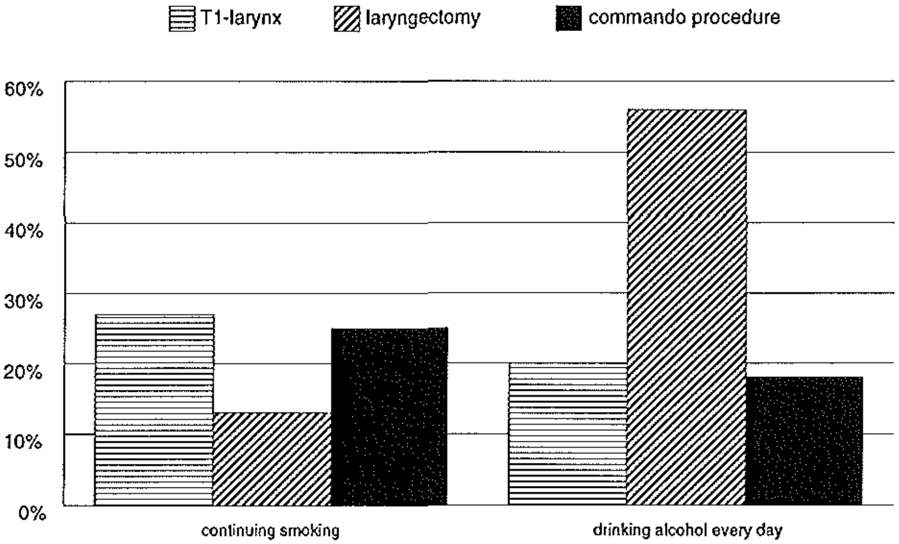

Figure 4. Smoking/drinking habits in the three treatment groups (radiotherapy for T1 larynx, laryngectomy and commando procedure). Percentages of high scores are given.

continue to smoke, of which 75% and 67%, respectively, reported reduced smoking (Figure 4). The drinking behavior of T1 larynx and laryngectomy patients shows a different pattern: only a third of them drink less. With respect to the amount of alcohol they consume 56% of the laryngectomees and 20% of the T1 larynx patients report drinking everyday. Seventy percent of the commando procedure patients have reduced their alcohol consumption. Of these patients 18% drink alcohol every day. Finally, we found that women patients drink less than men ($t = 2.93$; $p<.004$).

CORRELATIONS BETWEEN REHABILITATION PROCESS AND OUTCOME VARIABLES

In this study multivariate regression analyses were carried out by means of SPSS software.[29] With these analyses one cannot describe causal connections between process and outcome variables. It is possible, however, to predict a maximum amount of variance in rehabilitation outcomes from a minimum number of process variables. The data set was reduced by factor analyses, and by eliminating variables with a skewed distribution or those which were not relevant for all three treatment groups. Dummy variable coding[30] was used in order to establish the unique contribution made by the treatment groups (T1 larynx, laryngectomy and commando procedure) to each of the dimensions of the defined rehabilitation outcomes. Ultimately, 15 solid process variables and 15 outcome variables were entered in the multiple regression analyses. Table 3 shows the standarized beta weights for the process variables in a regression analysis performed for each of the 15 outcome variables (A to O) for which the multiple correlation coefficient R was significantly different from zero.

As can be seen in Table 3, three "social support and information" variables show a significant correlation with a considerable number of rehabilitation outcome variables. In particular, "openness to discussion of illness in the family" is related to 13 of 15 the outcome variables. The more openness to discussion patients experience, the fewer negative feelings (depression, loneliness and state anxiety) and less loss of control they report. Also this variable is associated positively with self-confidence in oral presentation and self-esteem (with respect to performing and social functioning). Receiving frequent "visits at home after discharge" is related to higher self-confidence, less uncertainty, fewer feelings of depression and less loneliness. High "appreciation of information given by the specialist" also correlates positively with eight outcome variables, eg, more self-confidence in oral presentation, fewer complaints (specific to head and neck physical and psychosocial), less uncertainty about how to cope with one's emotions, fewer feelings of depression, less loss of control, and greater self-esteem.

Patients with high "internal locus of control regarding the course of their illness" perceive themselves as having good speech abilities, show higher self-esteem with respect to the ability to perform, and experience less anxiety. "Swallowing difficulties after treatment" is a predictor for physical and psychosocial complaints, negative feelings (depression and anxiety) and threatened self-esteem with respect to the ability to perform. The more "time elapsed since treatment", the fewer physical and psychosocial complaints specific to head and neck cancer are reported.

The results of the multiple regression analyses show differences between the three treatments groups. Undergoing a laryngectomy is related with reporting decreased perceived abilities with respect to swallowing and food-intake, and with head and neck specific complaints. Also, having had a laryngectomy is a predictor of experiencing uncertainty in handling the practical consequences of the illness and uncertainty in coping with own

process variable	outcome variables														
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	0
Locus of Control															
Cause of the illness (Internal)	.02	–.02	–.08	–.07	–.04	–.02	.04	–.05	–.13	–.09	–.13	.03	–.02	.07	.01
Religious control	–.18	.00	.01	.04	.10	–.02	–.09	–.04	.03	.03	.11	–.04	–.02	.09	.01
Course of the illness (Internal)	–.08	.03	.13	.08	.24*	–.06	–.06	–.09	.01	–.01	.13	–.22*	.27**	.10	–.03
Illness related data															
Swallowing difficulties	.17*	.14	–.11	–.24**	–.02	.17*	.21*	.21*	–.22*	–.10	–.06	.21**	–.23**	–.15	.12
Time since treatment	–.08	–.04	–.05	.04	–.11	–.20**	–.11	–.09	–.07	–.05	–.08	.02	.12	.07	–.03
Health appreciation	–.11	–.05	.12	.20*	.11	–.16	.00	–.10	–.05	–.12	–.14	–.16	.11	.19*	–.17*
T1a Larynxcarcinoma	–.21	–.11	.27	.33	–.07	–.14	–.01	–.09	.19	.16	.16	–.16	.31	.16	–.30
Laryngectomy	–.08	.08	.47***	.09	–.22	.35*	–.04	–.03	.28	.57***	.39*	–.21	.07	–.02	.17
Commando	.04	.09	.02	–.06	–.12	.27*	–.06	.17	.24	.18	.19	.03	.03	.03	–.03
Social support and information															
Openness to discussion of illness in the family	–.34***	–.39***	.12	.27**	–.02	.19*	–.35***	–.36***	–.20*	–.24**	–.21*	–.35***	.25**	.25**	–.36**
Visit at home after treatment	–.19*	–.18*	.11	.24**	.15	–.08	–.06	–.12	–.19*	–.15	–.14	–.09	–.09	.08	.04
Appreciation information specialist	–.27**	–.14	.06	.27**	.07	–.22**	–.10	–.23**	–.12	–.12	–.32***	–.15	.25**	.22*	–.27**
Social support specialist	–.10	–.10	.04	.01	–.15	–.12	–.04	–.08	.06	.10	.15	–.06	–.04	.09	.01
Demographic data															
Education	.08	.21**	–.05	–.11	–.11	.06	.09	.05	–.14	–.03	–.05	.00	.00	–.04	.04
Age	–.02	–.09	–.16**	–.23**	–.24**	.05	–.06	–.02	–.09	–.08	–.06	–.10	.02	.04	–.01
Multiple R	0.60	0.57	0.77	0.61	0.45	0.64	0.49	0.57	0.45	0.60	0.56	0.56	0.62	0.49	0.66
R Square	0.36	0.33	0.59	0.37	0.20	0.41	0.24	0.33	0.21	0.36	0.31	0.31	0.38	0.24	0.44
Adjusted R Square	0.26	0.23	0.53	0.28	0.09	0.33	0.13	0.23	0.09	0.27	0.21	0.21	0.29	0.13	0.36
F	3.80***	3.32***	9.83***	4.05***	1.74*	4.76***	2.18**	3.34***	1.77*	3.85***	3.03***	3.12***	4.15***	2.19**	5.33***

* = p≤.05
** = p≤.01
*** = p≤.001

A Feelings of depression
B Loneliness

Self-Efficacy with respect to h&n tumors
C Perceived abilities in swallowing and food intake
D Self confidence in oral presentation
E Perceived speech abilities

Complaints
F Head and neck specific physical and psychological complaints
G Physical complaints
H General psychological complaints

Uncertainty
I Access to help/to solve problems
J How to handle practical consequences of the illness
K How to cope with own emotions
L State anxiety

Self esteem
M With respect to the ability to perform
N With respect to social functioning
O Loss of control

emotions. Finally, Table 3 shows that age is a predictor for self-efficacy with respect to head and neck tumors; getting older is associated with reduced abilities and reduced confidence in handling head and neck problems.

CONCLUSIONS AND DISCUSSION

General Conclusions The main goal of this exploratory study was to describe the rehabilitation outcomes in long-term survivors of head and neck cancer and to get insight in the rehabilitation process. While over half of the instruments used in the investigation were ones previously validated in earlier research, there were also some new instruments used in this research which were developed to be specific to head and neck patients and their problems and concerns. A few of these patient-specific instruments (eg, the ones designed to assess perceived self-efficacy in regard to speech abilities and self-confidence in oral presentations, control over the course of the illness, and self-esteem with respect to social functioning) were based on previously validated generalized measures. Concurrent validity of these new instruments could have been assessed had the validated generalized measures been included in the study. However, the length of time required for the completion of all the instruments would probably have proven too burdensome for many of the elderly patients so it was decided to include only the new instruments. Thus, future research with respect to validation of the new scales is needed. Importantly, the reliability coefficients of these scales are satisfactory.

A problem in this kind of research is the small sample size that seems to be a characteristic in many studies involving oral and pharyngeal cancer.[31] Also in the present study, for this reason, one has to be careful in drawing conclusions with respect to generalizing to populations (especially for the commando procedure group).

The most remarkable results from this study are (1) T1 larynx patients experience a considerable number of physical complaints between 2 and 6 years after treatment; (2) Laryngectomy patients and commando procedure patients experience severe psychosocial distress. The problems of the laryngectomy patients are often related to communication with others, while the commando procedure patients in particular have food intake problems and feel hindered by their disfigurement and its consequences; and (3) Open discussion off the illness in the family, social support, and adequate information from the specialist are the most important predictors of positive rehabilitation outcomes.

Commando Procedure and Laryngectomy Group Problems reported by the commando procedure patients are considerable, as are those of the laryngectomy group. The latter patients have the most complaints related to speech. It has to be mentioned that during the period in which the research was carried out no speech revalidation with the aid of an tracheoesophageal puncture was applied. The above-mentioned results could be more favorable with this method of speech rehabilitation.[32] The commando procedure patients in particular report problems with food intake.

Despite research findings[33] that have shown that the degree of dysfunction was associated with rehabilitation outcomes and facial disfigurement was not, more than half of both the laryngectomy and commando procedure group in the present study find that their appearance is damaged by the treatment; this disfigurement consists of the stoma, in particular, for the laryngectomy patients, and of the change in their appearance for the commando procedure patients.

T1 Larynx Treatment Group We know of no research on the physical and psychosocial rehabilitation of patients who have had only radiotherapy for a small larynx tumor. Because the treatment involves little mutilation and the prognosis for these patients is generally good it might be expected that they would report relatively few problems. However, our findings show that T1 larynx patients experience a considerable number of physical complaints such as sore muscles and fatigue, and complaints specific to head and neck tumors (phlegm, frequent colds), speech problems and problems in swallowing. This is striking because, if there should be any problems, we would expect them to be of psychosocial nature because of the cancer diagnosis. However, only 10% of the patients report such problems.

Psychosocial Functioning over Time Having psychosocial complaints specific to head and neck tumors is significantly associated with time elapsed since treatment. The longer the time since treatment, the fewer problems the patients experience. These results are in line with the study of Rapoport et al.[6] concerning 55 patients with head and neck cancer. They report an improvement over time with respect to psychological problems directly related to the disease such as coping with health problems and estimation of one's medical state. This is not surprising because the patients have actually survived and medical problems improve. However, almost all other conditions deteriorate. The authors ascribe this unexpected finding to "patient burnout" caused by chronic stress produced by having the disease and the emotional strain to keep up a normal and healthy appearance.

In three other studies that analyzed problems related to time since treatment, two authors found the most problems experienced between two and four years postsurgery/radiotherapy.[4,17] However, time did not seem the key factor in relieving problems. The third study found no relationship with elapsed time.[12] More research on this subject in a prospective study is needed.

Surprisingly, half of all the patients in our study are still troubled by feelings of uncertainty (about prospects for the disease and treatment) in spite of the fact that the treatment took place some time ago (between 2 and 6 years). Laryngectomy patients feel uncertain with regard to access to help and finding solutions, as well as with regard to managing their own emotions. It is also the laryngectomy group which feels a threat to their self-esteem with regard to their social functioning. This may indicate that this group needs psychosocial guidance for a longer posttreatment period.

Social Support and Information Further inspection of the data reveals that patients indicate that they have had important support from their partner, children and others, such as fellow sufferers and friends. Laryngectomy patients, in particular, say that they have had support from fellowsufferers. Fifty percent of the subjects in the present research have had contact with fellowsufferers; over half of these patients found this contact useful. Positive psychosocial effects following contact with fellow-sufferers were also found in the case of other types of cancer.[19]

Open discussion of illness in the family, social support from others after treatment and adequate information from specialists are predictors of positive rehabilitation outcomes. These findings are in line with the literature and provide further validation for the positive influence of social support on rehabilitation outcomes.[31]

Nearly half of the laryngectomy patients had experienced tensions and difficulties in the family, and for two-third of these patients, these problems continued more than 2 years after treatment. At the same time, it is found in all three treatment groups that personal contact with the partner improves following the disease. It appears, therefore, to be important that health care personnel involve the partner as much as possible in all communications, if this is appreciated by the patient. Caregivers also need to encourage the patient to talk at home about problems. In doing so they need to be aware that being so intensively involved in the process of the disease can lead to an extra load on the partner. For this reason it is advisable that the problems of the partner, in relation to the patient and his/her disease, should also be open to discussion. Also, Mah and Johnston[34] identified the need for support for care giving family members during the rehabilitation process.

Locus of Control A small majority of the patients believe that they themselves can influence (internal "locus of control") the course of the disease. Patients with a relatively high internal locus of control with regard to the course of the disease seem to rehabilitate better (self-confidence in speech, more self-esteem with regard to their achievements, and less anxiety). Patients with a high internal locus of control are also more inclined to health-related behavior, such as not smoking and careful eating.[24] These findings are consistent with other studies demonstrating that people with an internal locus of control are more inclined to exhibit behavior which improves or maintains their health, particularly if it is clear that changes are necessary for better physical functioning.[35] Research is needed on how patients' internal locus of control can be strengthened.

Smoking and Drinking From the present research, it appears that T1 larynx and laryngectomy patients smoke less following their treatment. Only 13% of the laryngectomy group continue smoking. In other studies, 9% is reported.[36,37] It is possible that this behavior change is partly brought about by information given by caregivers, in which the link between a doubled risk of recurrence in the larynx and continued, excessive smoking is frequently discussed. Another reason may be that it is, with respect to the tracheo-stoma, technically speaking, less attractive to smoke. A similar pattern of behavior is not found in the case of alcohol use; more than a half of the laryngectomy patients still drink alcohol every day. Although the literature indicates at least a synergistic role with exessive smoking in the etiology of cancer in the oral cavity or oropharynx,[38,39] alcohol use has penetrated public opinion less than has the relation with smoking. Reducing an excessive use of alcohol may also be more difficult than stopping smoking. Bronheim et al.[40] stated that alcoholism may need to be treated separately from the cancer. Eight of the 12 of the commando procedure patients who have received extensive postoperative radiotherapy in the area of the mouth and throat are found to have reduced their use of alcohol. A possible explanation for this is that increased sensitivity of the mucous membranes in the oral cavity after treatment and decreased sense of taste may have made the consumption of alcohol less attractive.

REFERENCES

1 Pruyn JFA, De Jong PC, Van den Borne HW, Bosman LJ, Poppel JWMJ van, Rijckman RM, and Mey K de. Psychosocial aspects of head and neck cancer: a review study. *Clin Otolaryngol* 1986;11:469-74.

2 Mathieson, CM, Stam, HJ, Scott, JP, Psychosocial adjustment after laryngectomy: a review of the literature. *J Otolaryngol* 1990;19 331-6.

3 Espie CA, Freedlander E, Campsie LM, Soutar DS, en Robertson, AG. Psychological distress at follow-up after major surgery for intra-oral cancer. *J Psychosom* Res 1989;33(4) 441-8.

4 Gamba A, Romano M, Grosso IM, Tamburini M, Cantú G, Molinari R, Ventafridda V. Psychosocial adjustment of patients surgically treated for head and neck cancer. *Head Neck* 1992;14:218-23.

5 Strauss RP. Psychosocial responses to oral and maxillofacial surgery for head and neck cancer. *J Oral Maxillofac Surg* 1989;47:343-8.

6 Rapoport Y, Kreitler S, Chaitchik S, Algor R, Weissler K. Psychosocial problems in head and neck cancer patients and their change with time since diagnosis. *Ann Oncol* 1993;4:69-73.

7 Bjordal K, Kaasa S, Mastekaasa A. Quality of life in patients treated for head and neck cancer: a follow-up study 7 to 11 years after radiotherapy. *Int J Radiat Oncol Biol Phys* 1994;28:847-56.

8 Gotay CC, Moore TD. Assessing quality of life in head and neck cancer *Qual Life Res* 1992;1:5-17.

9 Cella DF, Tusky DS. Measuring quality of life today: methodological aspects. *Oncology* 1990;4:29-38.

10 Aaronson NK, Bullinger M, Ahmedzai S. A modular approach to quality of life assesment in cancer clinical trials. *Recent Results Cancer Res* 1988;3:231-41.

11 Skeel RT. Quality of life assessment in cancer clinical trials-it's time to catch up. *J Natl Cancer Inst* 1989;81:472-3.

12 Browman GP, Levine MN, Hodson DI, Sathya J, Russell R, Skingley P, Cripps Ch, Eapen L, Girard A. The head and neck radiotherapy questionnaire: a morbidity/quality of life instrument for clinical trials of radiation therapy in locally advanced head and neck cancer. *J Clin Oncol* 1993;11:863-72.

13 Bjordal K, Kaasa S. Psychometric validation of the EORTC core quality of life questionnaire, 30-item version and diagnostic-specific module for head and neck cancer patients. *Acta Oncol* 1992;31:311-21.

14 Hassan SJ, Weymuller EA. Assessment of quality of life in head and neck cancer patients. *Head Neck* 1993;15:485-96.

15 Jones E, Lund VJ, Howard DJ, Greenberg MP, McCarthy M. Quality of life of patients treated surgically for head and neck cancer. *J Laryngol Otol* 1992;106:238-42.

16 List MA, Ritter-Ster Ch, Lansky SB. A performance scale for head and neck cancer patients. *Cancer* 1990;66:564-9.

17 Rathmell AJ, Ash DV, Howes M, Nichols J. Assessing quality of life in patients treated for advanced head and neck cancer. *Clin Oncol* 1991;3:10-16.

18 Padilla GV, Grant MM, Martin L. Rehabilitation and quality of life measurement issues. *Head Neck Surg* 1988;10: S156-S160.

19 Pruyn JFA. Coping with stress in cancer patients. *Patient Education Counseling*. 1983;5,2:57-62.

20 Borne HW van den, Pruyn JFA. Lotgenotencontact bij kankerpatiënten. (*Contacts between fellow cancer patients*). Thesis, Van Gorcum, Assen/Maastricht, 1985.

21 Borne HW van den, Pruyn JFA, Heuvel WJA van den. Effects of contacts between cancer patients on their psychosocial problems. *Patient Education Counseling*. 1987;9:33-51.

22 Cronbach LJ. Essentials of psycological testing. New York: Harper and Row, 1990.

23 Rijckman RM, Robbins MA, Thornton B and Cantrell P. Development and validation of a Physical Self-Efficacy Scale. *J Pers Soc Psychol* 1982;42:891-900.

24 Pruyn JFA, Borne HW van den, Reuver RSM de, Boer MF de, Bosman LJ, Pelkwijk MA ter, Jong PC de. De Locus of Control-schaal voor Kankerpatiënten. [The Locus of Control Scale for Cancer Patients.] *Tijdschrift voor Sociale Gezondheidszorg* 1988;66:404-8.

25 Watson M, Greer S, Pruyn JFA, Borne HW van den. Locus of control and adjustment to cancer. *Psychosocial Reports* 1990;66:39-48.

26 Luteijn F, Starren J and Van Dijk H. Handleiding bij de Nederlandse Persoonlijkheidsvragenlijst N.P.V. (*Manual to the Dutch Personality Questionnaire*), Lisse, Swets en Zeitlinger, 1975.

27 De Haes JCJM, Pruyn JFA, Knippenberg F. Klachtenlijst voor kankerpatiënten. Eerste ervaringen. (Item list for complaints in cancer patients. First experience) *Ned Tijdschrift voor Psychologie*. 1983;38:403-22.

28 De Haes JCJM, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *Br J Cancer*. 1990;62:1034-8.

29 Nie NH, Hull Ch, Jenkins JG, et al. *Satistical package for social sciences*. New York: McGraw-Hill, 1970.

30 Cohen J, Cohen P. *Applied Multiple Regression: relation analysis for the behavioral sciences.* Jersey: L.Erlbaum Assoc., 1983.

31 Langius A, Björvell H, Lind MG. Functional status and coping in patients with oral and pharyngeal cancer before and after surgery. *Head Neck* 1994;16:559-68.

32 Pindzola RH, Cain BH. Acceptability ratings of tracheoesophageal speech *Laryngoscope.* 1988;98 394-7.

33 Baker CA. Factors associated with rehabilitation in head and neck cancer. *Cancer Nursing* 1992;15:395-400.

34 Mah MA, Johnston C. Concerns of families in which one member has head and neck cancer. *Cancer Nursing* 1993;16:382-7.

35 Strickland BR. Internal-external expectancies and health-related behaviors. *J. Consult Clin Psychol* 1978;46:1192-211.

36 Ackerstaff AH, Hilgers FJM, Aaronson NK, Balm AJM. Communication, functional disorders and lifestyle changes after total laryngectomy *Clin Otolaryngol* 1994;19:295-300.

37 Jay J, Ruddy J, Cullen RJ. Laryngectomy: the patient's view. *J Laryngo. Otol* 1991;105:934-38.

38 Talamini R, Franscechi S, Barra S, and La Vecchia C. The role of alcohol in oral and pharyngeal cancer, and of tobacco in non-drinkers *Int J Cancer,* 1990;46:391-3.

39 Ng SKC, Kabat GC, Wynder EL. Oral Cavity Cancer in Non-Users of Tabacco *J Natl Cancer Inst,* 1993;85:743-45.

40 Bronheim H. Psychotherapie of the otolaryngology patient. *Gen Hosp Psychiatrie,* 1994;16:112-8.

Chapter 4

MEDICAL CORRELATES OF HEAD AND NECK CANCER RELAPSE AND SURVIVAL: A REVIEW OF THE LITERATURE

ABSTRACT

This chapter reviews recent literature on predictive factors with respect to overall survival and relapse in head and neck cancer, with a focus on medical prognostic factors, ie, patient-related factors, disease-related factors and treatment-related factors.

The value of statistical significance of prognostic factors was estimated by means of a simple procedure of calculating the so called "significance score", in which statistical significance, statistical analysis method applied and the number of patients involved in studies were accounted for.

It has been found that in over 70% of the 55 studies, involved in this review, a multivariate analysis model was used. However, only 6 factors (of the 97 factors in total) were analyzed in a population of more than 3000 patients. Of these factors, only N classification has reached a predictive significance score of importance in relation to both overall survival and relapse. Age, site, T classification and stage of disease showed inconsistent results. No correlation was found between patients' sex and prognosis. The factors, positive tumor margins and extra nodal spread might have prognostic value, although these factors do not meet the criterion of sufficient number of patients studied in the present review. The prognostic value concerning treatment outcome and survival of most of the histological and biological tumor factors, still needs to be confirmed in studies using multivariate analyses, involving large patient populations.

INTRODUCTION

Studies of prognostic factors are aimed directly, or indirectly, at explaining or accounting for the remarkable heterogeneity observed in the characteristics of patients and in the outcome of diseases in humans. A prognostic factor is a variable measured in an individual patient that singly, or in combination, with other factors, explains part of this heterogeneity.[56]

It is well recognized that both disease and treatment factors have a significant effect upon tumor control and survival rates in patients with head and neck cancer. Until now, the TNM classification system has been the most important determinant in estimating prognosis and hence in deciding the type of treatment. In particular, both high T and N classification, irrespective of the treatment given, are associated with a poorer prognosis. Cancer staging should ideally predict survival, response to therapy and tumor aggressiveness, eg, early regional metastasis in a small primary tumor, but the final prognosis is a complex issue and may depend on several other risk factors.

Many medical factors have been studied with respect to their prognostic value. These candidate prognostic factors can be classified into three groups, patient-related factors, disease-related factors (clinical tumor factors, histological factors, biological tumor factors) and treatment-related factors. However, the importance of each of these factors has not been unequivocally demonstrated. Many of these variables are in fact interrelated, and their apparent association with prognosis may be due to secondary relationships with genuine correlates of survival. In 1991 Kowalski et al.[51] stated that "the present knowledge about the relative importance of the factors has been mostly derived from studies based on univariate analyses of candidate prognostic factors". Reliable information on prognosis, however, can only be obtained by multifactorial analysis of survival data on a large patient population.[57]

The purpose of this study is to determine what prognostic factors have been identified in the literature and to ascertain the value of the statistical significance in relation to the type of statistical analysis and the number of patients included in the studies performed over the last five years.

MATERIALS AND METHODS

A literature search from 1990 to 1995 using Medline and CancerLit was performed including the key words *head and neck neoplasms*, *prognos**, *outcome*, **survival*, *recurrence*, *relapse* and *second primary tumor*. Only reports of studies were included. Two studies, published in 1996, were also included.[48,52] Reports not written in the English language were excluded. Studies that focused on a tumor location (eg, nasopharynx) or a type of treatment (eg, interstitial radiotherapy or chemotherapy) that did not pertain to the site or treatment of the three groups[a] being the subject of the descriptive and prospective study described in chapters 3 and 6, respectively, were excluded. Articles that focused on race as a possible prognostic factor were also excluded.

The studies reviewed were checked for tumor site, number of patients included, study design, prognostic factors studied, outcome parameters, the type of statistical analysis and the reported results. For each factor, evaluated by means of a multifactorial analysis, a weighted mean was calculated. This calculation was performed by dividing the sum of the number of patients studied in the articles in which the prognostic factor was significant ($p<.05$), by the sum of the number of patients included in each study in which the factor was evaluated (see example in footnote in Table 1, Appendix I, page 193). This calculated mean, coined "significance score", represents a figure between 0 and 1. The confidence of this score also depends on the number of studies in which the factor was evaluated.

An article by Wolfensberger was not analyzed in the aforementioned fashion.[57] In the two studies described in this article involving 920 head and neck cancer patients, 61 possible prognostic factors have been studied. Unfortunately, the way in which the results were presented was not suitable for analyzing these factors within the framework of our review study. For instance, of the 61 variables more than half, ie, 32, were not named. However, the results of this study, which has been cited in many articles on prognostic factors, together with some important studies preceeding 1989, as well as a few review studies, were used in the discussion, to comment on the results we found in our analysis.

RESULTS

Fifty-five reports that assessed prognostic factors were assessed. In 41 studies the design was retrospective and only in 12 the design was prospective. Two studies dealt with both a retrospective and a prospective design. The statistical analysis used in 16 studies was limited to a univariate model, and these studies

---

[a] T1 larynx carcinoma treated with irradiation alone, larynx carcinoma treated with laryngectomy and carcinoma of the oral cavity and oro-pharynx treated with surgery.

Table 1 Site of the primary tumor

tumor site	number of studies
Larynx	22
Larynx/hypopharynx	2
Oropharynx/base of tongue	2
Oral cavity	13
Several sites in the head and neck	18

had a total of 2434 patients, with numbers ranging from 28 to 763 patients. In the other 39 studies a multivariate model was used, with a total of 9429 patients involved, with numbers ranging from 47 to 1315.

Tumor site (location[b]) and treatment can be considered as selection criterion for patient inclusion and as a prognostic factor. Used as a selection criterion both were for the greater part determinative for the choice of possible prognostic factors under study. Tumor sites as well as treatment regimes were diverse in the studies reviewed. The head and neck sites involved are summarized in Table 1, and for each of the 55 studies listed in Table 3, Appendix I.

The majority of studies dealt with laryngeal carcinoma, three of which were limited to a T1 classification. Larynx-hypopharynx carcinomas and oropharynx/base of tongue carcinomas were studied in two articles. Oral cavity carcinoma was studied in 13 articles, of which 6 were confined to the mobile tongue. Nearly one-third of the studies dealt with head and neck squamous cell carcinoma. In these studies various sites were grouped together and the site of the tumor was not always specified.

In 29 studies the patient population studied was selected upon the basis of the treatment regime being either mono-therapy eg, local excision with neck dissection, external radiotherapy, or a combination therapy, eg, surgery followed by radiotherapy, and/or chemotherapy. In only 10 studies treatment was analysed as possible prognostic factor. The treatment regimes of the 29 studies are listed in Table 3, Appendix I.

Outcome parameters used in studies reviewed are: overall *3-year and 5-year* survival, and the treatment outcomes: the occurrence of a local, regional or distant recurrence/relapse, disease free survival/disease specific survival, and the occurrence of a second primary tumor. We classified the outcome variables in two categories: *overall survival (OS)* and *relapse* (local,

---

[b] The terms "tumor site" and "tumor location" were used interchangeably in the articles, meaning the situation of the primary tumor in the head and neck.

regional and distant recurrence, and second primary tumor).

We classified the prognostic variables according to the following categories: host factors, treatment factors, clinical tumor factors, histological tumor factors and biological tumor factors. All “candidate” prognostic factors analyzed in the 55 studies will be enumerated in the next paragraph.

“Candidate” Prognostic Factors A total of 97 prognostic factors were identified in the 55 studies. The full list of variables analyzed per study , the number of patients per study and reference number of the study are given in Table 1 (univariate analysis) and Table 2 (multivariate analysis) in Appendix I.

Of the *host-related factors* the most frequent studied factors were age[7,16-19,21-23,26,28,29,31-34,36,38,39,41,43,45-48,50-52D] , sex[12,16,17-19,21,22,24,26,28,30-32,36-39,44-50,52,53], tobacco use[2,17,21,23,34,48,49,52,53], alcohol use[2,17,21-23,34,52] and performance status[6,16,24,39,44,47,49]. Less frequently mentioned were the continuance of smoking and drinking after treatment [21,32,], hemoglobin[28,53], sedimentation rate[27] and rhesus blood group[28].

Serologic determinants of survival studied, included immunoglobulin A[41], prostaglandin E concentration[53], and the level of circulating macromolecules capable of binding the first component of complement C1q in vitro[41].

Concerning *treatment factors* the type of treatment as criterion of patient inclusion was determinative of the factors analyzed. In case of surgery as treatment modality, some of the following variables were found to be included in the analyses: type of surgery[33,43,46,51], (type of) neck dissection[35,48,51], paratracheal lymph node dissection [51], pretreatment tracheostomy in laryngectomy patients[17,22,48,51] and salvage surgical procedure[45], and post-operative wound infection[9]. When radiotherapy was given as the sole treatment or as part of a combined treatment regime, the following factors were analyzed: total dose of radiotherapy given[3,6,13,18,32,35,36,45,], radiotherapy field size [8,13,32,35,36,53], overall treatment time in days[18,24,36,], dose fraction[8,13,53], postoperative radiotherapy[1,51], radiotherapy delay more than 6 weeks post surgery[6,13], tumor response evaluation at 40 Gy.[3,8], response to radiotherapy[50],and voice quality after radiotherapy[45].

Finally other variables, such as response to chemotherapy[20,22], hemoglobin drop during treatment[24,52] and number of blood transfusion units administered[46], were occasionally studied.

Clinical tumor factors most frequently studied are: site[1,3,6,12,14,17,19,20,23,25,26,28,29,31,33,35,38-41,44,46,48,50-52,54,55], T classification[1,12,14,22-25,28,31,33,35,38,43,44,46,49-55], N classification[12,14,17, 22-25,29,31,33,35,38,46,48-52,54,55] and clinical Stage of

Disease [9,19,23,26-31,39,41,43,46,49,52,54]. The factors less frequently included in studies included lymph node level[35,44,48,51], vocal cord mobility[19,23,45], tumor extension on the vocal cord[13,32,36] and duration of symptoms [17,28,49] were less frequently included in studies. Finally, fixation of lymph nodes[35], tumor thickness[7] and exophytic growth pattern[48], dyspnea[17], and location of second primary tumors[21] were occasionally studied.

Concerning *histological tumor factors*, numerous attempts have been made to correlate the microscopic appearance of a tumor with its biological behavior and prognosis. In this review the factors, postoperative T classification[17,40] and tumor positive resection margins[6,17,30,40,42,46,51] with respect to the primary tumor, were evaluated. When the pathology of nodal metastasis was reviewed, it was found that the postoperative N classification[1,6,14,17,30,34,44,46,51] and extra nodal spread[1,6,30,46,51] were analyzed as possible prognostic factors. Microscopic tumor invasion of muscle, bone, skin and cartilage and neural invasion were entered into the multivariate analyses[6,17,40,51]. The histological classification most commonly used, as appears from this review as well, consisted of 3 differentiation grades (well, moderately, and poorly differentiated)[2,5,7,12,14,17,18,20,23,26,29-34,36,3739, 40,4 2,44-45,48,50,51,53-55]. The his- tologic malignancy grading system introduced by Jacobson uses 8 different morphologic parameters for the tumor cell population (growth pattern, keratinization, nuclear polymorphism, mitosis) and its relation to adjacent tissues (mode of invasion, stage of invasion, vascular invasion and cellular response)[29]. Also determinants of this system were studied separately[34,40,42,48,51,52]. In one study the degree of chronic inflammation and tumor associated desmoplasia as an expression of the tumor-host relationship were studied[42]. In other studies factors such as tumor associated tissue eosinophilia, lymphocytosis, tumor associated desmoplasia, and plasma cells were evaluated[12,42]. In addition to the morphologic features a stereomorphometric characteristic, such as nuclear volume[52], was studied.

Of the *Biological tumor factors,* quantification of the DNA content of individual cells is a more objective measure than histopathological grading systems, as it measures the cellular features of a tumor sample. Several variables were analyzed: DNA ploidy and DNA index[14,26,29,34,37-39], degree in nuclear DNA aberation[5], synthesis phase fraction[14], circulating prolactin level[11]. Futhermore, epidermal growth factor [20,33], squamous cell carcinoma antigen[27], tumor angiogenesis[43,50], serum thymidine kinase activity[27], proliferative activity[5,26], epidermal growth factor[11,14], insulin-like growth factor[11], P 53E[14], catepsin immuno reactivety[14], tissue polipeptide-specific antigen[11], have been studied. In one radiotherapy study other biological tumor factor were evaluated: median labeling index, duration of S-phase, potential doubling time and total labeling index.[4]

Univariate Analysis An overview of the results of the literature study concerning univariate analysis is presented in Table 1, Appendix I. With respect to the prognostic factors, Overall Survival (OS) and Relapse, the number of studies in which the possible prognostic factor was found statistical significantly (<.05) correlated with OS or relapse, and the number of patients included in the study are given.

Table 2 contains the summarized data concerning OS, the two columns representing the number of patients involved in the studies concerning the variable under investigation, and the number of studies in which the variable was evaluated. In the univariate analysis 7 factors were found to be of significance. Two of the 7 variables, ie, performance status and stage of disease, were also significant prognostic variables in studies using *multivariate* analyses. The other 5 factors (nutritional status/score, post-operative wound infection, tumor thickness, p-N classification and the circulating prolactin level) were studied in only a small number of patients.

Table 2 univariate/OS

Host factors	# pat	# sig	Histological tumor factors	# pat	# sig
Age	821	0	P - N classification	65	1
Sex	763	0	Histologic differentiation	123	0
Performance status	763	1	Histological grading (Broders)	52	0
Nutritional status/score	67	1	Growth pattern	65	0
Treatment factors			Vascular invasion	65	0
PO wound infection	134	1	Biological tumor factors		
RT field size	330	0	Insulin-like growth factor	52	0
Tumorresponse evaluation	330	0	P 53E	65	0
Clinical tumor factors			Catepsin immuno reactivity	65	0
Site	65	0	Tissue polipeptide-specific	52	0
T classification	65	0	Median labelling index (LI)	105	0
N classification	65	0	Duration of S-phase (Ts)	105	0
Tumor thickness	58	1	Potential doubling time (Tpot)	105	0
Stage of disease	134	1	Total labeling index (TLI)	105	0
			Synthesis phase fraction	65	0
			DNA ploidy (index)	65	0
			Circulating prolactine level	52	1

pat = number of patients involved in studies
sig = number of studies in which the variable is a significant predictor

In Table 3 the data with respect to relapse are presented. Eighteen factors were found to be of significance of which 7 factors (ie, site, stage of disease, p-N classification, extra nodal spread, histologic differentiation grade, growth pattern and mode of invasion) were also significant variables in studies using *multivariate* analyses. The other factors, ie, nutritional status/score, prostaglandin E, postoperative wound infection, total given dose of radiotherapy, tumor response evaluation at 40 Gy, the dose fraction relation, tumor thickness, tumor extension on the vocal cord, tumor associated tissue eosinophilia, proliferating cell nuclear antigen and degree of DNA aberration reached significant p-values in only 1 or 2 studies involving small numbers of patients.

Table 3 univariate/Relapse

Host factors	# pat	# sig	Histological tumor factors	# pat	# sig
Age	58	0	P - N classification	508	2
Sex	104	0	Extra nodal spread	443	1
Performance status	199	0	Tumor positive resection margins	199	0
Nutritional status/score	67	1	Histologic differentiation grade	284	1
Tobacco consumption	94	0	Growth pattern	47	1
Alcohol consumption	94	0	Nuclear differentiation	94	0
Prostaglandine E	53	1	Mode of invasion	47	1
Treatment factors			Vascular invasion	293	0
Treatment modality	104	0	Cellular response	47	0
PO wound infection	134	1	Neural invasion	199	0
Postoperative radiotherapy	244	0	Invasion	199	0
Total given dose RT	364	1	Tumor associated tissue eosinophilia	104	1
RT field size	395	0	Lymphocytosis	104	0
Tumorresponse evaluation at 40 Gy	430	2	Plasma cells	104	0
Treatm.delay po RT>6 wks.	264	0	Biological tumor factors		
Dose fraction	395	2	Epidermal growth factor	117	0
Clinical tumor factors			Proliferating cell nucl. antigen	28	1
Site	647	1	Degree nucl. DNA aberation	28	1
T classification	348	0			
N classification	104	0			
Tumor thickness	58	1			
Stage of disease	134	1			
Vocal cord tumor extension	65	1			

pat = number of patients involved in studies
sig = number of studies in which the variable is a significant predictor

Multivariate Analysis The results of studies using multivariate analysis are presented in Tables 4-7. In Appendix 1, Table 2 an overview of the significance (scores) and numbers of patients is given.

In Table 4 of this chapter a list is given of factors that showed *no* significant correlation with OS. In the first column the significance score (ss) as calculated according to the formula given in the methods section, is shown. In the second column the number of studies in which the factor was analyzed, is given. In the last column the total number of patients involved in these studies is noted.

It can be postulated that the greater the number of patients studied, the more reliable the predictive value with respect to disease course is. For instance, patients' sex was found to be unrelated to OS, analyzed in 18 studies, including 5270 patients in total. Less convincing with respect to their negative correlation to OS, but still analyzed in over 500 patients, were factors such as p-T classification, p-N classification and duration of symptoms.

The opposite of a solid predictive value is found in a factor such as "response to radiotherapy", which was found to be significantly correlated with OS, investigated in a single study (significance score = 1) involving only 48 patients. In Table 5 the figures with respect to significant prognostic factors are presented.

In order to give an orderly picture of the relative value of the statistical significant correlation of prognostic factors with OS, a plot was constructed as can be seen in Figure 1. Cut-off points were set at the .25 and .75 significance score levels and at a number of 500 patients. By this means three fields were created, containing prognostic factors that were studied in more that 500 patients; below .25, between .25 and .75 and over .75. One field with less than 500 patients was also evaluated. In the field with scores over .75 and more than 500 patients (1) N classification and (2) pre-treatment tracheostomy are encompassed. In the second field (scores between .25 and .75, and more than 500 patients) the following were seen (1) site, (2) stage of disease, (3) age, (4) level of lymph node, (5) alcohol consumption (6) vocal cord mobility and (7) performance status. In the border area, near the "500 patients-line", 2 factors were located: (1) fixation of lymph node and (2)extra nodal spread. In the third field (with scores between 0 and .25, and more than 500 patients) the factors (1) T classification, (2) histological differentiation grade and (3) treatment modality were seen. The plots on the zero X-axis represent the unrelated (non-significant) factors that are listed in Table 4, such as sex.

Table 4 Multivariate/OS
Not significant factors

Host factors	ss	#art	#pat
Sex	0	18	5270
Continuing smoking/alc.	0	1	165
Sedimentation rate	0	1	189
Immun globulin A	0	1	103
Serum C1q-binding molecules	0	1	103
Treatment factors			
Type of surgery	0	2	485
(Type of) neck dissection	0	3	991
Para-tracheal node dissection	0	1	278
Salvage surgical procedure	0	1	148
Postoperative radiotherapy	0	1	278
Total given dose RT	0	4	834
RT field size	0	3	704
Dose fraction	0	1	109
Clinical tumor factors			
Exophytic growth pattern	0	1	221
Dyspnea	0	1	551
Vocal cord tumor extension	0	1	103
Duration of symptoms	0	3	688
Histological tumor factors			
P - T classification	0	1	511
P - N classification	0	3	1943
Vascular invasion	0	2	499
Neural invasion	0	1	278
Invas.muscle/bone/skin/ cartilage	0	2	789
Biological tumor factors			
Epidermal growth factor	0	1	109
Squamous cell carc. antigen	0	1	189
Serum thymidine kinase activity	0	1	189
Tumor angiogenesis	0	1	48
DNA ploidy (index)	0	1	171

Table 5 Multivariate/OS
Significant factors

Host factors	ss	#art	#pat
Age	42	18	4989
Performance status	38	3	1525
Tobacco consumption	0.1	6	1368
Alcohol consumption	44	4	1202
Hemoglobin	1	2	220
Rhesus bloodgroup	1	1	111
Treatment factors			
Treatment modality	14	8	1700
Pretreatment tracheostomy	77	4	1306
Overall treatm. time RT (days)	47	2	194
Response to radiotherapy	1	1	48
Voice quality after radiotherapy	1	1	148
Response to chemotherapy	68	2	339
Blood transfusion units	1	1	207
Clinical tumor factors			
Site	0.47	16	6053
T classification	0.22	13	5342
N classification	0.83	12	4460
Level lymp node	43	4	2168
Fixation lymph node	1	1	492
Location sec. prim. tumor	1	1	165
Stage of disease	0.57	9	2765
Vocal cord mobility	75	3	589
Histological tumor factors			
Extra nodal spread	43	2	485
Tumor positive resection margins	1	3	485
Histologic differentiation grade	0.24	15	5446
Biological tumor factors			
Proliferative activety (SPF)	1	1	171

ss = significance score
# art = number of articles in which studies are described
# pat = number of patientsinvoleved in studies

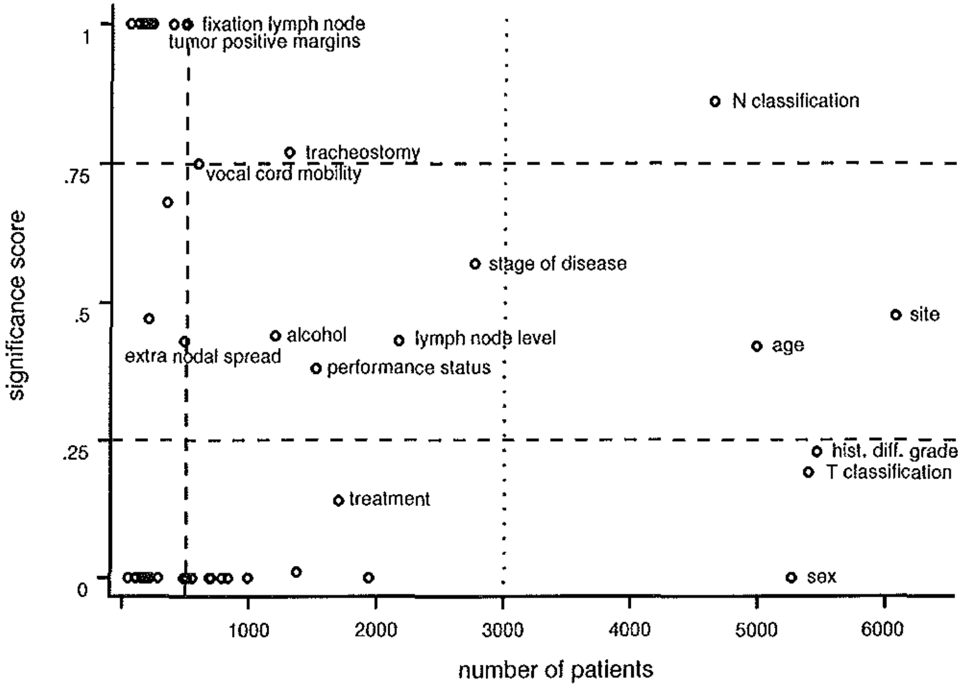

Figure 1 Significance score with respect to overall survival

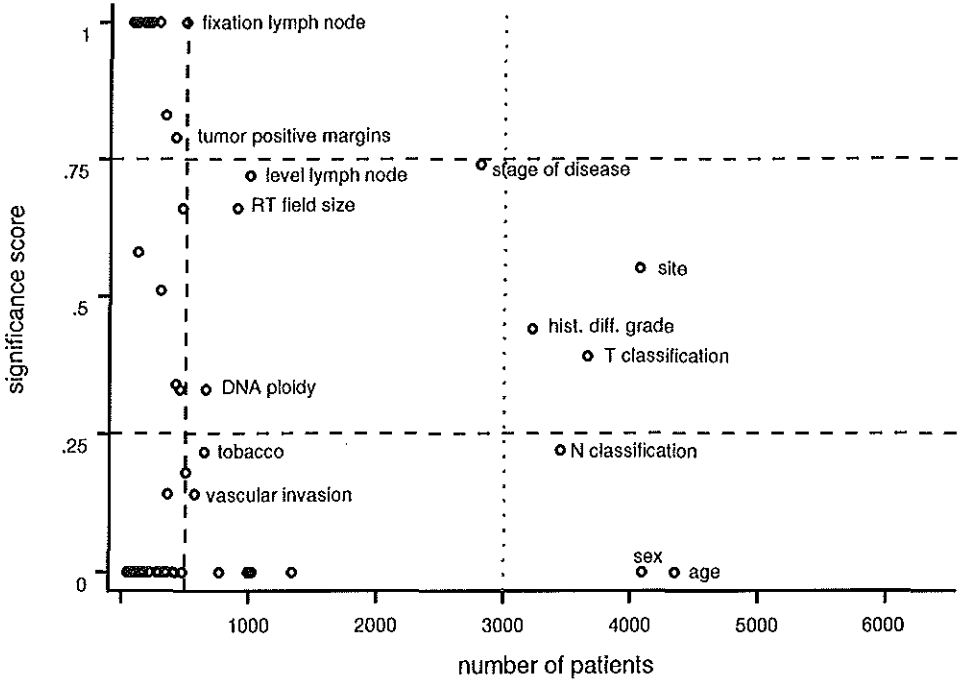

Figure 2 Significance score with respect to relapse

In Table 6, similarly as for the OS a list is presented of factors that showed no significant correlation with the occurrence of a relapse in the literature reviewed. Again, the number of articles (studies) and patients involved were considered as a measure of reliability. Age, sex, performance status and tobacco consumption showed no significant correlation with relapse; nor did the treatment modality or the total dose of radiation given. In Table 7 the figures concerning the significant prognostic factors correlated to relapse are shown.

In the same manner as in Figure 1, Table 4 and Table 5 were visualized by means of a plot-diagram in Figure 2. Three fields, enshrined by the the same significance score levels (.25 and .75) and the 500 patients-limit as in figure 1, encompass areas of high value with respect to significant correlation (upper field), of moderate value (middle field) and of little or no significant correlation (bottom field). The upper field contains no factor. Stage of disease, lymph node fixation and tumor positive resection margins are borderline cases (ss=.74; 2809 pat., ss=1; 492 pat. and ss=.79; 413 pat., respectively). The middle field contains (1) level of lymph node, (2) tumor site, (3) histological differentiation grade, (4) T classification, (5) radiotherapy field size and (6) DNA ploidy. The bottom field contains (1) N classification, (2) tobacco consumption and (3) vascular invasion. The plots on the zero X-axis represent the non-significant factors that are listed in Table 6, eg, age and sex.

As well as for the outcome OS as the outcome relapse 500 patients was considered minimum to draw any conclusions. When we selected the factors studied in 3000 patients, the same 6 factors in both OS and relapse can be distinguished, ie, sex, age, histological grade, T classification, site, N classification. With the limitations of a review study like this in mind cautious conclusions concerning the predictive value of these 6 variables can be drawn.

DISCUSSION

Central to the design, conduct, and interpretation of clinical studies is thorough consideration of prognostic factors, which might have an impact on the outcome of treatment. Knowledge of prognostic factors is an indispensable tool in judging the effectiveness of a treatment procedure. Prognostic factors can also guide the clinician in tailoring a treatment plan for the individual patient. In studying the influence of possible predictors of outcome in a standard treatment, known reliable prognostic factors must be considered in the analysis. The first goal of this review was to make an inventory of all

Table 6 Multvariate/relapse
Not significant factors

Host factors	ss	#art	#pat
Age	0	20	4354
Sex	0	20	4094
Performance status	0	4	994
Alcohol consumption	0	3	479
Immun globulin A	0	1	103
Treatment factors			
Treatment modality	0	6	1344
Type of surgery	0	3	418
(Type of) neck dissection	0	2	770
Para-tracheal node dissection	0	1	278
Salvage surgical procedure	0	1	148
Pos-operative radiotherapy	0	1	278
Total given dose RT	0	4	1028
Response to radiotherapy	0	1	48
Dose fraction	0	1	109
Response to chemotherapy	0	2	339
Clinical tumor factors			
Tumor thickness	0	1	47

Table 7 Multivariate/relapse
Significant factors

Host factors	ss	#art	#pat
Continuing smoking/alc.	1	1	194
Tobacco consumption	0.24	5	645
Serum C1q-binding molecules	1	1	103
Hemoglobin	1	12	220
Rhesus bloodgroup	1	1	111
Treatment factors			
Pretreatment tracheostomy	1	1	278
RT field size	66	4	898
Overall treatm. time RT (days)	18	3	500
Voice quality after radiotherapy	33	2	454
Hemoglobin drop	66	2	467
Clinical tumor factors			
Site	55	16	4064
T classification	0.39	15	3889
N classification	0.22	13	3675
Level lymp node	72	2	1000
Fixation lymph node	1	1	492
Stage of disease	0.74	13	2809
Vocal cord mobility	51		293
Histological tumor factors			
P - N classification	34	3	421
Extra nodal spread	83	2	333
Tumor positive res. margins	79	4	413
Histologic differentiation grade	0.44	19	3224
Histological score (Jacobson)	1	1	72
Growth pattern	1	2	168
Mode of invasion	1	1	161
Depth of invasion	14	4	356
Vascular invasion	14	4	568
Nuclear volume	1	1	161
Biological tumor factors			
Epidermal growth factor	1	2	183
Tumor angiogenesis	58	2	114
DNA ploidy (index)	33	6	660
Proliferative activety (SPF)	1	1	171

ss = significance score
# art = number of articles in which studies are described
# pat = number of patients involved in studies

possible prognostic factors studied in the literature. Also, an effort was made to quantify the impact on survival and tumor relapse of a wide range of medical factors. An extensive and in recent years very popular procedure for this purpose is a meta-analysis of published results.[58] Considering the ultimate aim of this review study, namely to justify the choice of medical co-variates in a multiple regression analysis studying psycho-social correlates of survival and tumor-relapse (reported in chapter 6), we preferred a more simple method of reviewing studies, in which statistical significance, statistical method and sample size were accounted for.

Statistics In search for reliable prognostic factors a variety of patient factors, treatment factors, and tumor factors have been studied in the literature. However, the possible interrelationships of these factors have only recently received attention, due previously to the lack of appropriate statistical methods, for which multivariate analysis is necessary in order to identify the independent significance of the factors under consideration.[17] In this review, 39 studies used a multivariate analysis and in only 16 studies was the analysis limited to the univariate technique. This means an improvement in comparison with what was found in studies before 1990.[48]

The more factors analyzed in a multivariate model the greater number of patients are needed. A large number of patients in a disease of relatively low incidence, such as head and neck cancer thus leads to combining different locations with a considerable heterogeneity in tumor and treatment features.

Criteria for Patient Selection As the histology of more than 90% of head and neck carcinomas is squamous cell carcinoma, it is not surprising that patients with this type of histology were included in the majority of studies (n=30). A great number of studies were concerned with a limited number of head and neck cancer sites (Table 1). However, in 18 studies "cancer of the head and neck" was the eligibility criterion, in which many sites were grouped together. The latter causes a heterogeneity that has implications for treatment, prognosis, and hence for the set of possible prognostic factors, as is the case with other selection criteria. In 29 studies the type treatment was a criterion for study entry. Only in 10 studies was treatment evaluated as a possible correlate of prognosis. In 17 studies T and N classification or stage of disease was a selection criterion.

The following discussion concerning the predictive value of factors will be confined to results of studies with a multivariate study design.

Host Factors Two of the host factors, age and sex, were evaluated with respect to survival in nearly 5000 patients showing diverging significance scores. It was found that in studies that evaluated age, in approximately 50% there was a significant correlation between this factor and survival. In the earlier literature, contradictory statements were found, seldomly based on proper analysis.[59,16] The problem is that age can affect survival in various ways for which "confounding" factors must have been corrected and this was not always so, eg, the death rate from intercurrent disease rises with increasing age, and the stage of presentation might change with increasing age. Huygen et al. performed in 1980 a careful analysis on patients with laryngeal cancer with respect to age and mortality allowing for most of these pitfalls.[60] They found that both the chance of survival and the length of survival fell significantly with increasing age. With respect to age, it might be concluded that the findings in the recent literature are in accordance with results of earlier publications. The results of the influence of patients' sex with respect to survival and relapse are clear: no correlation has been found.

Treatment Factors Treatment modality did not prove to correlate with overall survival and only slightly (ss=.14) with relapse, perhaps due to the fact that the majority of studies were focused on a selected tumor site and/or one treatment modality/regime.

In 4 of the 22 articles that focused on the larynx, pretreatment tracheostomy was evaluated with respect to survival and in only 1 study with respect to relapse. Significance scores were high. This factor might be of some importance especially with respect to overall survival (n=1306 patients), and needs to be studied in a large patient population with respect to relapse, considering the relative small sample with respect to relapse (n=278). In other studies dealing with treatment parameters, overall treatment time in radiotherapy, response to radiotherapy and response to chemotherapy show only in small samples sizes statistical significance concerning overall survival, .47, 1, and .68, respectively. With respect to the response to chemotherapy, Deyfuss[61] concludes in reviewing the literature, that this factor is of predictive value concerning the course of disease, and thus might identify groups of patients with unfavorable disease with subsequent adjustment of therapy regime.

Clinical Tumor Factors It is generally believed that substantial heterogeneity exists in the natural history of tumors arising from the different sites within the head and neck region, possibly resulting in differences in treatment outcome and survival. In this review, tumor site was analyzed in 23 studies in a large sample of patients resulting in inconclusive significance scores concerning both overall survivall and relapse, .47 and .55, respectively. Wolfensberger reported in his study, involving 920 head and neck carcinoma patients, that tumor location was predictive of prognosis in the larynx and tonsil.[57] A bias in analysing this factor might be that tumor extension to another *site* in the larynx is representing a higher *T classification,* making these 2 factors inter-related, whereas in the oropharynx it is not the involvement of other sites, but the total dimension of tumor that determines the T classification. In a large series of 1021 patients, Platz et al. reported that no influence of tumor location on prognosis has been found, concerning oral cavity and oropharynx carcinomas.[62]

In three of the studies involving 589 patients, in which vocal cord mobility was analyzed in T2-larynx carcinomas, a high significance score was found. This finding could be a justification of the tendency to split up the existing T2 classification into T2a, with normal vocal cord mobility and T2b, with impaired mobility. The influence of T classification per se on overall survival and relapse appears to be relatively low, .22 and .39, respectively. With respect to the larynx, a possible explanation for this weak correlation is the difficulty of exact clinical assessment of local tumor extent. The newer generation CT- and/or MRI scanners are indispensible for assessing the accurate T category, and might become mandatory in the future.

In contrast to the primary tumor the neck nodes are more easily accessible for clinical examination. The significance score calculated for N classification in relation to *overall survival* was the highest of all factors (.83, in 4460 patients), meaning that N status provides independent prognostic information. In a review article on prognostic factors in laryngeal cancer it is stated that it has been recognized since a long time that the presence of palpable lymph nodes is the most important factor determining prognosis.[59] Staging the neck only by palpation is less accurate than with the aid of diagnostic imaging and can lead to false negative results. In the present TNM classification the N classification is determined by clinically detectable lymph nodes, including detection by CT-scan, MRI and Ultra Sound.[63-65] Once metastatic neck disease from squamous cell carcinoma in the head and neck is esthablished, overall survival was found to be strongly correlated with N classification.[35] In contrast, the effect of N classification on *tumor relapse* is much less clear. This finding may be influenced by the fact that local, regional and distant control in the present evaluation were combined. Moreover, in this literature review conflicting results with respect to the effect of N classification on local control were found.[22,24,25,29,51]

The correlation of the factor "fixation of lymph nodes" both with OS and relapse was found to have a high significance score in a smallish patient population (both, n=492). Before 1987 the accepted staging systems of the American Joint Committee on Cancer (AJC) and the International Union Against Cancer (UICC) were different with respect to lymph node fixation.[66-69] Since 1987 both the staging systems are identical and fixation is no longer a criterion for N classification, because the assessment of size is less subjective than the assessment of fixation[c].

Another factor with respect to neck nodes, the level of lymph node(s), was found to have less predictive value. However, by the UICC '87 the level of lymph node metastasis is commented upon as having a bearing on prognosis. It is recommended that the level should always be recorded but it is not incorporated in its classification. Notably, stage of disease is absent in the field of *highest* significance score with respect to overall survival and relapse, although the scores are rather high. An underlaying assumption of the TNM staging system is that tumor growth progresses from local to regional to distant sites, with corresponding decreases in survival. The classification of different TNM categories into stage groups is such that each group is homogeneous with respect to survival and the survival rates for different stage groups are distinctive.When both N classification and M classification are highly predictive for prognosis, it is hard to understand that stage of disease is not. An explanation could be found in the publication of Snyderman and Wagner, who argue against the existing TNM staging system that the results of studies show that different combinations of T and N classifications within stage groups did not have comparable outcomes.[70] For example, it is doubtfull that patients with relatively early primary cancers (T1-T3) with manageable neck disease (N2) would have the same prognosis as patients with advanced primary and/or neck disease (T4 N3), despite the fact that both groups are stage IV.[71] Modifications of the staging system in 1987 altered the N description but did not change the stage groupings. It was not until 1997 that in the fifth edition of TNM classification of the UICC[72] and the AJCC[73] stage

---

c A major change has been introduced in the 4th edition of the UICC classification system. The neck node classification is now based on size, on presence of single or multple nodes, as well on the ipsilateral, bilateral or contralateral neck involvement. The subjectivity of esthablishing fixation has been eliminated

IV is subdivided in three categories, IVA, IVB and IVC, reflecting a worsening prognosis.

Histological and Biological Tumor Factors In this study, both positive tumor margins and extra nodal spread show high significance scores concerning relapse, evaluated in samples less than 500 patients. These factors are incorporated in treatment protocols of many institutions as an indication for postoperative irradiation and are regarded as important determinants of outcomes research.[74] Also, Wolfensberger and Platz reported that tumor positive margins were found to be prognostically significant with respect to survival studied in large series of patients.[57,62] Weymuller et al. stated that the fact that some studies fail to show a significance of surgical margin status may well be caused by poor "surgical quality control", ie, lack of uniform understanding in reporting surgical features, that is confounding data analysis in multi-institutional trials.[75] In a series of 1713 patients with respiratory and digestive tract carcinomas Richard et al. found that extra nodal spread was the most important prognostic factor regardless the primary site of the tumor.[76] Although these factors do not meet the criterion of sufficient number of patients studied in the present review, it can be concluded that positive tumor margins and extra nodal spread might provide prognostic information.

Since 1920 different histological classification systems have developed such as the grading system of Broders[77], with 4 grades of malignancy, and the invasive front grading according to the system of Bryne[78]. The grade of histologic differentiation, ie, well, moderately, and poorly differentiated, the only grading system studied in more than 5000 patients, turned out to be a prognostic factor of low confidence with respect to survival. Also the correlation with relapse was often contradictory. There are many difficulties inherent in histological grading systems, including wide inter and intra-observer error by the histopathologist, various differences between different parts of the same tumor and differences at different times. However, some authors believe that an undifferentiated carcinoma metastasizes early and has a poor prognosis.[55] Other histological tumor factors, such as growth pattern, mitosis, and mode of invasion, composite factors of the histological malignancy grading system according to Jacobson[29], have been reported as significant, but were only evaluated in a small number of patients.

Of the biological tumor factors, DNA ploidy, proliferation activity and epidermal growth factor showed some correlation with relapse. In a review study, Joensuu states that there is some evidence that DNA aneuploid carcinomas are more easily destroyed by irradiation than diploid carcinomas.[79] In conclusion, the predictive value concerning treatment outcome of all these factors, still needs to be confirmed in multivariate studies involving large patient populations. The factor p53 expression evaluated only in 1 study in the present review using univariate analyses, is a subject of interest in an increasing body of articles in the last few years, but failed to provide significant prognostic information with regard to tumor behavior.[80,81]

It is assumed that as new and more effective therapies are developed for patients with head and neck cancer, previously significant prognostic factors will cease to have clinical value. Similarly, as new diagnostic tests and staging tools are developed, a new generation of prognostic factors with greater biological and clinical relevance is likely to emerge.[61]

CONCLUSIONS

1. This literature review was conducted in order to quantify the impact on survival and tumor relapse of a wide range of medical factors. Considering the ultimate aim of this review study, namely to justify the choice of medical co-variates in a multiple regression analysis studying psychosocial correlates of survival and tumor relapse, a relative simple method of reviewing studies, in which statistical significance, statistical method and sample size are accounted for, by means of the significance score formula proved to be usefull.
2. Of the 55 studies evaluated more than 70% used a multivariate analysis model. This means an improvement in comparison with what was found in studies before 1990.
3. The majority of articles reported on a limited number of tumor locations or treatment modalities, but dealt with small numbers of patients. Only a few studies were found in which a large number of patients were involved. In this literature review 97 factors in total have been evaluated. However, only a limited number of factors (6 factors concerning both OS and relapse) were analyzed in a large patient population (3000 patients).
4. Of the factors that have been studied in a large series of patients, only N classification has reached a significance score of importance with respect to overall survival.
5. Age, site and T classification showed inconsistent results concerning prognosis.
6. For stage of disease the prognostic value calculated with the aid of the significance score formula was less than expected given the results

found with regard to N classification concerning overall survival.

7. No correlation has been found between patients' sex and prognosis.
8. Positive tumor margins and extra nodal spread can be considered as prognostic variables with respect to treatment outcome, although these factors do not meet the criterion of sufficient number of patients studied in the present review.
9. The prognostic value concerning treatment outcome and survival of most the histological and biological tumor factors, still needs to be confirmed in multivariate studies involving large patient populations.

REFERENCES

1 Leemans CR, Tiwari R, Nauta JJP, Van der Waal I, Snow GB. Recurrence at the primary site in head and neck cancer and significance of neck lymph node metastases as a prognostic factor. *Cancer* 1994;73:187-90.

2 Odell EW, Jani P, Sherriff M, Ahluwalia SM, Hibbert J, Levison DA, Morgan PR. The prognostic value of individual histologic grading parameters in small lingual squamous cell carcinomas. *Cancer* 1994;74:789-94.

3 Inoue T, Matayaoshi Y, Inoue T, Ikeda H, Teshima T, Shigeyuki M. Prognostic factors in telecobalt therapy for early supraglottic carcinoma. *Cancer* 1993;72:57-61.

4 Cooke LD, Cooke TG, Foster G, Jones AS, Stell PM. Prospectve evaluation of cell kinetics in head and neck squamous carcinoma: the relationship to tumour factors and survival. *Br J Cancer* 1994;69:717-20.

5 Munck-Wikland E, Fernberg JO, Kuylenstierna R, Lindholm J, Auer G. Proliferating cell nuclear antigen (PCNA) expression and nuclear DNA content in predicting recurrence after radiotherapy of early glottic carcinima. *Eur J Cancer B Oral Oncol* 1993;29B:75-9.

6 Peters LJ, Goepfert H, Kian Ang K, Byers RM, Maor MH, Guillamondegui O, Morrison WH, Weber RS, Garden AS, Frankenthaler RA, Oswald MJ, Brown BW. Evaluation of the dose for post operative radiation therapy of head and neck cancer: first report of a prospective randomized trial. *In J Radiat Oncol Biol Phys* 1993;26:3-11.

7 Nathanson A, Ågren K, et al. Evaluation of some prognostic factors in small squamous cell carcinoma of the mobile tongue: a multicenter study in Sweden. *Head Neck* 1989;11:387-92.

8 Inoue T, Inoue T, Ikeda H, Teshima T, Shigeyuki M. Prognostic factors of telecobalt therapy for early supraglottic carcinoma. *Cancer* 1992;70:2797-801.

9 Grandis JR, Snyderman CH, Johnson JT, Yu VL, D'Amico F. Postoperative wound infection: a poor prognostic sign for patients with head and neck cancer. *Cancer* 1992;70:2166-70.

10 Kaplan I, Katić V, Čulo F, Ćuk V. Prognostic significance of plasma prostaglandin E concentration in patients with head and neck cancer. *J Cancer Res Clin Oncol* 1992;118:308-13.

11 Bhatavdekar JM, Patel DD, Vora HH, Balar DB. Circulating markers and growth factors as prognosticators in man with advanced tongue cancer. *Tumour Biol* 1993;14:55-8.

12 Thompson AC, Bradley PJ, Griffin NR. Tumor-associated tissue eosinophilia

and long-term prognosis for carcinoma of the larynx. *Am J Surg* 1994;168:469-71.

13 Shimm DS. Early-stage glottic carcinomas: effect of tumor location and full-length involvement on tumor recurrence after radiotherapy. *Radiology* 1994;192:873-5.

14 Resnick MJM, Uhlman D, Adams G, Niehans GA, Knapp D, Gapany M, Jaszcz W. Cervical lymph node status and survival in laryngeal carcinoma: prognostic factors. *Ann Otol Rhinol Laryngol* 1995;104:685-94.

15 Lopez KJ, Robinson P, Madden T, Highbarger T. Nutritional support and prognosis with head and neck cancer. *J Surg Oncol* 1994;55:33-6.

16 Stell PM. Prognosis in laryngeal carcinoma: host factors. *Clin Otolaryngol* 1990;15:111-9.

17 Manni JJ, Terhaard CHJ, De Boer MF, Croll GA, Hilgers FJ, Annyas AA, Van der Meij AGL, Hordijk GJ. Prognostic factors for survival in patients with T3 Laryngeal carcinoma. *Am J Surg* 1992;164:682-7.

18 Rudoltz MS, Benammar A, Mohiuddin M. Prognostic factors for local control and survival in T1 squamous cell carcinoma of the glottis. *Int J Radiat Oncol Biol Phys* 1993;26:767-72.

19 Kowalski LP, Batista MBP, Santos CR, Scopel AA, Salvajoli JV, Novaes PE, Trippe N. Prognostic factors in glottic carcinoma clinical stage I and II treated by surgery or radiotherapy. *Am J Otolaryngol* 1993;14:122-7.

20 Dassonville O, Formento JL, Francoual M, Ramaioli A, Santini J, Schneider M, Demard F, Milano G. Expression of epidermal growth factor receptor and survival in upper aerodigestive tract cancer. *J Clin Oncol* 1993;11:1873-8.

21 Schwartz LH, Ozsahin M, Ni Zhang G, Touboul E, De Vataire F, Andolenko P, Lacau-Saint-Guily J, Laugier A, Schlienger M. Synchronous and metachronous head and neck carcinomas. *Cancer* 1994;74:1933-8.

22 Nyman J, Mercke C, Lindström J. Prognostic factors for local control and survival of cancer of the oral tongue: a retrospective analysis of 230 cases in western Sweden. *Acta Oncol* 1993;32:667-73.

23 Pradier R, González A, Matos E, Loria D, Adan R, Saco P, Califano L. Prognostic factors in laryngeal carcinoma. *Cancer* 1993;71:2472-6.

24 Van Acht MJJ, Hermans J, Boks DES, Leer JWH. The prognostic value of hemoglobin and a decrease in hemoglobin during radiotherapy in laryngeal carcinoma. *Radiother Oncol* 1992;23:229-35.

25 Nair MK, Sankaranayanan R, Krishnan E, Padmanabhan TK, Mayadevi S, Mathew A. Independent predictors of response and disease-free survival in oral cancer treated with radical radiation therapy. *Cancer* 1992;69:2221-26.

26 Fietkau R, Iro H, Tulusan AH, Dressel V, Altendorf-Hofmann, Sauer R.

Prognostic value of s-phase fraction in head and neck squamous cell carcinomas and nodal negative breast carcinomas. *Strahlenther Onkol* 1994;170:13-24.

27 Fontana X, Dassonville O, Neri J, Vallicioni J, Santini J, Milano G, Combon P, Lapalus F, Demard F. Sedimentation rate and serum thymidine kinase activity: prognostic factors in squamous cell head and neck cancer. *Head Neck* 1993;15:425-32.

28 Bryne M, Eide GE, Lilleng R, Langmark F, Thrane PS, Dabersteen E. A multivariate study of prognosis of oral squamous cel carcinomas: are blood group and hemoglobin new prognostic factors? *Cancer* 1991;68:1994-8.

29 Zätterström UK, Wennerberg J, Ewers SB, Willén R, Attewell R. Prognostic factors in head and neck cancer: histological grading, DNA ploidy, and nodal status. *Head Neck* 1991;13:477-87.

30 Foote RL, Olson KD, Davis DL, Buskirk SJ, Stanley RJ, Kunselman SJ, Schaid DJ, DeSanto LW. Base of tongue carcinoma: pattern of failure and predictors of recurrence after surgery alone. *Head Neck* 1993;15:300-7.

31 Wiernik G, Millard PR, Haybittle JL. The predictive value of histological classification into degrees of differentiation of squamous cell carcinoma of the larynx and hypopfarynx with survival of patients. *Histopathology* 1991;19:411-7.

32 Terhaard CHJ, Snippe K, Ravasz LA, Van der Tweel, Hordijk GJ. Radiotherapy in T1 laryngeal cancer: prognostic factors for locoregional control and survival, uni- and multivariate analysis. *Int J Radiat Oncol Biol Phys* 1991;21:1179-86.

33 Maurizi M, Scambia G, Benedetti Panici P, Ferrandina G, Almadori G, Paluderri G, De Vincenzo R, Distafano M, Brinchi D, Cadoni G, Mancuso S. EGF receptor expression in primary laryngeal cancer: correlation with clinico-pathological features and prognostic significance. *In J Cancer* 1992;52:862-6.

34 Truelson JM, Fisher SG, Beals TE, MacClatchey D, Wolf GT. DNA content and histological growth pattern correlate with prognosis in patients with advanced squamous cell carcinoma of the larynx. *Cancer* 1992;70:56-62.

35 Cerezo L, Milian I, Torre A, Aragon G, Otero J. Prognostic factors for survival and tumor control in cervical lymph node metastasis from head and neck cancer. *Cancer* 1992;69:1224-34.

36 Small W, Mittal BB, Brand WN, Shetty RM, Rademaker AW, Beck GG, Hoover SV. Results of radiation therapy in early glottic carcinoma: multivariate analysis of prognostic and radiation therapy variables. *Radiology* 1992;183:789-94.

37 Munck-Wikland E, Kuylenstierna R, Lind M, Lindholm J, Nathanson A, Auer G. The prognostic value of cytometric DNA analysis in early stage tongue cancer. *Eur J Cancer B oral oncol* 1992;28B:135-8.

38 Kearsley JH, Bryson G, Battistutta D, Collins RJ. Prognostic importance of cellular DNA content in head-and-neck-squamous-cell cancers. A comparison of retrospective and prospective series. *Int J Cancer* 1991;47:31-7.

39 Cooke LD, Cooke TG, Forster G, Helliwell TR, Stell PM. Cellular DNA content and prognosis in surgically treated squamous carcinoma of the larynx *Br J Cancer* 1991;63:1018-20.

40 Ravasz LA, Slootweg PJ, Hordijk GJ, Smit F, Van der Tweel I. The status of the resection margins as a prognostic factor in the treatment of head and neck carcinoma. *J Craniomaxillofac Surg* 1991;19:314-8.

41 Lydiatt DD, Savage HE, Clayman GL, Liu FJ, Sample D, Schantz ST. Serologic deteminants of survival in patients with head and neck cancer: validating a clinical prediction model. *Laryngoscope* 1993;103:13-6.

42 Jones KR, Lodge-Rigal RD, Reddick RL, Tudor GE, Shockley WW. Prognostic factors in recurrence of stage I and II squamous cell cancer of the oral cavity. *Arch Otolaryngol Head Neck Surg* 1992;118:483-5.

43 Williams JK, Carlson GW, Cohen C, Derose P, Hunter S, Juriewicz MJ. Tumor angiogenesis as a prognostic factor in oral cavity tumors. *Am J Surg* 1994;168:373-80.

44 Jones AS, Roland NJ, Field JK, Phillips DE. The level of cervical lymph node metastases: their prognostic relevance and relationship with head and neck squamous carcinoma primary sites. *Clin Otolaryngol* 1994;19:63-9.

45 Kersh CR, Kelly MD, Hahn SS, Constable WC. Early glottic carcinoma: patterns and predictors of relapse after definitive radiotherapy. *South Med J* 1990;83:374-8.

46 Barra S, Barzan L, Maione A, Cadelano A, Pin M, Franceschi S, Comoretto R. Blood transfusion and other prognostic variables in the survival of patients with cancer of the head and neck. *Laryngoscope* 1994;104:95-8.

47 Stell PM. Prognosis in mouth cancer: host factors. *J Laryngol Otol* 1992;106:399-402.

48 Kowalski, LP, Batista BP, Santos CR, Scopel A, Salvajolli JV, Torloni H. Prognostic factors in T3, N0-1 glottic and transglottic carcinoma. A multifactorial study of 221 cases treated by surgery or radiotherapy. *Arch Otolaryngol Head Neck Surg* 1996;122:77-82.

49 Mak-Kregar S, Schouwenburg PF, Baris G, Hilgers FJM, Hart AAM..Staging and prognostic factors in carcinoma of the base of the tongue. *Clin Otolaryngol* 1992;17:107-12.

50 Zätterström UK, Brun E, Willén R, Kjellén , Wennerberg J. Tumor angiogenesis and prognosis in squamous cell carcinoma of the head and neck. *Head Neck* 1995;17:312-8.

51 Kowalski LP, Franco EL, De Andrade Sobrinho J, Oliveira BV, Pontes PL. Prognostic factors in laryngeal cancer patients submitted to surgical treatment. *J Surg Oncol* 1991;48:87-95.

52 Bundgaard T. Bentzen SM, Wildt J, Sørensen FB, Søgaard H, Nielsen JE. Histopathologic, stereologic, epidemiologic, and clinical parameters in the prognostic evaluation of squamous cell carcinoma of the oral cavity. *Head Neck* 1996;18:142-52.

53 Fein DA, Lee W, Hanlon AL, Ridge JA, Langer CJ, Curran WJ, Coia LR. Pretreatment hemoglobin level influences local control and survival of T1-T2 squamous cell carcinomas of the glottic larynx. *J Clin Oncol* 1995;13:2077-83.

54 Corvò R, Giaretti W, Sanguinetti G, Geidi E, Orecchia R. Guenzi M, Margarino G, Bacigalupo A, Garaventa G, Barberi M, Vitale V. In vivo cell kinetics in head and neck squamous cell carcinomas predicts local control and helps guide radiotherapy regimen. *J Clin Oncol* 1995;13:1843-50.

55 Stell PM. Prognosis in laryngeal carcinoma: tumour factors. *Clin Otolaryngol* 1990;15:69-81.

56 George SL. Identification and assessment of prognostic factors. *Semin Oncol* 1988;15:462-71.

57 Wolfensberger M. Using Cox's proportional hazards model for the prognostication in carcinoma of the upper aero-didestive tract. *Acta Otolaryngol (Stokh)* 1992;112:376-82.

58 Thacker SB. Meta-analysis: a quantative a quantative approach to research integration. *Jama* 1988;259:1685-9.

59 Stell PM. Review. Prognostic factors in laryngeal cancer. *Clin Otolaryngol* 1988;13:399-409.

60 Huygen PLM, Van Den Broek P, Kazem I. Age and mortality in laryngeal cancer. *Otolaryngol* 1980; 5:129-37.

61 Dreyfuss AI, Clark JR. Analysis of prognostic factors in squamous cell carcinomas of the head and neck. *Hematol Oncol Clin North Am* 1991;5:701-12.

62 Platz H, Fries R, Hudec M, Tjoa AM, Wagner RR. The prognostic relevance of various factors at the time of first admission of the patient. *J Maxillofac Surg* 1983;11:3-12.

63 Van den Brekel MWM, Castelijns JA, Croll GA, Stel HV, Valk J, Van de Waal I, Snow GB. Magnetic resonance imaging vs palpation of cervical lymph node

metastasis. *Arch Otolayngol Head Neck Surg* 1991;117:666-73.
64 Baatenburg de Jong RJ, Rongen RJ, De Jong PC, Lameris JS, Knegt PP. Sreening for lymph nodes in the neck with ultra sound. *Clin Otolaryngol* 1988;13:5-9.
65 Takes RP, Knegt PP, Manni JJ, Meeuwis CA, Marres HAM, Spoelstra HAA, De Boer MF, et al. Regional metastasis in head and neck squamous cell carcinoma: revised value of US with US-guided FNAB *Radiology* 1996;198:819-23.
66 Levendag PC, Veeze-Kuijpers B, Knegt PP, De Boer, MF, Eijkenboom WMH, Reichgelt BA, Van Putten WLJ. Cancer of the supraglottic larynx with neck node metastasis treated by radiation therapy only. The revised 1987 UICC classification system as prognostic indicator. *Acta Oncol* 1990;29:603-9.
67 TNM Classification of Malignant Tumors (3rd edition). UICC International Union Against Cancer, Geneva, 1978.
68 TNM Classification of Malignant Tumors (4th edition). UICC International Union Against Cancer, Geneva, 1987.
69 American Joint Committee on Cancer. Manual for staging of cancer. Third ed. Philadelphia: JB Lippincott Co., 1988.
70 Snyderman CH, Wagner RL. Superiority of the T and N integer score (TANIS) staging system for squamous cell carcinoma of the oral cavity. *Otolaryngol Head Neck Surg* 1995;112:691-4.
71 Mendenhall WM, Parsons JT, Million RR, Cassisi, NJ, Devine JW, Greene BD. A favorable subset of AJCC stage IV squamous cell carcinoma of the haed and neck. *Int J Radiat Oncol Biol Phys* 1984;10:1841-3.
72 TNM Classification of Malignant Tumors (5th edition). UICC International Union Against Cancer, New York: Wiley and Sons Inc., 1997.
73 American Joint Committee on Cancer. Manual for staging of cancer. Fifth ed. Philadelphia: JB Lippincott Co., 1997.
74 Deleyiannis FWB, Weymuller EA. Outcomes research in head and neck oncology. *Cur Opnion Otolaryngol Head Neck Surg* 1996:4:73-7.
75 Weymuller EA, Ahmad K, Casiano RR, Schuller D, Scott CB, Laramore G, Al-Sarraf M, Jacobs JR. Surgical reporting instrument designed to improve outcome data in head and neck cancer trials. *Ann Otol Rhinol Laryngol* 1994;103:499-509.
76 Richard JM, Sancho-Garnier H, Micheau C, Saravane D, Cachin Y. Prognostic factors in cervical lymph node metastasis in upper respiratory and digestive tract carcinomas: a study of 1,713 cases during a 15-year period. *Laryngoscope* 1987;97:97-101.
77 Broders AC. Squamous epithelioma of the lip: a review study of five hundred

and thirty cases. *Jama* 1920;74:656-64.

78 Bryne M. Prognostic value of various molecular and cellular features in oral squamous cell carcinomas: a review. *J Oral Pathol Med* 1991;20:413-20.

79 Joensuu A. DNA flow cytometry in prediction of survival and response to radiotherapy in head and neck cancer: a review. *Acta Oncol* 1990;29:513-6.

80 Shin DM, Lee JS, Choi G. Shah T, Hyne K, Earley C, shin HJ, Ro JY, Hong WK, Hittelman. Prognostic significance of p53 expression in head and neck squamous cell carcinmoma (meeting abstract). *Proc Annu Meet Am Soc Clin Oncol* 1994;13:A914.

81 Portugal L, Goldenberg JD, Wenig BL, Ferrer KT, Nodzenski E, Jaishiri B, Javier C, Weichselbaum RR, Vokes EE. Human Papillovirus and p53 gene mutations in squamous cancer. *Arch Otolaryngol Head Neck Surg* 1997;123:1230-4.

Chapter 5

LITERATURE REVIEW OF PSYCHOSOCIAL CORRELATES OF CANCER RELAPSE AND SURVIVAL

ABSTRACT

This article reviews literature on the psychosocial correlates of cancer relapse and survival from 1979 through 1995. The factors studied were structured according to a theoretical model of coping with cancer. Reviewed studies have shown that factors most frequently evaluated were depression, anxiety, hopelessness/helplessness, hostility, marital status and social involvement. Mainly inconsistent results were found. The strongest evidence for a relationship between psychosocial variables and prognosis was found for social involvement/social support; in 7 of 15 studies a positive relationship was demonstrated, while no negative associations were found. Coping styles eg, fighting spirit and stoic acceptance, and severe/stressful life events were found to have no conclusive influence on the length of survival. Important determinants of the coping model, such as uncertainty and information given by the specialist were not studied as possible predictors of survival and/or relapse free period. Among the factors that showed no correlation at all was multidimensional health locus of control. For the inconsistent findings, a considerable number of methodologic shortcomings with respect to study design, sample size, measure and statistical analysis are enumerated.

INTRODUCTION

The idea that there is a relationship between psychosocial variables and the causation and development of cancer goes back over two thousand years to ancient Greece. Hippocrates believed that health was a state which depended on the balance of four humors of the body: blood, phlegm, yellow bile and black bile.[1] Any distortion of the balance of the humors could cause a disease. For example, women with an excess of black bile were melancholic and more likely to suffer from cancer than the ones with an excess of blood who were sanguine. Also Galen, a famous Roman doctor (200 A.D.), stated in "De Tumoribus" that cancer occurred more frequently in "melancholic" women than in the "sanguine" women.[2] This belief was substantiated by careful, systematic observations, but not by statistical or experimental research.

During the eighteenth and nineteenth centuries, many observers commented on this relation. For instance, Gendron noted in 1701 that anxious and depressed women were more cancer prone.[3] In that time a number of references related cancer to emotional factors; for example Berchelman in 1764 maintained that cancer was caused by a severe disturbance of emotions.[4] In 1846 Walshe commented that mental dysphoria and the stresses of a difficult life resulted in "defective innervation", which he felt was an aspect of cancer pathogenesis.[4] Although, as late as 1911, Sir William Osler[5], known as "the father of British medicine", stated that it was often more important to know which person had the disease than which disease the person had, the first scientific work was published by Snow in 1893[6], in which he reported the first statistical analysis of the effects of psychosocial factors on the development of cancer in 250 patients. Stressful life events were seen in the majority of patients.

An extensive review of the literature on psychosocial factors and the pathogenesis of cancer from the 19th century to the end of the 1950s has been published by LeShan.[7,8] He concluded that the characteristics of hopelessness, loss and depression frequently emerged as predictive in these studies. The investigator used factors such as loss of a crucial relationship, inability to express hostility and not getting over the death of a parent, to successfully discriminate between cancer patients and controls.[8] From 1950 to 1970, although psychology was not systematically integrated into clinical oncology programs, there was substantial research activity in the field. In 1952 Bard outlined a 4-stage sequence of emotional reactions to mastectomy.[10] Simultaneously, Renneker et al. elucidated the psychosocial problems of distorted body image, anxiety, depression, and self deprecation associated with surgical treatments for breast cancer.[11] As mentioned previously, many early clinicians and investigators perceived an association between psychosocial status and the emergence of cancer. However, these observers may have had difficulty separating antecedent from consequent factors. Until now there are a number of relations between psychological disorders and cancer that investigators remain eager to explore, including the potential psychogenic etiology of cancer, psychological symptoms as possible prodromal signs of neoplasia, and psychological integrity in response to cancer.

The first reports suggesting that cancer patients' psychological characteristics were systematically related with length of survival appeared during the 1950s. Individuals who rapidly succumbed to the disease were described as polite, cooperative, and unable to express negative affects, particularly hostility. Longer survivors were described as emotionally expressive, and in some cases bizarre.[12,13] Subsequently,Stavraky et al. observed similar relations between emotional expression and survival. In two population based studies, higher mortality rates among patients with few social community ties were revealed.[14] A loss of social support through the death of a spouse has also been shown to be related to an increased risk of cancer death.[7,15]

In a review study of psychogenic effects on cancer etiology and prognosis, Fox suggested that if psychosocial factors are considered to have any effect at all, there was more theoretical reason to expect that psychological factors influence the course, rather than the occurrence of disease.[16] The author argues that the mechanisms involved in the prognosis question are more restricted and the findings from therapy and animal experiments are much less subject to suspicion than the extrapolating to psychosocial factors in the etiology of cancer. Contradictory scientific data and controversial theories, such as the type C behavior[17], high corticosteroid level, and poor immune function being associated with depression[18], exist concerning the belief that psychological factors can influence the onset, and can predict progression of cancer. In this article we will present an overview of the literature on psychosocial prognostic factors in all cancer sites from 1979 through 1995.

MATERIALS AND METHODS

The purpose of this review is to establish an impression of the most important psychosocial determinants of survival and freedom of relapse. Relevant studies and reviews were used for an exploratory investigation of this field of research. The relationships between psychosocial characteristics of cancer patients, and survival and recurrence were evaluated on the basis of reports

Table 1 Overview of studies concerning psychosocial variables related to the course of cancer

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Derogatis et al. (20)	35	Breast cancer, metastatic Stage IV	After diagnosis of metastasis 3 yr Prospective	– Joy – Contentment – Affection – Vigor – Clinical judgement measures – Obsessive/compulsive – Interpersonal sensitivity	OS (short-term/long-term survivors) – High state anxiety↑[a] – Psychotism↑ – Depression, guilt ↑ – Good adjustment ↓[b] – Low hostility ↓ – Positive mood ↓	Short and long-term surv. groups no significant differences on: age, disease-free interval, menopause status, distribution of metastases, Karnofsky performance status, initial response to treatment.
Rogentine et al. (21)	64	Melanoma Stage I and II	Within 1 wk after radical surgery 1 yr Prospective	– Locus of control – Somatization – Depression – State anxiety – Hostility – Phobic anxiety – Paranoid ideation – Psychotism – Stressful life events	RFP – Minor adjustment to cope with illness ↓	Clinical stage, number of positive nodes, clinical enlargement nodes, histology and location primary tumor, Clarck level, age, sex , time from first symptom
Greer et al. (22) Petting dale et al (23) and Greer et al. (24)	57	Breast cancer Stage I and II	Before and 3, 12 mo after operation, annually for 4 yr 5-10-15 yr Prospective	– Depression – Hostility – Neurotism – Extrovertism – Social adjustment – Psychological response to cancer after 3 months	OS/RFP – Denial ↑ – Fighting spirit ↑ – Stoic acceptance ↓ – Helpless, hopelessness ↓ – [Alone/poor-relationship ↓ weak association[c]	Age, social class, tumor size, histological grading, delay in seeking medical advice, menopausal status, clinical stage, radiation therapy, type of surgery. not for: histological node status

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Funch et al. (25)	208	Breast cancer Stage I and II	After diagnosis 20 yr Prospective	– Marital status – Number of friends and relatives	OS – High social involvement ↑ – High objective stress (old) ↓ – High subjective stress (young) ↓	Age, stage of disease, meno pausal status, past health status, socioeconomic status, (not for: treatment regimes)
Marshall et al. (26) (same patient population as Funchs')	283	Breast cancer All stages, all died	Before initial treatment 20 yr Prospective	No other psychosocial variables evaluated	OS – Stress ↓ – High social involvement ↑	Stage at diagnosis, age and prior cancer history, physical condition
Cassileth et al. (27)	359	Group I: unresectable cancers Group II: melanoma, stage I-II and breast cancer, stage II	2-8 wk after diagnosis Until relapse Prospective	– Marital history – Social ties – Job satisfaction – Psychotropic drug use – Life satisfaction – Hopeless/helplessness – Adjustment to cope illness – Subjective view of adult health	OS (group I)/RFP (group II) No effect	Stage of disease, performance status, socioeconomic status, sex, age, treatment status
Kukull et al. (28)	53	Lung cancer Advanced stage Inoperable	1 and 2 mo after diagnosis 4 yr Prospective	– Pain – Personality traits – Social dependence – Mood state – Current concern – Acknowledged awareness of illness	OS – High symptom distress ↓	None, except age and delay in reporting symptoms (all patients received same treatment-modality and were in a similar stage of disease)

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Neale et al. (29)	1261	Breast cancer Stage I-IV	At the time of admission to the hospital 10 yr Prospective	No other psychosocial variables evaluated	OS – Married status ↑	Socio-economic status, age, stage, delay seeking treatment
Holland et al. (30)	346	Breast cancer Stage II	Prior to chemotherapy Until relapse Prospective	– Somatization – Obsessive-compulsive – Interpersonal sensitivity – Depression – State anxiety – Hostility – Phobic anxiety – Paranoid ideation – Psychotism	RFP No effect	Estrogen receptor (ER), stage, adjuvant therapy
Goodwin et al. (31)	25706	All cancer sites All stages	At time of diagnosis 5 yr Retrospective	No other psychosocial variables evaluated	OS – Married status ↑	Socioeconomic status, ethnicity, site, type of cancer, stage, treatment
Jamison et al. (32)	49	Breast cancer Metastatic	13-167 mo after treatment Until death Prospective	– General well-being – Subjective valuation of health – Self-esteem – Hostility – Depression (Zung) – Multiple health locus of control – Trait anxiety (Spielberger)	OS (short-term/long-term survivors) No effect	Age, people at home, education level, other illness, lymph nodes, metastases, menopausal status, ER, Karnofsky performance status

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Jensen (33)	52	Breast cancer 27 treated for recurrence 25 no recurrence.	After treatment Average 624 days Prospective	No other psychosocial variables evaluated	RFP – Repressive personality style ↓ – Reduced expression of negative affect ↓ – Comforting day-dreaming ↓ – Helpless/ hopelessness ↓ – Chronic stress ↓	Age at diagnosis, stage of disease, length of disease course, medical status at study onset, genetic and hormonal factors, socioeconomic status, IQ, family cancer (not for: treatments)
Hislop et al. (34)	133	Breast cancer All stages	Within 3 mo of diagnosis 4 yr Prospective	– Instrumental activities: at home, away from home – Neurotism – Self-esteem – Recent life events – Recent life changes – Coping behavior – State anxiety – Depression	OS/RFP – Extroversion ↑ – Anger ↓ – Expressive activities: at home ↑ away from home ↑ – Low cognitive disturbance ↑ (RFP) [– High Internal locus of control ↑ (RFP), weak association[c]]	Age, stage, pathological axillary nodal status, histological grade, ER, (not for: treatment regimes)

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Leigh et al. (35)	101	All sites (eg, breast cancer and prostate cancer) All stages	During radiotherapy period 3 yr Prospective	– Self assessment seriousness disease – Psychotropic drugs – Nausea	OS (survivors/non-survivors) – High trait anxiety ↑ – More pain ↓ [– State anxiety and depression tended to be higher in survivors]	Demographic data (age, sex, education, living alone, ethnicity), site, expected 5-year survival rate, weight, skin complications, psychotropic drugs, nausea, number of visits, number of radical treatments, months since diagnosis made
Cassileth et al (36)	204 and 155	Group I: intestinal cancer, Advanced stages Group II: cutaneous melanoma and breast Stage II	After diagnosis, group I: 8 yr group II: until recurrence Prospective	– Social relationships – Job satisfaction – Life satisfaction – Subjective view of adult health – Hopeless/helplessness – Adjustment required to cope with diagnosis – General life evaluation – Psychotropic drugs	RFP no effect, exept a weak correlation for [– positive life evaluation ↑ (OS), weak association[c]] [– married status ↓ (OS), weak association[c]]	Group I: performance status, extent of disease, age, marital status, race, gender Group II: diagnosis, extent of disease, performance status, marital status, age
Levy et al. (37)	36	Breast cancer Recurrence	At diagnosis first recurrence and 4 wk later 3,5 yr Prospective	– Dysphoric mood – Hostility (Affect-Balance scale same as in Derogatis' study, opposite findings)	OS (short-term/long-term survivors) – More joy at baseline ↑	Age, disease-free interval, number and location of metastatic sites, cell histology of primary tumor, karnofsky status

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Dean et al. (38)	122	Breast cancer Stage I-III	Before and 3 mo after operation 6-8 yr Prospective	– Eysenck personality inventory (extroversion, neurotism) – psychiatric status	RFP – Psychiatric illness before operation ↑ – General health questionnaire ↑ – Coping using denial after operation ↑ – Fighting spirit, stoic acceptance – Hopeless/helplessness↓ (difficulties in measuring coping strategies!)	Age, social class, marital status, employment status, menopausal status, histological node status, tumor size, clinical staging, therapy regime
Kaasa et al (39)	102	Non-small cell lung cancer (NSCLC) Stage II and III, inoperable	Before start of chemotherapy 3 yr Prospective	– Physical functioning – Everyday activity	OS – Little general symptoms ↑ – Good psychosocial well-being ↑	Stage, prior weight loss, WHO performance status, treatment
Ramirez et al. (40)	100	Breast cancer 50 recurrence 50 free of recurrence Case-control study	After surgery From date of surgery to date of recurrence Retrospective	No other psychosocial variables evaluated	RFP (occurrence of relapse) – Severe life events/difficulties ↓	Case and control were matched for type of operation, chemotherapy, menopausal state, affected lymph nodes, tumor size, histological type of tumor, sociodemographic variables

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Richardson et al. (41)	141	Hematologic cancer and rectal cancer	1-2 wk of diagnosis / 1-3 mo of surgery and both groups 6 mo later 2 yr or more and 3 yr or more Prospective	– Depression (Beck, Zung) – Coping styles (Moos) – Multiple health locus of control (Walston)	OS No effect	Demographics: gender, ethnicity, marital status, education, income, age, disease severity: high/ moderate/low, treatment, hospital stay
Levy et al (42)	90	Breast cancer Stage I-II	5 d after surgery and 15 mo 5 yr Prospective	– Familial social support	RFP – Positive mood (POMS) ↑	Age, stage of disease, pathology staging, number of positive nodes, estrogen receptor, treatment, Natural Killer cell activity
Waxler et al. (43) (Same material as study of Hislop)	133	Breast cancer All stages	Within 3 mo after diagnosis 3-4 yr Prospective	– Expressive (emotional, relational) activities at home, away from home – Extroversion – Anger – Problem tackling	OS – Number supportive persons ↑ – Having a job ↑ – Size of social network ↑ – Married status ↓ – Daydreaming ↑	Age, clinical stage, pathological nodal status, histological tumor grade, estrogen receptor, type of initial treatment,, time to first recurrence, (not the treatment)
Buddeberg et al. (44)	107	Breast cancer Stage I-III	Every 3 mo from 6-36 mo after surgery 3 years Prospective	– Depressive coping – Self-encouragement/ distraction	OS/RFP No effect	Involvement axillary lymph nodes, post surgical tumor stage, treatment, age

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Forsén (45)	87	Breast cancer All stages	After surgery 8 yr Prospective	– Important losses – Preceding difficult life situations – Psychiatric symptoms	OS/RFP – Stressful life event ↓ – Lower social class ↓	Age, marital status, education, stage of disease, radiotherapy, axillary node status, chemotherapy, ER, histology
Ganz et al (46)	40	Lung cancer (NSCLC) Advanced (metastatic) stage	Before treatment 20 mo Prospective	No other psychosocial variables evaluated	OS – High quality of life (FLIC) ↑ – Married status (interaction with QOL) ↑	Histological cell type, Karnofsky performance status, weight loss, number of distant metastatic sites, age, gender
Siberfarb et al. (47)	290	Multiple myeloma	Before initial treatment and at 3 mo of therapy 2 yr Prospective	– Mood state (POMS) – State anxiety, depression, hostility (MAACL) – Physician-completed handicap-rating scale	OS/response duration No effect	Age, tumor-cell load and creatinine level
Barraclough et al. (48)	204	Breast cancer Stage I-III	4, 24 and 42 mo after surgery 42 mo Prospective	– Severe life events (LEDS) – Social difficulties (LEDS) – Depressive illness (DSM-III) – Availability of confiding relationships	RFP No effect	Marital status, non manual occupation, menopausal status, size of tumor, number histological positive axillary nodes, treatment

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Coates et al (49)	262	Breast cancer advanced stage	Before treatment and after 3 cycles chemotherapy 3-4 yr Prospective	– Pain	OS – Physical well being ↑ – High quality of life index (Spitzer) ↑ – Overall quality of life ↑	Subset of patient and disease prognostic factors significant for survival from an earlier study in the same patients: performance status, metastatic pattern, treatment, allocation, tumor response
Ell et al. (50)	294	Breast cancer, lung cancer and colorectal cancer All stages	Within 3-6 mo of diagnosis 21 d to 83 mo Prospective	– Availability of social integration – Psychological distress	OS Breast cancer: – Married status ↓ – Adequacy of emotional support ↑ Lung and colorectal cancer: – Role-limitations ↓	Age, socio-economic status (income, education, occupational status),site, stage of illness
Fawzy et al. (51)	68	Malignant melanoma Stage I and II	Before treatment and 6 wk after intervention and after 6 mo 5-6 yr Prospective	– change in variables over the 6 mo	OS/RFP – Baseline affective distress (POMS TMD) ↑ – Baseline effective coping ↑	Age, sex, Breslow depth, tumor site, natural killer cell activity

Table 1 Continued

Author (Ref. no.)	No. of patients	Cancer site Stage	Time of measurement Follow-up time Design	Variables not associated with (relapse free) survival	Variables associated with overall (OS) and relapse free period (RFP)	Control for sociodemografic and medical variables
Reynolds et al. (53)	1011	Breast cancer All stages	3-6 mo of diagnosis 5 yr Prospective	– Social network (structural, Berkman's NSI)	OS – Close social ties ↑ – Many perceived sources of emotional support (functional) ↑	Age, race, study area, education, presence of symptoms, co-morbidity, stage of disease
Maunsell et al. (54)	224	Breast cancer Stage I-III	3 mo after initial surgery 7 yr Prospective	– Stressful life events – Emotional distress – Daily activities	OS – Social support ↑	Age, presence of axillary lymph nodes, therapy variables

[a] (↑=positive correlation)
[b] (↓=negative correlation)
[c] mentioned by the authors as having a relationship with OS and/or RFP, while the p-value varied between .05 and .09

of studies and review studies. Therefore, a literature search was done, using Medline, CancerLit and PsycLIT, including the key words *neoplasms*, *psych **, *social support*, prognos *, *predict **, *survival* and *recurrence*, from 1979 through 1995. Reports written not in the English language were excluded. Also excluded were articles on cancer in childhood.

The key words "intervention" and "psychotherapy" were not used in the literature searches. Interventions influence particular psychosocial variables, which in measuring outcome on survival are difficult to disentangle. Articles of this kind only were included, if psychosocial factors were related to survival and/or relapse.

A total of 33 studies were found. Besides these studies, 17 review articles from the same period of time were found. On the basis of studies described in the articles that could be obtained in a reasonable time span, a table was made containing the following sections: author, number of patients, time of measurement, follow-up time, study design, psychosocial variables that were not associated with survival and relapse of tumor, psychosocial variables that were associated with survival and relapse and sociodemographic and medical co-variates controlled for (Table 1). The review articles that were found by means of the literature search were analyzed with respect to concluding remarks on methodological and psychosocial issues relating to treatment outcome concerning longevity and tumor status.

RESULTS OF THE REVIEW

Tumor Site The great majority, ie, 20 studies, focused on breast cancer as the only tumor site. Two studies were limited to malignant melanoma, whereas two other studies dealt with breast cancer and melanoma, amongst others. Lung cancer patients were the subject of study in 4 studies, and miscellaneous sites were studied in the remaining reports.

Number of Patients The number of patients that were involved in the 33 studies could be classified into four categories: 1) 35-68 patients (n=10), 2) 87-141 patients (n=10), 3) 204-359 patients (n=10), and 4) 1011-25706 patients (n=3). In the majority of studies (n=20) only less than 142 patients were included.

Stage of Disease Patients in different stages of disease were studied. For most tumor sites it is usually accepted that stages I and II are mentioned as early-stage cancer, whereas stages III and IV are referred to as being advanced-stage cancer. Of the 22 studies dealing with breast cancer, 9 reported on early-stage cancer, 3 on advanced-stage, and in 10 studies all stages were present. Of the melanoma patients all 4 studies were of early-stage. Both studies on lung carcinomas and combined sites were predominantly advanced-stage.

Time Point of Assessment Psychosocial assessments were carried out at different time points before and after diagnosis or treatment. The time point of measurement in studies was: (1) after diagnosis (n=12), (2) before treatment (n=5), and (3) after treatment (n=9). In 5 studies there was an assessment on multiple points, one before and one after treatment, and in 2 studies there were multiple measurements after treatment. In the "measurement after diagnosis", there was a range from 1 week to 6 months, or the elapsed time after diagnosis was not mentioned at all.

Study Design As can be seen in Table 1, only two studies had a retrospective design, the study of Goodwin et al.[31] concerned population-based data and Ramirez et al.[40] studied severe life events, looking back at the point of disease relapse. All other reviewed studies were prospective of design. It is not always possible to draw a clear distinction between a retro and prospective design, eg, life events are always assessed retrospectively, while one is studying the relationship between life events and disease progression/survival prospectively. We did not find a study with a "real" prospective design, ie, psychosocial assessment before diagnosis.

Follow-Up Time The mean follow-up time was 5.5 years, ranging from 21 days to 20 years. In some studies the occurrence of relapse was the end point of study (all of the patients that were the subject of a study had a relapse) and in other articles death was the end-point of study (all of the patients had died).

Control Variables In most articles the evaluation of the relationships between psychosocial variables and treatment outcomes was controlled for a number of sociodemographic and clinico-pathological variables. The relevant control-variables can be subdivided in 4 groups: 1) socio-demographic, 2) tumor status/treatment, 3) general-medical and 4) site-specific. The groups are listed here, along with the number of studies in which the factor was analyzed as a "control" variable, in parenthesis.

Group 1: age (24), sex (6), socio-economic status (5), marital status (4), ethnicity (4), educational level (4), social class (2), living alone (1), people at home (1), number of visits (1), Intelligence Quotient (I.Q.) (1),employment status (1), and income (1).

Group 2: clinical stage (17), aspects of treatment (13), number of (positive) lymph nodes (11), histology/grading primary tumor (8), time from first symptom (5), number/distribution metastatic sites (4), location primary tumor (3), length of disease course (1), expected 5-year survival rate (1), disease severity (1) skin complications (1), use of psychotropic drugs (1), and nausea (1).

Group 3: performance status (7), co-morbidity (2), physical condition (1), medical status at onset of study (1), past health status (1), prior cancer history (1), and family history of cancer (1).

Group 4: menopausal status (6), estrogen receptor status (6), natural killer cell activity (2), genetic and hormonal factors (1), tumor cell load (1), creatine level (1), Clark level (1), and Breslow depth (1).

Outcome Variables The outcome measures differed considerably. We have tried to subdivide outcome measures into two groups: overall survival (OS) and the occurrence of relapse or tumor. In 20 studies, variables were correlated with overall survival. Several investigators have split up the patient population into short- and long-term survivors, using a common cut-off point of 1-2 years. In this manner, criteria of lengths of survival have been applied instead of analyzing data using life table analyses. In 8 studies relapse free period (RFP) was studied, and in the remaining studies, both criteria were applied. In the concept "relapse free period", the frequently used outcome measures, "occurrence of relapse/recurrence", "disease-free survival" and "cause specific survival" were included.

Statistical Analysis In general we can conclude that there is no uniformity in statistical analysis in the studies reviewed here. More sophisticated and more uniform analysis methods were employed in more recent years, in which multivariate analytic methods, with Cox proportional hazards model, were more frequently used. In the past, univariate models were also applied statistically , independently of the study design; however, an approach in which the combined influence of interacting psychosocial variables is examined, is more conclusive than the influence of separate factors.

Application of Theories The research literature is generally atheoretical. It seems more important to researchers to use well-established instruments than it is to select and use psychometrically-sound measures that are grounded in theory. In only 3 studies there was an indication of what one could call a theory or model concerning the interaction between psychosocial factors and the course of malignant disease. Kukul et al. evaluated "key psychosocial variables" that influenced the quality of the daily life of people with cancer in a model of coping with a life threatening illness.[28] The basis of the study of Jensen is the "disregulation theory" and progression of cancer.[32] Levy et al. used the theory that emotional and behavioral factors might well affect hormonal and immunological regulatory mechanisms related to breast cancer outcome by biological pathways linking higher cortical function and potential tumor response.[42]

Model of Coping with Cancer Of the studies reviewed, the predictive variables were structured according to a theoretical model of coping with cancer of Van den Borne and Pruyn.[19] This model is based on the assumption that *uncertainty*, *negative feelings*, eg, feelings of depression, loneliness and psychosocial and physical complaints, *loss of control*, and *threatened self-esteem* are the four most important problems experienced by cancer patients. Efforts of the patients themselves are directed to prevent or reduce these problems as much as possible. These efforts are called *coping strategies*. In this process of coping with cancer, *person-related* factors like socio-demographic variables, eg, income, education, age, marital status, smoking and drinking habits and daily activities, *intra-personal*, eg, trait-anxiety and locus of control, *inter-personal (social)* concepts, such as information and support they received from others, and *illness-related* factors (eg, stage of disease, type of treatment), together with the physical and psychosocial problems experienced by patients, can possibly influence the course of disease.

Psychosocial Correlates Psychosocial variables that are studied with respect to their relation to overall survival (OS) and relapse free period (RFP) are presented according to the model of coping with cancer described in the previous paragraph.

Basic Problems With respect to *Negative feelings*, high state-anxiety, high depression and guilt were associated significantly with longer OS in the study of Derogatis.[25] State-anxiety and depression tended to be higher in survivors in the study of Leigh.[35] In four studies state-anxiety showed no association with OS and/or recurrence[21,30,34,47] and in eight studies depression was not associated.[21,24,30,32,34,41,44,47] Greater helplessness and/or hopelessness in three studies by Greer & Pettingdale and Jensen was associated with reduced OS/RFP.[22,23,24,33,38] In two other studies measuring hopelessness and helplessness, no association was found.[27,36] Hostility was found to associate with longer OS in the Derogatis study.[20] In six other studies hostility was not associated.[21,24,30,32,37,47] Both phobic anxiety (in two studies) and anger (in one study) showed no association with OS/RFP[21,43], while anger was positively associated in one study.[34] Of the physical problems, increased pain turned out to be correlated with shorter OS.[35] In two studies no association was found between pain and outcome variables.[28,49] Having few general symptoms is associated with longer OS in the study of Kaasa[39], whereas in another study physical problems, such as skin complications and nausea, showed no correlation.[35]

Loss of control: Hislop reported that low cognitive disturbance, eg, forgetfulness and difficulty concentrating, was correlated with longer OS.[34] Less functional status, assessed in terms of role limitations, was found to correlate with shorter OS by Ell.[50] In two studies every-day activities were found to be uncorrelated with outcome variables.[39,54]

Threatened self-esteem: In two studies inter-personal sensitivity as an indicator of problems in the area of self-image, was not associated with survival.[20,30]

Coping Strategies In the study of Greer and Pettingale, denial and fighting spirit were associated with longer OS/RFP.[22-24] Fighting spirit in another study was associated with shorter RFP.[33] Coping by stoic acceptance was associated with shorter OS/RFP in the studies of Greer and Pettingale[22-24] and Dean.[38] The results with respect to comforting day-dreaming are contradictory. In the study of Jensen[33], comforting day-dreaming was associated with poor prognosis, whereas in the study of Waxler[43], it was related with a good prognosis. Both reduced expression of negative affect in the study of Jensen[33] and minor adjustment that is needed to cope with the illness in the study of Rogentine[21], were associated with shorter OS. In the study of Derogatis good adjustment to the illness was correlated with shorter OS/RFP.[20] In two other studies adjustment to coping with illness[24] and social adjustment[27] showed no correlation with outcome variables. Coping styles such as tackling problems[43], self encouragement[44], distraction[44], extrovertism[43] and depressive coping (distrust, pessimism, regressive tendency)[44], were not associated with OS and/or RFP. In the study of Fawzy "effective" coping (no further explanation of this concept was given in this report) was associated with longer OS/RFP.[51] In other studies coping style (Moos)[41] and coping behavior (chance, control, stress)[34] showed no association with prognosis.

Person-Related Factors Concerning *socio-demographic factors,* being married was associated in 3 studies with longer OS.[29,31,46] Correspondingly, in the study of Greer and Pettingale, being alone and having a poor relationship were weakly associated with shorter OS/RFP. However, in the study of Cassileth[36] a weak association and, in the studies of Waxler[43] and Ell[50], a significant association between married status and shorter OS was found. In two studies no correlation between married status and OS/RFP was seen.[25,27] Having a job and a higher social class were associated with longer OS/RFP.[43,45]

Social factors: In several studies, social factors were found to be associated significantly with good prognosis. These social factors, ie, high social involvement[25,26], high involvement in expressive (social) activities[34], large social network and a great number of supportive persons[43], close social ties[53], good adequacy of emotional support[50], high perceived sources of emotional support[53] and extensive social support[54], were correlated with longer OS. In a similar number of studies no significant correlations were found for social factors. These factors were: number of friends and relatives[25], social ties[27], social network[53], social dependence[28], social relationships[36], familial support[42], availability of confiding relationships[45], availability of social integration[50] and involvement in social activities.[34]

Personality factors: In the study of Leigh, high trait-anxiety was significantly associated with longer OS/RFP.[30] Trait-anxiety showed no correlation in another study.[32] Internal locus of control was found to have a weak correlation with a longer RFP.[34] A locus of control scale in another study had no relation with prognosis[21]. In the study of Jensen a repressive personality style was associated with shorter OS.[33] Extroversion was positively related to OS/RFP in one study[34] and had no influence on suvival in another study.[24] In two studies Multidimensional health locus of control had no relation with OS and/or RFP.[32,41]

Container and Miscellaneous Factors Several, more global, concepts studied that were used in some of the studies can not be described according to our theoretical model of coping with cancer. These so-called container and miscellaneous factors will be addressed below.

In the study of Cassileth "positive life evaluation" was correlated weakly with longer survival[27] In three studies[46,49,52] "high quality of life", and, in one study[39] "good psychosocial well-being" were associated with longer OS. In other studies "life satisfaction" and "general life evaluation" were not correlated with survival.[27,36] In the study of Ramirez[35] having experienced severe life events and difficulties in the past was associated with shorter RFP. However, the factors - recent life events[34] and preceding difficult life situations[40], and in 3 studies, severe/stressful life events[21,48,56] -produced only null results. Also, general well-being[32] was found to be uncorrelated with OS and/or RFP, while general health had a positive relationship with RFP.[38] In a study by Levy[42] positive mood was associated with a longer RFP. However, in a study of Derogatis[20] positive mood was associated with shorter OS. In three other studies mood state was not correlated with prognosis.[28,37,47]

Psychiatric factors, such as psychotism[20] and psychiatric illness measured before the operation[38] were associated with longer OS. On the other hand, factors such as psychotism (two studies)[21,30], psychiatric symptoms[45], psychiatric status[38] paranoid ideation (in two studies)[21,30], and neurotism (in two studies)[24,34], did not correlate with prognosis. Experiencing more joy at baseline measurement was associated with longer OS.[37] In another study the variable "joy" had no influence.[20] With respect to stress variables it was found that high objective/subjective stress[25] and chronic stress[33] were associated with shorter OS/RFP. High affective distress[51] and high symptom distress[28] were associated with shorter OS. The factors psychological distress[50] and emotional distress[56] did not show any correlation with survival or disease progression. In the study of Coates[49] physical well-being was correlated with longer OS. Other miscalleneous factors such as subjective view of adult health[36], subjective evaluation of health[32], acknowledged awareness of illness[28], self assessment of seriousness of the disease[30], physician completed handicap-rating scale[47], somatisation (in two studies)[21,30], contentment[20], affection[20], vigor[20], obsessive/compulsive (in two studies)[20,30], using psychotropic drugs (in three studies)[27,35,36], job satisfaction[36] and social difficulties[48] were found to be not associated with OS and/or RFP.

Studies with No Associations In 8 studies investigators have not found any significant association with the length of survival or (the time to) relapse.[27,30,32,36,41,44,47,48]

CONCLUSIONS

Head and Heck Cancer No studies were found concerning patients with head and neck cancer in which correlations were analyzed between psychosocial factors and survival or tumor relapse.

Associations with Survival and Tumor Relapse

a. Factors most frequently evaluated with respect to their association with survival and/or relapse were depression, anxiety, hopelessness/helplessness, hostility, marital status and social involvement. Mainly inconsistent results were found. Against two studies which found a positive correlation between depression and OS/RFP, in eight studies no significant correlation was found. State-anxiety was also found to correlate positively with OS/RFP in two studies while no relations were found in four studies. Feelings of hopelessness and helplessness were found to correlate negatively with OS/RFP in five studies against two studies in which no relations were found. In only one out of seven studies a positive correlation between hostility and OS/RFP was found, while the other studies showed no significant correlations. These inconsistencies with respect to the predictive value of psychological factors are in line with the conclusions of other reviewers.[6,57,58] However, Watson concluded that there is some indication of a correlation between depression and hopelessness/helplessness, and prognosis.[59]

Marital status was analyzed in eight studies. In two of these studies being married was positively related, wherease three studies yielded a negative relation with OS, and one study a negative relation with RFP. In two studies no relation was found. Interestingly, in two extensive studies involving many cancer patients (n=1262 and n=25706 respectively) both found married patients to have an increased survival.[29,31] In reviewing the literature Blanchard found no evidence that marital status had an influence on prognosis.[60]

Probably the strongest evidence for a relationship between psychosocial variables and OS/RFP was found for social involvement/social support. In seven studies a positive correlation was found between a measure for social involvement/social support and OS. In eight studies no relationship between a social involvement/social support variable and OS/RFP was found. The conclusions of other reviewers of the literature are consistent with our findings. Several review authors concluded that social support is a predictor of a good prognosis.[61,63,64] However, Blanchard[60] stated that there is no conclusive evidence for a correlation, and Hilakivi found some indication of a relationship with the length of survival.[62]

b. Other inconclusive results regarding a predictive value for OS/RFP were found with respect to psychosocial variables that were less frequently studied. There were contradictory findings with respect to outcome measures, such as day dreaming and mood. Moreover, we found inconsistent findings with respect to variables such as pain, functional status/every-day activities, coping mechanisms, fighting spirit and stoic acceptance, locus of control, trait anxiety, anger, extroversion, severe/stressful life events, psychotism and experience of joy. Three earlier reviewers of the literature mentioned coping styles as having influence on prognosis[64,65,66], while Hürney concluded that coping styles showed no conclusive evidence of correlation.[67] With respect to stressful life events three reviewers concluded equally that there was no evidence of association with the length of survival.[60,62,68]

c. In addition, we considered a result as inconclusive when a variable showed an association with OS/RFP only in one study. These variables are social class, quality of life, physical and psychological well being, and several stress variables, ie,chronic stress, high objective/subjective stress, reduced affective distress. In other review studies, Osoba[69] stated that (pretreatment) health quality of life in late stage disease was predictive of survival, and Turns concluded that contradictory results were found with respect to stress.[70]

d. No correlation was found between prognosis and multidimensional health locus of control, phobic anxiety, neurotism and somatization. For each of the variables this was found in two studies, while there were no studies that described the opposite.

e. In none of the reviewed studies we found results concerning the concepts which were included in our model of coping with cancer such as: uncertainty (the need for information), the amount of information given by health care providers, support from fellow patients, and the appreciation of the information. Also, loneliness was not studied as a predictor of OS/RFP.

Methodological Problems and Reasons for Inconsistent Findings In our review of the literature we found a considerable number of methodological shortcomings, which were:

a. In many studies the sample sizes were small and the selection of patients was not always specified. This is also in concordance with the conclusions of Carlsson.[63]
b. In some studies patients with different types of cancer and patients in

different stages of disease were studied, also concluded by Mulder[57], Richardson[41] and Watson.[59]

c. With respect to the study design we come to the conclusion that many studies were prospective/longitudinal but the follow-up time was variable and usually short. Moreover, psychosocial assessments were carried out at different time points before and after diagnosis/treatment. Bleiker[6], Carlsson[63] and Mulder[57] have commented on these issues in the same sense.

d. With respect to the measures we observed that the outcome variables were different in several studies, which made it difficult to compare the studies. Few studies measured constructs using the same instruments and the instruments were not always reliable and/or valid. Many earlier reviewers came to the same conclusions.[6,41,65,57,60,63]

e. There were differences in statistical analyses. In most studies confounding behavioral factors, such as compliance with medical treatment, smoking and alcohol abuse, were ignored and in some studies clinical-pathological prognostic factors were left uncontrolled, shortcomings that were also mentioned by Mulder[57], Richardson[41], van der Pompe[68] and Bleiker.[6]

f. In most studies there is a lack of substantive theoretical models, as was also mentioned by Blanchard[60] and Temoshok.[17]

DISCUSSION

In this review we choose to give the state of affaires concerning psychosocial prognostic factors. We did not describe the strengths an weaknesses of each study. Therefore no priority/weight is given to results obtained in stronger studies (with larger patient groups, prospective study design, and including control of several variables by using multivariate analyses). Also no specific studies have been described which are suspected because of methodological shortcomings and what this says with respect to conclusions drawn.

A possible explanation for the many contradictory and inconsistent findings from our review is that the stage of disease is a confounding factor in analyzing the relation between psychosocial variables and prognosis. It is possible that in the beginning phase of the disease, a negative feeling, eg, anxiety, is related to an active way of coping, which leads to seeking information and support from others. On the other hand, this same negative feeling could be related to "passive" coping and poor outcomes when it is experienced in a late stage of the disease.

Another explanation is that the diversity of types of tumors and tumor locations may partially account for the inconsistent findings. It is possible that different mechanisms are related to tumor progression (eg, hormonal factors in breast cancer) that might have results in psychosocial responses and conversely. Tumor type can also play a role when confounding behavioral factors such as smoking and alcohol abuse, and dietary factors, which are intimately related to the onset as well as the progression of cancer of the upper and lower aerodigestive tract, are left uncontrolled. For example, we know that people with lung cancer and head and neck cancer, on average, smoke more than others and that continued smoking among head and neck cancer patients has been shown to lead to as much as a fourfold increased relative risk compaired with the risk of nonsmokers, and a doubled risk compaired with that of patients who had quit smoking.[71]

Contradictory and inconclusive results could also be explained by possible non-linear relations between psychosocial factors and prognosis. For instance, when a psychosocial variable, such as anxiety, is not linearly related to survival time, both a low and a high level of anxiety may be associated with short survival, while a medium anxiety score may be associated with long term survival.

Finally, an explanation for inconsistent findings could be the fact that in so many studies only small numbers of patients were included, leading to many type II errors. Therefore, it is possible that factors significant in one study are not significant in another.

RECOMMENDATIONS

We make the following recommendations for future research:

1. There is still a need for a good meta-analysis of the studies in which the study results are valued according to the strength of the study.
2. The starting point of a study on the relations between psychosocial variables and prognosis should be a theoretical model on coping with cancer. From such a model the choice of the independent variables can be derived. By doing so the chances that possible, important predictive factors are missed will be reduced. Subsequently it is advised to define and add relevant confounding factors to be measured. At least age and stage of disease should be included as well as tumor-specific variables.
3. Only homogeneous patient groups of large enough numbers should be included in the study. When the incidence of a tumor site is (relatively) rare, multicenter studies are mandated.

4. The point of first measurement should be as early as possible; at the time of diagnosis or before the revelation of the disease.
5. Uncertainty is an important problem in cancer patients. As we did not find any study in which uncertainty was addressed in relation to prognosis we recommend that in future studies the concept of uncertainty will be incorporated.
6. Last but not least, only measures with well established levels of reliability and validity should be used.

REFERENCES

1 Rigatos GA, Scarlos DB. Psychosomatic concepts in writings of ancient Greek philosophers. In G. Christodoulou (Ed.), *Psychosomatic Medicine. Past and Future* New York/London: Plenum Press, 1987:pp. 43-46.

2 Goldfarb C, Driesen J, Cole D. Psychophysiologic aspects of malignancy. *Am J Psychiatry* 1967; 123: 1545-52.

3 Gendron D. *Enquiries into the nature, knowledge and cure of cancer.* London: J. Taylor, 1701.

4 Derogatis LR. Psychology in cancer medicine: a perspective and overview. *J Consult Clin Psychol* 1986; 54: 632-8.

5 Eysenck HJ. Prediction of cancer and coronary heart disease mortality by means of a personality inventory: results of a 15-year follow-up study. *Psychological Reports* 1993; 72: 499-516.

6 Bleiker EMA. Personality factors and breast cancer; A prospective study of relationship between psychological factors and the development of breast cancer. Academic Thesis, Amsterdam, 1995.

7 LeShan LL, Worthington RE. Personality as a factor in the pathogenesis of cancer: a review of the literature. *Br J Med Psychol* 1956; 29: 49-56.

8 LeShan LL. Psychological states as factors in development of malignant disease: a critical review. *JNCI* 1959; 22: 1-18.

9 LeShan LL. *You can fight for your life: emotional factors in the causation of cancer.* 1977; New York: M. Evans.

10 Bard M. The sequence of emotional reactions in radical mastectomy patients. *Public Health Reports* 1952;67:1144-8.

11 Renneker R, Cutler M. Psychosocial problems of adjustment to cancer of the breast. *J Am Med Assoc* 1952;148:633-8.

12 Bacon CL, Renneker R, Cutler M. A psychosomatic survey of cancer of the breast. *Psychosom Med* 1952; 14: 453.

13 Blumberg EM, West PM, Ellis FW. A possible relationship between psychological factors and human cancer. *Psychosom Med* 1954; 4: 277-86.

14 Stavraky KM, Buck CN, Lott JS, Worklin JM. Psychological factors in the outcome of human cancer. *J Psychosom Res* 1968; 12: 251-9.

15 Kissen DM. The present status of psychosomatic cancer research. *Geriatrics* 1969; 24: 129.

16 Fox BH. Current theory of psychogenic effects on cancer incidence and prognosis. *J Psychosoc Oncol* 1983; 1: 17-31.

17 Temoshok L, Heller B. On comparison between apples and oranges and fruit salad: a methodological overview of medical outcome in psychosocial onco-

logy. In Cooper CL. *Psychosocial Stress and Cancer.* London: Wiley, 1984: 231-60.

18 Solomon GF, Amkraut AA. Psychoneuroendocrinological effects on the immun response. *Ann Rev Microbiol* 1981;35:155-84.

19 Pruyn JFA. Coping with stress in cancer patients. *Patient Education Counseling* 1983;5:57-62.

20 Derogatis LR, Abeloff MD, Melisaratos N. Psychological coping mechanisms and survival time in metastatic breast cancer. *JAMA* 1979;242: 1504-8.

21 Rogentine GN, Van Kammen DP, Fox BH, Docherty JP, Rosenblatt JE, Boyd SC, Bunney WE. Psychological factors in the prognosis of malignant melanoma: a prospective study. *Psychosom Med* 1979; 41: 647-55.

22 Greer S, Morris T, Pettingale KW. Psychological response to breast cancer: effect on outcome. *Lancet* 1979; 13:785-7.

23 Pettingale KW, Morris T, Greer S, Haybittle JL. Mental attitudes to cancer: an additional prognostic factor. *Lancet* 1985; 30: 750.

24 Greer S, Morris T, Pettingale KW, Haybittle JL. Psychosocial response to breast cancer and 15 year outcome. *Lancet* 1990; 335: 49-50.

25 Funch DP, Marchall J. The role of stress, social support and age in survival from breast cancer. *J Psychosom Res* 1983; 27: 77-83.

26 Marshall JR, Funch DP. Social environment and breast cancer A cohort analysis of patient survival. *Cancer* 1983; 52: 1546-50.

27 Cassileth BR, Lusk EJ, Miller DS, Brown LL, Miller C. Psychosocial correlates of survival in advanced malignant disease. *N Engl J Med* 1985; 312: 1551-5.

28 Kukull WA, McCorkle R, Driever M. Symptom distress psychosocial variables and survival from lung cancer. *J Psychosoc Oncol* 1986; 4: 91-100.

29 Neale AV, Tilley BC, Vernon SW. Marital status delay in seeking treatment and survival from breast cancer. *So. Sci Med* 1986; 23: 305-13.

30 Holland JC, Korzun AH, Tross S, Cella DF, Norton L, Wood W. Psychosocial factors and disease free survival in stage II breast carcinoma. (Abstract) *Proc Am Soc Clin Oncol* 1986; 5: 237.

31 Goodwin JS, Hunt WC, Key CR, Samet JM. The effect of marital status on stage, treatment, and survival of cancer patients. *JAMA* 1987; 258: 3125-30.

32 Jamison RN, Burish TG, Wallston KA. Psychogenic factors in predicting survival of breast cancer patients. *J Clin Oncol* 1987; 5: 768-72.

33 Jensen MR. Psychobiological factors predicting the course of breast cancer. *J Pers* 1987; 55: 317-42.

34 Hislop T, Waxler NE, Coldman AJ, Elwood JM, Kan L. The prognostic significance of psychosocial factors in women with breast cancer. *J Chron Dis* 1987; 40: 729-35.

35 Leigh H, Percarpio B, Opsahl C, Ungerer J. Psychological predictors of survival in cancer patients undergoing radiation therapy. *Psychother Psychosom* 1987; 47:65-73.

36 Cassileth BR, Walsh WP, Lusk EJ. Psychosocial correlates of cancer survival: a subsequent report 3 to 8 years after cancer diagnosis. *J Clin Oncol* 1988; 6: 1753-9.

37 Levy SM, Lee J, Bagley C, Lippman M. Survival hazards analysis in first recurrent breast cancer patients: seven years follow up. *Psychosom Med* 1988; 50: 520-8.

38 Dean C, Surtees PG. Do psychological factors predict survival in breast cancer? *J Psychosom Res* 1989; 33: 561-9.

39 Kaasa S, Mastekaasa A, Lund E. Prognostic factors for patients with inoperable non-small cell lung cancer, limited disease. *Radiother Oncol* 1989; 15:235-42.

40 Ramirez AJ, Craig TKJ, Watson JP, Fentiman IS, North WRS, Rubens RD. Stress and relapse of breast cancer. *Br Med J* 1989; 298:291-3.

41 Richardson JL, Zarnegar Z, Bisno B, Levine A. Psychosocial status at initiation of cancer treatment and survival. *J Psychosom Res* 1990; 34: 189-201.

42 Levy SM, Herberman RB, Lippman M, D'Angelo T, Lee J. Immunological and psychological predictors of disease recurrence in patients with early stage breast cancer. *Behav Med* 1991; 17: 67-75.

43 Waxler-Morrison N, Hislop TG, Mears B, Kan L. Effects of social relationships on survival for women with breast cancer: a prospective study. *Soc Sci Med* 1991; 33(2): 177-83.

44 Buddeberg C, Wolf C, Sieber M, Riehl-Emde M, Bergant A, Steiner R, Landolt-Ritter C, Richter D. Coping strategies and course of disease of breast cancer patients; results of a three year longitudinal study. *Psychoth Psychosom* 1991; 55: 151-7.

45 Forsén A. Psychosocial stress as a risk for breast cancer. *Psychoth Psychosom* 1991; 55: 176-85.

46 Ganz PA, Lee JJ, Siau J. Quality of life assessment. An independent prognostic variable of survival in lung cancer. *Cancer* 1991; 67: 3131-5.

47 Silberfarb PM, Anderson KM, Rundle AC, Holland JCB, Cooper MR, McIntyle OR. Mood and clinical status in patients with multiple myeloma. *J Clin Oncol* 1991; 9: 2219-24.

48 Barraclough J, Pinder P, Cruddas M, Osmond C, Taylor I, Perry M. Life events and breast cancer prognosis. *Br Med J* 1992; 304:1078-81.

49 Coates A, Gebski V, Murray P, McNeil D, Byrne M, Forbes JF. Prognostic value of quality-of-life scores during chemotherapy for advanced breast can-

cer. *J Clin Oncol* 1992; 10: 1833-8.

50 Ell K, Nishimoto R, Mediansky L, Mantell J, Hamovitch M. Social relations, social support and survival among patients with cancer. *J Psychosom Res* 1992; 6: 531-41.

51 Fawzy FI, Fawzy NW, Hyun CS, Elashof R, Gurthrie D, Fahey JL,Morton DL. Malignant Melanoma - Effects of an early structured psychiatric intervention, coping, and affective state on recurrence and survival 6 years later. *Arch Gen Psychiatry* 1993; 50:681-9.

52 Fraser SCA, Ramirez AJ, Ebbs SR, Fallowfield LJ, Dobbs HJ, Richards MA, Bates T, Baum M. A daily dairy of life measurement in advanced breast cancer trials. *Br J Cancer* 1993; 67: 341-6.

53 Reynolds P, Boyd PT, Blacklow RS, Jackson JS, Greenberg RS, Austin DF, Chen VW, Edwards BK. The relationship between social ties and survival among black and white breast cancer patients. *Cancer Epidemiol Biomarkers Prev* 1994; 3: 253-9.

54 Maunsell E, Brisson J, Deschênes L. Social support and survival among women with breast cancer. *Cancer* 1995; 76: 631-7.

55 Weeks J. Quality-of-life assessment: performance status upstaged? [editorial]. *J Clin Oncol* 1992; 12: 1827-9.

56 Derogatis LR. Psychology in cancer medicine: a perspective and overview. *J Consult Clin Psychol* 1986; 54: 632-8.

57 Mulder CL, Van der Pompe G, Spiegel D, Antoni MH, De Vries MJ. Do psychosocial factors influence the course of breast cancer? *Psycho-Oncology* 1992; 1:155-67.

58 Stam, HJ, Steggles, S. Predicting the onset or progression of cancer from psychological characteristics: psychometric and theoretical issues. *J Psychosoc Oncol* 1987; 5(2): 35-46.

59 Watson M. Breast cancer: psychological factors influencing progression. In: Cooper CL, Ed. *Stress and breast cancer*. New York: John Wiley & Sons, 1988: 65-75.

60 Blanchard CG, Albrecht TL, Ruckdeschel JC, Grant CH, Hemmick RM. The role of social support in adaptation to survival. *J Psychosoc Oncol* 1995; 13(1/2): 75-95.

61 Spiegel D. Effects of psychosocial support on patients with metastatic breast cancer. *J Psychosoc Oncol* 1992; 10(2): 113-20.

62 Hilakivi-Clarke L, Rowland J, Clarke R, Lippman ME. Psychosocial factors in development and progression of breast cancer. *Breast Cancer Res Treatment* 1993; 29: 141-60.

63 Carlsson M, Harim E. Psychological and psychosocial aspects of breast cancer;

a literature review. *Cancer Nurs* 1994; 17(5): 418-28.

64 Bauer SM. Psychoneuroimmunology and cancer: an integrated review. *J Adv Nurs* 1994;19: 1114-20.

65 Levy SM. Psychosocial risk factors and cancer progression. In: Cooper CL, ed. *Stress and breast cancer.* New York: John Wiley & Sons, 1988: 77-96.

66 Royak-Schaler R. Psychological Processes in breast cancer: a review of selected research. *J Psychosoc Oncol* 1991; 9(4): 71-89.

67 Hürny C, Bernhard J. Coping and survival in patients with primary breast cancer: a critical analysis of current research strategies and proposal of a new approach integrating biomedical, psychological, and social variables. In: Herfarth Ch, Senn HJ, eds. *Recent Results in Cancer Research Volume 115.* Berlin Heidelberg: Springer-Verlag, 1989: 255-71.

68 Van der Pompe G, Antoni MH, Mulder CL, Heijnen C, Goodkin K, De Graef A. Psychoneuroimmunology and the course of breast cancer: an overview. *Psycho-Oncology* 1994; 3: 271-88.

69 Osoba D. Lessions learned from measuring health related quality of life in oncology. *J Clin Oncol* 1994; 12(3): 608-16.

70 Turns DM. Psychosocial factors. In: Donegan WL, Spratt JS, eds. *Cancer of the breast.* Philadelphia London: Saunders Company, 1995: 778-86.

71 Stevens MH, Gardner JW, Parkin JL, Johnson LP. Head and neck cancer survival and life style changes. *Arch Otolaryngol* 1983;109:746-9.

Chapter 6

PSYCHOSOCIAL AND PHYSICAL CORRELATES OF SURVIVAL AND RELAPSE IN HEAD AND NECK CANCER: RESULTS OF A 6-YEAR LONGITUDINAL STUDY

ABSTRACT

Background. Studies which have examined the relations between psychosocial factors and survival in cancer patients do not permit any definitive conclusions. No studies have examined the relationship between medical as well as quality of life variables and survival in head and neck cancer patients. The present study will focus on the complex interactions among psychosocial, medical, behavioral and demographic variables as they relate to prognosis in this type of patients.

Methods. A total of 133 consecutive head and neck cancer patients were included in a prospective study at pretreatment. In addition to clinical variables, psychosocial and physical functioning was assessed by means of a self report questionnaire.

Results. During the observation period 57 patients died whereas 76 were still alive at 6 years after treatment. Results of the multivariate survival analysis indicate that patients without neck metastasis had a better prognosis than patients with positive neck nodes. Pretreatment smoking showed a negative correlation with overall survival.

Patients who are more physically self-efficacious (ie, higher in perceived physical abilities) were more likely to survive and less likely to suffer a relapse. Also, patients who expressed a high intensity of psychosocial complaints prior to the treatment had a better prognosis than had those who did not express such negative feelings.

Conclusions. The current findings linking physical self-efficacy and prognosis are suggestive, but clinical trials are necessary to examine the direct and indirect mediational pathways of the variables which underly physical efficacy and influence survival and relapse. Also, the negative correlation between pretreatment smoking and survival suggests a need for increased efforts to address smoking status of newly diagnosed patients.

INTRODUCTION

For many years researchers have focused on the quantitative dimension of survival as the main outcome of cancer therapy, attempting to maximize overall survival time and the relapse-free time period. Unfortunately, in the last decade not much progress has been achieved with respect to survival time in many cancer sites. For example, the 5-year survival in head and neck cancer patients has stabilized at approximately 50% in the last 15 years.[1, 2] However, in recent years there has been an increasing amount of attention paid to the second important outcome parameter, the quality of life for patients, with some encouraging results.[3] Increases in the quality of the patients' lives has been achieved by means of improvement in surgical skills, along with refinement of reconstructive techniques, more sophisticated radiotherapy, and organ preservation by combined modality treatment.[4] Constructive changes have also been accomplished in rehabilitation outcomes by means of psychosocial intervention programs, eg, by providing information, guidance, offering fellow patient contact, psychotherapy, and improving the communication between physician and patient. Indeed, these psychosocial intervention programs have prepared patients to cope better with the stresses of their illness during and after treatment, resulting in reduced levels of uncertainty, anxiety, and loss of control, as well as increased levels of self-esteem.[5-8]

Despite these advances, the impact of psychosocial intervention programs on survival and tumor control still remains problematic. Recent reviews of outcome studies involving such interventions do not yet show consensus, indicating that this field of research is still in an early stage of development.[9,10] In addition, many other studies examining the relations between psychosocial factors and survival have been conducted.[11] The factors most frequently studied include depression, anxiety, hopelessness and helplessness, hostility, social involvement, and marital status. Other less frequently studied factors in relation to prognosis include coping strategies, locus of control, and stressful life events. Unfortunately, the results of these studies do not permit any definitive conclusions to be drawn.[12-25]

These inconsistent findings could possibly be explained by deficiencies in study design, measurement technique, and/or data analysis. Also, most investigations lack an explicit theoretical model or utilize different operational definitions of psychosocial concepts. In addition, samples tend to confound cancer types and stage and/or severity of the disease and, in longitudinal studies, standardization of assessment time periods. Finally, results may be inconsistent in respect to data analysis: in many studies there is no statistical control for confounding variables such as age, sex, type of treatment, smoking, and alcohol consumption.

In reviewing the literature, it is also striking that there is a lack of studies concerning the relations among medical, as well as quality of life variables, and survival in head and neck cancer patients. The only two exceptions are the work of Fawzy [26] and the Simonton-Atchley [27] study, both involving patients with tumors in the head and neck region. While both studies were prospective in design, the first utilized a sample of 68 patients, only 11 of which were head and neck cancer patients. Also the study of Simonton-Atchley examined a mixed group of 17 patients after completion radiotherapy for head and neck, breast, or lung cancer. Since results in both studies were presented for the total sample only, no specific judgments about head-and-neck patients were made. Given the limited amount of data available about quality of life variables in relation to survival in head and neck patients, the current investigation was conducted to provide preliminary data to help rectify the situation. Specifically, this study will focus on the complex interactions among psychological, tumor-biological, behavioral and social variables, and sociodemographic factors as they relate to survival and relapse of the disease. These interactions will be studied in a prospective design over several years.

PATIENTS AND METHODS

Patients Participants in the study consisted of head and neck cancer patients from the Rotterdam University Hospital Dijkzigt and the Daniel den Hoed Cancer Center. The intake of new subjects started July 1 1986 and continued for 18 months as a part of an on-going research project involving medical/physical and psychosocial correlates of head and neck cancer, and prognosis. The baseline assessment of patients' medical and psychosocial characteristics occurred just before the treatment. The medical histories of the patients in study were reviewed during September and October, 1994. Elapsed follow-up time depended on when patients were initially enrolled in the study.

Eligible were all patients who received one of the following treatments:
Group I. A full course of radiotherapy for a carcinoma confined to the vocal cords (T1 [28]), no regional lymph node metastasis (N0).
Group II. Total laryngectomy without neck dissection for a primary laryn-

geal carcinoma or relapse following prior radiotherapy.
Group III. Surgery for carcinoma in the oral cavity and/or oropharynx.

For patients in Group II and III, surgery was performed as primary treatment or as salvage treatment, and in case of primary treatment, postoperative radiotherapy was given in advanced tumors per protocol requirement. Patients with a distant metastasis at first visit were not included. Of the initially selected 185 patients, 52 patients were excluded. Of these 52 patients, ten patients did not react to the invitation to participate in the study on time (eg, before the medical treatment), eight patients refused to join the study, and 34 patients dropped out because of various reasons, such as language barriers, living in another part of the country or undergoing preoperative tracheostomy, due to dyspnea. Finally, there were 133 patients who consented to participate in the study, after they received the essential information. Of these patients, 47 were in group I, 42 were in group II, and 44 were in group III. Of group II and III, a total 57 patients entered the study after a tumor relapse at the primary site had been detected, following curative radiotherapy. This group will be referred to as "prior radiotherapy".

In the follow-up study there were two main outcome variables: the time from treatment to relapse and the time from treatment to death. Discrimination between metastases to the lung and a second primary tumor located in the lung remained arbitrary. Therefore, in this study it was decided to add this "second primary of the lung" group (n=6) to the "recurrence" group and label this combined group as "tumor relapse". Also second primary tumors in the head and neck region (n=3) were added to the relapse group. There were no cases lost to follow-up. All patients had a histopathologic diagnosis of squamous cell carcinoma.

Measures The gross morphologic extent of the tumor, characterized by the TNM (tumor, node, metastasis) classification system, is often cited as the single most important prognostic factor.[29] Apart from the T and N classification and Stage of Disease, the variable "prior radiotherapy" was entered at first measurement as a possible prognostic factor. In this study we did not assess histological factors such as surgical margins, status of cervical nodes, tumor depth and microvascular invasion which may provide independent prognostic information.[30] These variables exclusively concern surgically treated patients. Because the number of patients in the different treatment groups is small, only variables that were applicable to all three treatment groups were included.

Prognosis might also be dependent on sociodemographic data such as age, gender, marital status and educational level, and behavioral data, including tobacco and alcohol, so these variables were entered at first visit. Smoking behavior and use of alcohol was measured by the questions "how many cigarettes a day do you smoke" and "how many units of alcohol do you consume per day". When patients had quit smoking or drinking alcohol less than one year before, the last amounts used were rated. Results concerning smoking and alcohol intake were categorized as follows. No = none; not much = less than 20 cigarettes, less than 6 units of alcohol; much = more than 20 cigarettes, more than 6 units of alcohol.

With respect to psychosocial studies, it is important that the development of instruments used, fits a theoretical basis.[31] In a retrospective study, involving 118 head and neck cancer patients, published elsewhere [32], we used a theoretical model of coping with cancer.[33,34] This model is based on the assumption that uncertainty, negative feelings (eg, feelings of depression, loneliness and psychosocial complaints), loss of control, and threatened self-esteem are the four most important psychosocial problems experienced by cancer patients. Efforts of the patients themselves are directed at preventing or reducing these problems as much as possible. These efforts are called coping strategies. Also the environment of the patient (eg, his/her family, medical specialist) can help by offering information and support. In this process of coping with cancer, person-related factors, such as locus of control, and illness-related factors, such as relapse after prior radiotherapy, can possibly influence outcomes of treatment and rehabilitation. This theoretical framework has been applied succesfully in a study on the effects of coping with cancer in relation to social contacts between cancer patient.[34,35,36]

The questionnaire used in this study is based on the same concepts as used in the retrospective study.[32] In this retrospective study we used validated scales from a study of the Van den Borne and Pruyn[34] on psychosocial functioning of breast cancer patients and Hodgkin patients, ie, loss of control, openness to discussion of the illness in the family, the cancer locus of control scale and a self-esteem scale. Also, Ryckman's Physical Self-efficacy Scale, the physical and psychosocial complaints of the Rotterdam Symptom Checklist (RSCL) and a number of new scales, specific to head and neck cancer patients, were used. These new scales which were developed to be specific to their problems and their concerns are instruments designed to assess uncertainty (two subscales: about how to handle the practical consequences of the illness and uncertainty about how to cope with one's own emotions) and head and neck specific complaints, covering both physical and the psychosocial domains. Internal reliability of the new developed scales has been proven to be

Table 1 Review of psychosocial scales

Scale	Mean	S.D.	No. items	Min. score	Max. score	α1*	α2†	α3‡
Uncertainty how to handle practical consequences of the illness	31.564	8.461	11	11	44	.91	.93	–
Uncertainty how to cope with one's own emotions	18.229	6.261	7	7	28	.90	.93	–
General physical complaints	10.333	2.976	7	7	28	.71	.70	.76
General psychosocial complaints	14.718	5.224	8	8	32	.90	.88	.91
Head and neck specific complaints	30.180	6.505	21	21	84	.81	.89	–
Loss of control	10.603	2.311	8	8	16	.79	.76	.77
Physical Self-Efficacy	29.026	6.925	7	7	42	.75	.75	–
Cancer Locus of Control with respect to the course of the illness	20.834	3.907	7	7	28	.65	.66	–
Self-esteem with respect to social functioning	11.845	2.074	5	5	15	.53	.65	–
Openness to discussion of the illness in the family	25.514	4.996	8	8	32	.85	.71	.81
Multidimensional Health Locus of Control-Internal	20.265	6.702	6	6	36	.78	.76	.77§

* Cronbach's alpha in this study.[37]
† Cronbach's alpha in a previous study involving head and neck cancer patients.[32]
‡ Cronbach's alpha in a previous study involving breast cancer and Hodgkin patients.[34,35]
§ Cronbach's alpha in a previous study involving colo-rectal cancer patients.[46]

satisfactory.[32] For an overview of the psychosocial scales see Table 1.

Uncertainty The need for information was assessed by a list of questions assessing uncertainty with respect to speech, food intake, and physical appearance. The uncertainty scale has two sub-scales: (1) uncertainty about how to handle the practical consequences of the illness and (2) uncertainty about how to cope with one's emotions.[32] Sample items for the eleven-item "handling illness" scale are: "How to learn to talk better" and "How to dress better so that you minimize the chances that others will notice your handicap". For the seven-item "coping with emotion" scale sample items are: "How to learn to control yourself" and "How to do relaxation exercises" (eg, yoga, respiratory exercises). A four point scale, including (1) "not at all", (2) "a little", (3) "rather much", and (4) "very much" was used. Cronbach's α for these scales are .91 and .90 , respectively.[37]

General Physical/Psychosocial Complaints (RSCL) Negative feelings can refer to psychosocial/emotional status and physical well-being. These feelings can be expressed by complaints. To assess the patients' complaints, the

Rotterdam Symptom Checklist was used.[38,39] Patients reported the extent to which they were suffering from a variety of physical and psychosocial problems. We used the two basic scales: general psychosocial complaints and general physical complaints. Sample items of the 8-item psychosocial complaints scale are: "during the past three days I suffered from worrying" and "from feeling tense". Sample items of the 7-item physical complaints scale are: "during the past three days I suffered from dizziness" and "from shortness of breath". These items were measured on a four-point scale, ranging from (1) "not at all", (2) "a little", (3) "rather much", and (4) "very much". Cronbach's α for these scales are .90 and .71 , respectively.

Head and Neck Specific Complaints Psychosocial and physical complaints more specific to head and neck cancer patients were assessed by means of the 21-item head and neck specific complaints scale.[32] Sample items on this head and neck specific complaints list are: "during the last three days I suffered from hoarseness", "from coughing", from phlegm formation", "from feelings of shame during eating" and "from feelings of not being able to make oneself intelligible". These items were measured on a four-point scale, ranging from (1) "not at all", (2) "a little", (3) "rather much", and (4) "very much". Cronbach's α for these scale is .81.

Loss of Control An inability to act upon events, to deal with and to cope with events is referred to as loss of control because of one's illness. Loss of control involves two important domains of life, ie, physical and social activities and losing hold in psychological sense. In the Van den Borne and Pruyn's study[34], 8 items were formulated to measure the extent of loss of control in cancer patients. Sample items of this 8-item scale are: "since/by my illness and/or treatment I am not quite my usual (old) self again", "I am not or am only partly able to work or keep house", and "I became more dependent on others". Patients were asked to tick as whether or not appropriate. Cronbach's α for this scale is .79.

Physical Self Efficacy Patients' perceived physical abilities and confidence were assessed by the Physical Self Efficacy Scale. On basis of the reliability analysis of the Self Efficacy Scale of Ryckman[40] a number of items were removed from the original list of 22 items. In this study a 7-item Physical self efficacy scale is used. Sample items of this scale are: "I have physical defects that sometimes bother me", "I am sometimes embarrassed by my voice", and "I have poor muscle tone". These items were measured on a six-point scale, including (1) "I strongly agree", (2) "somewhat agree", (3) "slightly agree", (4) "slightly disagree", (5) "somewhat disagree", and (6) "I strongly disagree". Cronbach's α of this subscale is .75.

CLOC with respect to Course of Illness The cancer locus of control scale measures the extent to which patients perceive control with respect to their illness.[41,42] In this study the sub-scale internal locus of control with respect to the course of the illness was used. Sample items for the 7-item "course of illness scale" are: "I have a strong influence on the course of my illness" and "by fighting against my illness I can influence its course". Cronbach's α for this scale is .65.

Self-esteem with respect to Social Functioning As a consequence of the tumor and/or its treatment, the patients' self-image with respect to bodily appearance and functioning can be changed.[43] The self-esteem with respect to social functioning assesses patients' competence in social situations and is a sub -scale of the self-esteem scale based on the California Psychological Inventory [32,35]. Sample items for the five-item social functioning scale are: "Other people do not perceive me as attractive" and "I am pleasant to associate with". Patients were asked to score these statements as correct or incorrect. Cronbach's α for this scale is .53.

Openness to Discussion of the Illness in the Family Talking about one's cancer within the family can be a way which enables patients to cope with the disease. Openness of discussion can be considered as a component of social support. An instrument to assess the openness of discussion was developed and validated by our group.[32,34,44] Sample items of the eight-item scale are: "My partner doesn't like to talk about my problems", "My partner often doesn't know what to say or to do when I'm feeling down", and "Talking about emotions related to my illness upsets my family". These items were measured on a four-point scale, ranging from (1) "agree very much", (2) "agree", (3) "not agree", and (4) "not agree at all". Cronbach's α is .85.

Multidimensional Health Locus of Control - Internal The internal locus of control scale is a sub-scale of the Multidimensional Health Locus of Control scale developed by Wallston and Wallston to measure internal control with respect to health and illness.[32,45] Sample items of the 6-item scale are: "If I get sick, it is my own behavior which determinates how soon I get well again" and "I am in control of my health". These items were measured on a six-point scale, ranging from (1) "I strongly agree", (2) "somewhat agree", (3) "slightly agree", (4) "slightly disagree", (5) "somewhat disagree", and (6) "I strongly disagree". Conbrach's α is .78.

Statistics All prognostic variables were categorized and their association with overall survival and disease free survival was evaluated using Kaplan-Meier Curves and log rank tests.[47] Survival analysis using Cox proportional hazards regression was performed to evaluate the simultaneous effects of a selected set of variables.[48] Given the relatively small number of patients and high correlation between some of the prognostic variables it was necessary to reduce the number of possible prognostic variables for inclusion in the Cox regression. This selection was based on content (all four categories of psychosocial problems from our theoretical model needed to be included), on requirements for multivariate data analysis, particularly non-multicollinearity and non-singularity of prognostic variables, and on preliminary univariate statistical analysis using Kaplan Meier Curves and logrank tests.

For all variables included in the analysis the assumptions of proportional hazards and log linearity of effects were carefully checked using graphical methods and statistical tests based on residuals. There was no significant indication of non-proportionality and all "continuous" variables (test scores) could be fitted linearly. Missing values were coded with the median value when there were only a few patients with missing values. All analyses were done using the SAS Statistical Package.[49]

RESULTS

The main purpose of the present study is to increase the understanding of factors which explain survival and tumor relapse in head and neck cancer patients. In particular, the focus in this study has been on the possible relations of psychosocial variables to these outcome criteria, in addition to medical , sociodemographic, and behavioral factors.

A total of three medical variables, ie, prior radiotherapy, T-classification, and N-classification, three sociodemographic variables, ie, age, level of education, and marital status, two behavioral variables, ie, smoking and drinking at pretreatment, and eleven psychosocial prognostic variables were included in the initial analyses with the two outcome variables. As there were only 21 females in the study, gender was excluded from the list of potential study variables. Also, treatment group was not included because groups II and III were heterogeneous with respect to disease site and stage of disease.

These multiple group differences would make between any group differences on outcome variables uninformative. Kaplan-Meier Curves were used for preselection of variables and to highlight specific relations of prognostic variables with outcomes. The univariate analysis using Kaplan-Meier Curves and Logrank tests on the medical, demographic, and behavioral variables further showed that, marital status, level of education, and amount of alcohol use at pretreatment were not significantly related to any of the two outcome variables. Because of the many prognostic variables relative to the number of patients in the sample, these variables were also excluded from the subsequent multivariate analysis. Finally, a total of 16 variables were included in subsequent multivariate analyses using the Cox proportional hazards regression procedure.

The number of patients in the three treatment groups, sociodemographic data, smoking and drinking habits, primary site, TNM classification, stage of disease, data on earlier treatment, cause of death and survival/relapse figures are presented in Table 2.

In Table 3 the Pearson correlation coefficients for the psychosocial variables as well as the variable "prior radiotherapy" that were included in the Cox regression analysis are presented.

In the present analysis the majority of patients were male (84%) and married/living together (76%). Ages ranged from 30 to 85 yr. (mean = 63.6 yr., SD = 11.27).

The first endpoint studied was death with 57 patients dying during the observation period and 76 still alive at 6 years of follow up. From the 57 deceased patients 30 died of cancer. The mean age of the deceased was 67.1 versus 59.2 among survivors. There were no differences by gender, married status and educational level with respect to survival.

Results of the multivariate Cox regression model with respect to overall survival including 16 prognostic variables, are presented in Table 4. From the medical variables N classification (Risk Ratio 5.124, 95% Confidence Interval 2.161 - 12.147) and T classification (Risk Ratio 2.243, 95% Confidence Interval 1.161 - 4.960) were found to be significantly associated with overall survival.

Most significantly, patients with no neck metastases (N0) had a better survival prognosis than patients with N classifications of 1,2, or 3. Patients who had salvage surgery for a relapse following prior radiation therapy had no significantly worse survival rates than patients who had their primary treatment. Smoking at pretreatment was found to have a significant negative

Table 2 Sociodemographic and disease related characteristics

Treatment group	I T_I-larynx	II laryngectomy	III surgery oral cavity/oropharynx	total
Number of respondents	47	42	44	133
Gender (male/female)	42/5	40/2	30/14	112/21
Median age	64.4	62.3	61.0	62.6
Marital status (living together/ single)	38/9	33/9	30/14	101/32
Educational level (elementary school/ vocational school/high school-university)	20/21/6	25/17/3	18/20/6	60/58/15
Smoking (none/<20/≥20 cigarettes)	1/9/37	2/12/28	4/19/20	7/40/85
Alcohol (none/<6/≥6 units)	22/11/14	19/9/14	21/6/17	63/26/45
Primary Site				
Oral cavity	–	–	37	37
Oropharynx	–	–	7	7
Hypopharynx	–	6	–	6
Supraglottic	–	16	–	16
Glottic	47	20	–	67
T classification				
T1	47	13	5	64
T2	–	8	18	26
T3	–	15	12	27
T4	–	6	9	15
N classification				
N0	47	33	5	107
N1	–	5	18	18
N2	–	3	12	4
N3	–	1	9	4
Stage of disease				
I	47	12	5	64
II	–	6	11	17
III	–	15	16	31
IV	–	9	12	21
Prior radiotherapy	–	37	20	57
Tumor-free/relapse	36/11	27/15	28/16	91/42
Alive/death	34/13	22/20	20/24	76/57
Death by tumor/by other cause death	2/11	13/7	15/9	30/27

influence on survival duration (Risk Ratio 1.955, 95% Confidence Interval 1.022 - 3.740). Older age was found to have a highly significant negative prognostic value with respect to survival.

From the psychosocial factors, three variables were significant predictors for overall survival, ie, physical self-efficacy, uncertainty about handling practical consequences of the illness, and psychosocial complaints. Patients

Table 3 Correlations between psychosocial variables and “prior radiotherapy”#

Variable	A	B	C	D	E	F	G	H	I	J	K	L
A) Prior radiotherapy												
B) Physical Self-Efficacy	–.01											
C) Multidimensional Health Locus of Control-Internal	.02	.17										
D) Cancer Locus of Control with respect to the course of illness	.22**	.15	.21**									
E) Self-esteem with respect to social functioning	.22**	.15	.07	.06								
F) Openness to discussion of the illness in the family	.03	.17*	–.07	.08	–.13							
G) Uncertainty how to handle practical consequences of the illness	.40***	–.04	.03	.34***	–.09	–.04						
H) Uncertainty how to cope with own emotions	.31***	.01	.15	.33***	–.05	.01	.77***					
I) Loss of control	.19*	–.25***	–.10	.17	.03	–.14	.39***	.37***				
J) Physical complaints	–.01	–.40***	–.16	–.12	–.04	–.20**	.19*	.10	.40***			
K) Psychosocial complaints	.18*	–.15	–.01	.10	–.08	–.20**	.35***	.27***	.50***	.39***		
L) Head and neck specific complaints	.08	–.03	.01	.08	.06	–.01	.07	.05	.03	–.05	.05	

Pearson correlation coefficient, r.
Levels of 2-tailed significance: * (p ≤ .05), ** (p ≤ .025), *** (p ≤ .01).

Table 4 Summary of regression analysis of predictors of overall survival

Predictors	Bèta-coefficient	Standard error	P-value
Prior radiotherapy	−0.267	.375	.477
T 2,3,4 (versus 1)	0.814	.405	.046
N 1,2,3 (versus 0)	1.634	.440	.000
Age at pretreatment measurement	0.056	.016	.001
Smoking at pretreatment measurement	0.671	.331	.043
Physical Self-Efficacy	−0.048	.023	.040
Multidimensional Health Locus of Control-Internal	0.044	.025	.074
Cancer Locus of Control with respect to the course of illness	−0.031	.049	.531
Self-esteem with respect to social functioning	0.087	.083	.294
Openness to discussion of the illness in the family	0.032	.029	.266
Uncertainty how to handle practical consequences of the illness	0.107	.037	.040
Uncertainty how to cope with own emotions	−0.074	.043	.085
Loss of control	0.115	.078	.139
Physical complaints	0.072	.064	.262
Psychosocial complaints	−0.121	.040	.003
Head and neck specific complaints	−0.003	.023	.889

with a high level of perceived self-efficacy at pretreatment have a better chance for survival. Patients with a higher score on uncertainty on how to handle practical consequences of their illness (eg, I would like to know more about how to make yourself better understood and about how and where to get contact with patients or ex-patients) have worse survival than patients with a low score. Notably, patients with more psychosocial complaints (eg, during the past three days, I suffered from worrying, and from feeling tensed) were found to have significantly better survival. Overall survival curves for self-efficacy, uncertainty, and psychosocial complaints based on the Cox regression model adjusted for the mean values of the other co-variates are presented in figures 1, 2, and 3.

The second endpoint studied was tumor relapse. Ninety-one patients had no tumor relapse. The mean age of patients who relapsed was 63.8 versus 61.9 among patients who were disease free. Also, there were no significant differences by gender, married status and educational level. Results of the Cox regression analysis model including 16 prognostic variables in predicting relapse of the tumor as outcome, are presented in Table 5.

In terms of the medical variables, the N classification was found again to be significantly associated with relapse. Patients without neck metastases

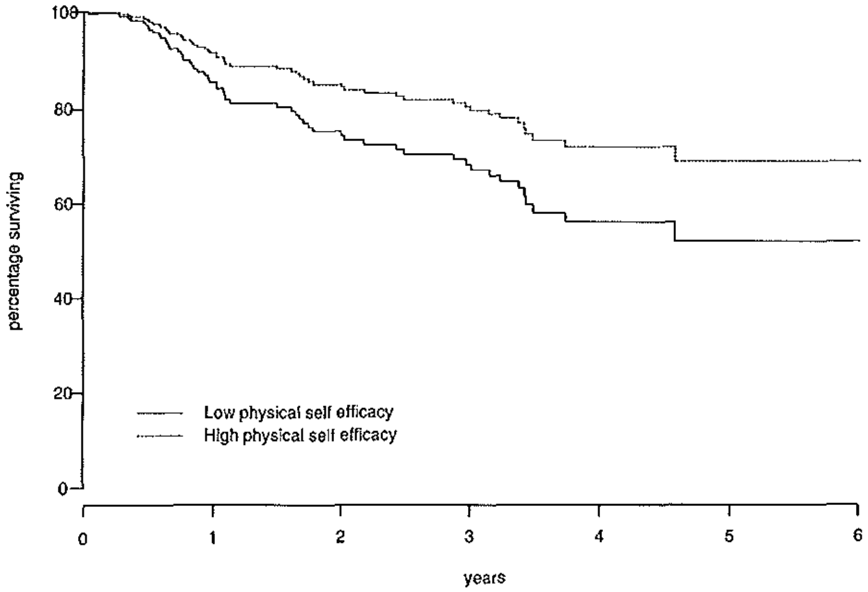

Figure 1 Overall survival curves according to perceived Physical Self-Efficacy based on the Cox regression model adjusted for the mean values of the other co-variates. Low physical self-efficacy score = 24 (25th. centile), high physical self-efficacy score = 34 (75th. centile).

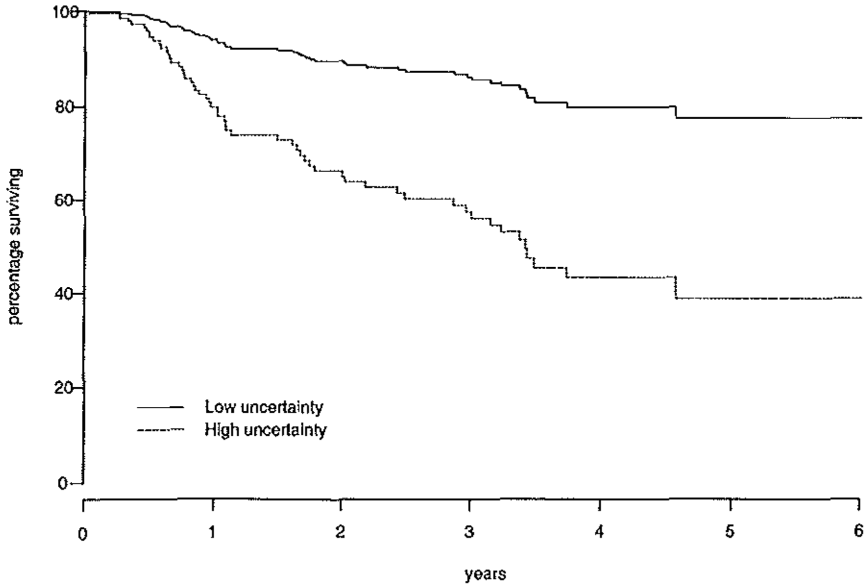

Figure 2 Overall survival curves according to perceived uncertainty how to handle the practical consequences of the illness based on the Cox regression model adjusted for the mean values of the other co-variates. Low uncertainty score = 26 (25th. centile), high uncertainty score = 38 (75th. centile).

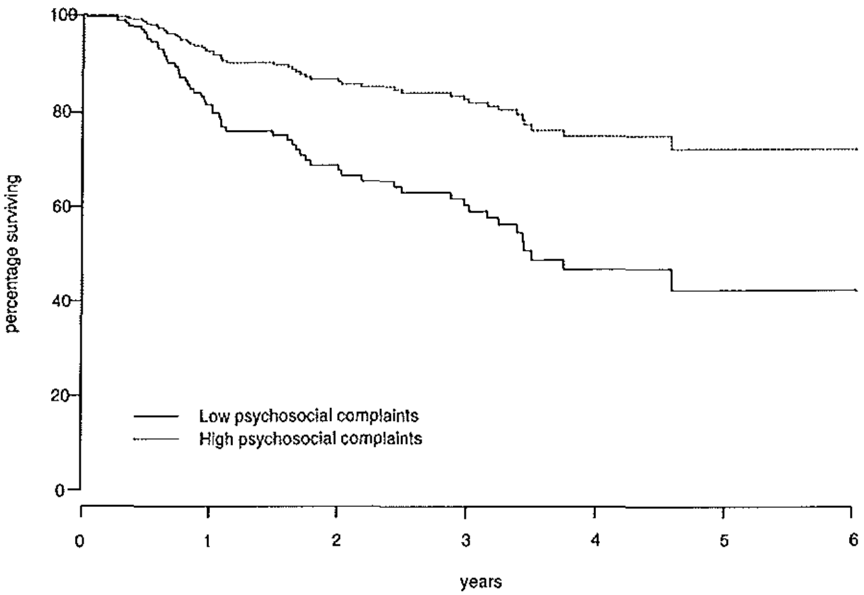

Figure 3 Overall survival according to expressed psychosocial complaints based on the Cox regression model adjusted for the mean values of the other co-variates. Low psychosocial complaints score = 11 (25th. centile), high psychosocial complaints = 18 (75th. centile).

(N0) had lower rate of relapse than N1-3 patients (Risk Ratio 4.455, 95% Confidence Interval 1.653 - 12.005).

Neither T classification nor "prior radiotherapy" were found to be predictive for this outcome. Neither age at pretreatment, nor smoking, were found to have prognostic value for relapse. From among the psychosocial factors only three variables were significant predictors for tumor relapse, ie, physical self-efficacy, psychosocial complaints, and loss of control. Patients with a high level of self-efficacy at pretreatment have a lower rate of relapse. Also, patients with more loss of control at pretreatment (eg, since/by my illness and/or treatment I am not quite my usual (old) self again, I am not or only partly able to work or to do the house-keeping, and I became more dependent on others), have a higher rate of relapse. Again, as with overall survival, patients with more psychosocial complaints were found to have significant lower rate of tumor relapse.

DISCUSSION

In the current investigation there are three variables that are related consistently to survival as well as to occurrence of relapse of disease: N classifica-

Table 5 Summary of regression analysis of predictors of disease relapse

Predictors	Bèta-coefficient	Standard error	P-value
Prior radiotherapy	0.058	.400	.885
T 2,3,4 (versus 1)	0.360	.464	.438
N 1,2,3 (versus 0)	1.494	.505	.003
Age at pretreatment measurement	0.006	.017	.730
Smoking at pretreatment measurement	−0.242	.402	.547
Physical Self-Efficacy	−0.064	.027	.018
Multidimensional Health Locus of Control-Internal	0.044	.026	.094
Cancer Locus of Control with respect to the course of illness	0.036	.055	.507
Self-esteem with respect to social functioning	0.108	.095	.253
Openness to discussion of the illness in the family	0.048	.035	.163
Uncertainty how to handle practical consequences of the illness	0.030	.038	.424
Uncertainty how to cope with own emotions	−0.016	.043	.711
Loss of control	0.190	.089	.034
Physical complaints	0.073	.066	.270
Psychosocial complaints	−0.112	.041	.007
Head and neck specific complaints	−0.009	.025	.720

tion, physical self-efficacy, and psychosocial complaints.

In regard to the medical data, we found, in agreement with previous results, that tumor dissemination to the neck is a bad prognostic sign for the length of survival following diagnosis and the chance of occurence of tumor relapse.[50-52]

With respect to psychosocial predictors, we found that patients who perceived themselves as more physically self-efficacious were more likely to survive and less likely to suffer a relapse. There are several possible explanations for these effects. In general, patients high in physical self-efficacy are more physically fit [38,53] and therefore probably better able to cope with the illness itself and its attendant stresses.[32] For example, chemotherapy, radiation therapy, and surgery all can produce serious side-effects, such as nausea and energy depletion [54], which high physical self-efficacy patients because of their greater strength and stamina should be better able to withstand. Also, physical self-efficacy refers, not only to the patients' judgments of their physical ability, strength, and fitness, but also importantly to their ability to generate and test alternative forms of behavior and strategies that could possible influence the course of the illness.[55] Judgments of self-efficacy also determine how much effort patients will expend and how long they will persist in the face of aversive experiences. The greater the self-efficacy of patients, the more vigorous and persistent are their efforts, possibly increasing their chances for survival.

In a recent literature review, Stepto has concluded that stresses do influence various types of illness and that these stresses can be mediated by specific dispositional resources of the individual, eg, by differences in the level of perceived hopefulness, control, and physical self-efficacy.[56] For example, Kaplan et al. have found that high physical self-efficacy patients are better able to cope with the stresses associated with their disease and to be more likely to survive 5 years after the diagnosis of their illness than were patients low in self-efficacy.[57] Moreover, patients can generate fear-related thoughts themselves that create new stresses that go beyond those that are ordinarily associated with the disease. Thus, patients low in physical self-efficacy who judge themselves incapable of coping with serious illness may dwell on their personal deficiences and think about potential difficulties in their treatment regimens as being more formidable than they actually are.[58] Conversely, patients high in self-efficacy should experience fewer fear-related thoughts which, in turn, should result in less stress. Support for this argument is found in prior research by De Boer et al.[32] which showed that highly efficacious patients reported fewer fears with respect to treatment and the consequences of the disease. Also, consistent with the finding of De Boer et al., Jerusalem and Schwarzer [59] found that high self-efficacy individuals were less prone to fears, anxieties and worries when confronted with highly aversive experiences. The ability to cope with such painful experiences may increase chances for patients' survival and make relapse less likely.

Given the positive correlation between perceived physical self-efficacy and actual strength and fitness, there is clearly a need for well-designed clinical trials in which the variables which underly physical self-efficacy are systematically varied to assess more precisely their differential impact on survival and freedom from relapse. These variables include the level of actual strength and fitness of the patients, their tendencies to generate adaptive strategies to cope with the stresses inherent in the disease, and their ability to generate constructive or destructive thoughts. Research using linear structural equation modeling needs to be conducted to examine the indirect pathways which mediate between self-efficacy and prognosis.[60] Assuming that these studies yield generally positive results, one tentative recommendation would involve the need to encourage especially those patients low in self-efficacy to physically exercise regularly to improve their strength and stamina. In terms of head and neck cancer patients, speech therapists may encourage their patients to do relaxation exercises to improve the link between breathing and speech abilities. Physiotherapists could help their patients, especially those who have undergone neck dissections, to do arm raising exercises to improve their mobility. Also, care givers could implement swimming activities for groups of laryngectomies to help them overcome their fear of being in the water in relation to their stoma. Also, by performing these activities in a group, they have the additional benefit of social support from other companions in distress. These benefits include a reduction in negative feelings, uncertainty, and loss of control, and to an increase in self-esteem.[35]

A third major finding in the current investigation involved the intensity of psychosocial complaints acknowledged by the patients before the start of treatment. Those patients who expressed a higher intensity of negative feelings in regard to their illness, ie, had recently felt high levels of anger, irritability, tension, and anxiety were more likely to survive and less likely to suffer a relapse than were those who were unable to express such feelings. These findings are consistent with a growing body of research knowledge which shows that a lack of awareness and an inability to express negative emotions is related to the progression of cancer. [61-68] The lack of awareness and inability to express negative feelings has been discussed in terms of a repressive personality style called Type C.[69] Repressive defensiveness may be associated with inattention to signals of distress which, according to deregulation theory, could have adverse effects on the body and could also lead to a failure to adopt more active coping responses, which could result in lessened chances for survival.[70] Patients who do not express psychosocial complaints may also be less likely to seek out or be referred for available support services. This may also have adverse effect on healing and survival.

The view that an expression of negative emotions increases the time of survival is not completely accepted by other researchers and reviewers. They insist that the actual contribution of psychosocial factors like emotional expressivity to cancer is very small.[71,72] In a more recent review of the literature, Gross concludes that there is some support for the view that emotional expression may be directly implicated in cancer progression, but argues that, in order to increase the likelihood of replication, variables important to the progress of the disease must be taken into account in measurement and analysis.[73] In the current investigation we were able to control for many of these variables, such as TNM classification, age, and smoking, in the multivariate analysis and found a significant effect for emotional expressivity. However, we did not control for other possible relevant factors, like histological grading, loss of weight, and daily activities, so that our conclusion that expressions of negative emotions increase the chances of survival still needs to be confirmed by future experimental research.

Finally, smoking status and continued tobacco use have been shown generally to result in poorer disease outcomes in head and neck cancer patients.[74,75] The results of the present investigation also indicate a negative correlation of pretreatment smoking and overall survival thus suggesting a need for increased efforts to address smoking status of newly diagnosed head and neck cancer patients. Physicians should intervene early and decisively in their patients' smoking behavior. Patients less able to quit might benefit from a psychosocial intervention program, including pharmacological adjunctive treatment.[76-78]

In conclusion, the results of this study add to an increasing body of knowledge which shows that certain psychosocial factors are related to relapse and survival in cancer patients. In this study the measurement of psychosocial factors was restricted to pretreatment, but patient outlook and psychosocial measures may vary markedly with time depending on treatment morbidity and this would potentially have an influence on disease control. As already has been stated only measures applicable across all three groups were included, thus eliminating histological factors and surgical margins. Also we indicated that variables were included in the Cox regression based on content, but also completeness of response. Therefore, results must be interpreted cautiously in light of these limitations.

Unfortunately, this study is the only one that has focused explicitly on head and neck cancer so that it is clear that more research of this particular type of cancer should be conducted. Given the small number of patients who suffer from this type of cancer, more 'multi-center' approaches are needed. For future research, we also recommend longitudinal studies in which change processes in psychosocial variables, including those from our own investigation, are studied over time (eg, processes from right before treatment through the first year after diagnosis) as predictors of long-term survival and freedom from relapse. Concurrently, more basic research is needed in which biobehavioral mechanisms that influence the course of the disease are examined, eg, through multivariate modeling using structural equation analyses.[60]

REFERENCES

1 Coebergh JWW, Van der Heijden LH, Janssen-Heijnen MLG, editors. Cancer incidence and survival in the Southeast of the Netherlands 1955-1994. Eindhoven: Comprehensive Cancer Center South, the Netherlands: 1995:p.101.

2 Muir c, Weiland l. Upper aerodigestive tract cancers. *Cancer* 1995; 75: 147-53.

3 De Boer MF, McCormick LK, Pruyn JFA, Ryckman RM, Van den Borne HW. Physical and psychosocial correlates of head and neck cancer: a review of the literature. *Otolaryngol Head Neck Surg* in press.

4 Dibb CR, Urba S, Wolf GT. Organ preservation in advanced head and neck cancer. *Cancer Treat Res* 1995;74:199-219.

5 Trijsburg RW, Knippenberg FCE, Rijpma SE. Effects of psychological treatment on cancer patients: a critical review. *Psychosom Med* 1992;54:489-517.

6 Anderson BL. Psychological Interventions for cancer patients to enhance the quality of life. *J Consult Clin Psychol* 1992;60:552-68.

7 Spiegel D. Psychosocial intervention in cancer. *J Nat Cancer Inst* 1993; 85:1189-1205.

8 Van Wersch A, De Boer MF, Van der Does E, De Jong P, Knegt P, Meeuwis CA, et al. Continuity of information in cancer care: evaluation of a logbook. *Patient Education Counseling* 1997;31:223-36.

9 Sherman AC, Simonton-Atchley S. Psychological aspects of treating oncology patients. In: Meyers EN, Suen JY. *Cancer of the Head and Neck, Third Edition* Philadelphia: WB Saunders, Co., 1996:917-25.

10 Classen C, Hermanson KS, Spiegel D. Psychotherapy, stress, and survial in breast cancer. In: Lewis CE, O'Sullivan c, Barraclough J. *The psycho immunology of cancer: mind and body in the fight for survival* Oxford Medical Publications, 1994:123-62.

11 Richardson JL, Landrine H, Marks G. Does psychological status influence cancer patient survival? A case still in need of evidence. In: Lewis CE, O'Sullivan c, Barraclough J. *The psycho immunology of cancer: mind and body in the fight for survival* Oxford Medical Publications, 1994:228-45.

12 Bauer SM. Psychoneuroimmunology and cancer: an integrated review. *J Adv Nurs* 1994;19: 1114-20.

13 Carlsson M, Harim E. Psychological and psychosocial aspects of breast cancer; a literature review. *Cancer Nurs* 1994;17(5):418-28.

14 Hilakivi-Clarke L, Rowland J, Clarke R, Lippman ME. Psychosocial factors in development and progression of breast cancer. *Breast Cancer Res Treatment* 1993;29:141-60.

15 Spiegel D. Effects of psychosocial support on patients with metastatic breast

cancer. *J Psychosoc Oncol* 1992;10(2):113-20.

16 Royak-Schaler R. Psychological Processes in breast cancer: a review of selected research. *J Psychosoc Oncol* 1991; 9(4):71-89.

17 Levy SM. Psychosocial risk factors and cancer progression. In: Cooper CL. *Stress and breast cancer.* New York: John Wiley & Sons, 1988:77-96.

18 Watson M. Breast cancer: psychological factors influencing progression. In: Cooper CL. *Stress and breast cancer.* New York: John Wiley & Sons, 1988: 65-75.

19 Osoba D. Lessons learned from measuring health related quality of life in oncology. *J Clin Oncol* 1994; 12(3): 608-16.

20 Hürny C, Bernhard J. Coping and survival in patients with primary breast cancer: a critical analysis of current research strategies and proposal of a new approach integrating biomedical, psychological, and social variables. In: Herfarth Ch, Senn HJ. *Recent Results in Cancer Research Volume 115.* Berlin Heidelberg: Springer-Verlag, 1989:255-71.

21 Blanchard CG, Albrecht TL, Ruckdeschel JC, Grant CH, Hemmick RM. The role of social support in adaptation to survival. *J Psychosoc Oncol* 1995; 13(1/2):75-95.

22 Van der Pompe G. Antoni MH, Mulder CL, Heijnen C, Goodkin K, De Graef A. Psychoneuroimmunology and the course of breast cancer: an overview. *Psycho-Oncology* 1994; 3:271-88.

23 Turns DM. Psychosocial factors. In: Donegan WL, Spratt JS. *Cancer of the breast.* Philadelphia London: Saunders Company, 1995:778-86.

24 Mulder CL, Van der Pompe G, Spiegel D, Antoni MH, De Vries MJ. Do psychosocial factors influence the course of breast cancer? *Psycho-Oncology* 1992;1:155-67.

25 Stam, HJ, Steggles, S. Predicting the onset or progression of cancer from psychological characteristics: psychometric and theoretical issues. *J Psychosoc Oncol* 1987; 5(2):35-46.

26 Fawzy FI, Fawzy NW, Hyun CS, Elashoff R, Gurthrie D, Fahey JL, et al. Malignant Melanoma - Effects of an early structured psychiatric intervention, coping, and affective state on recurrence and survival 6 years later. *Arch Gen Psychiatric* 1993; 50:681-9.

27 Simonton-Atchley S. The influence of psychological therapy on the immune system in patients with advanced cancer. *Dissertation Abstracts* 1994;Intl 55-05-B:1-86.

28 TNM Classification of Malignant Tumors (Third edition). UICC International Union Against Cancer, Geneva, 1987.

29 Deleyiannis FWB, Weymuller EA. Outcomes research in head and neck

oncology. *Curr Opin Otolaryngol Head Neck Surg* 1996:4:73-7.

30 Weymuller EA, Ahmad K, Casiano RR, Schuller D, Scott CB, Laramore G, et al. Surgical reporting instrument designed to improve outcome data in head and neck cancer trials. *Ann Otol Rhinol Laryngol* 1994;103:499-509.

31 Padilla, GV, Grant, MM, Martin, L. Rehabilitation and quality of life measurement issues. *Head Neck Surg* 1988;10:S156-S160.

32 De Boer MF, Pruyn JFA, Borne B vd, Knegt PP, Rijckman RM, Verwoerd CDA. Rehabilitation outcomes of long-term survivors treated for head and neck cancer. *Head Neck* 1995;17:503-15.

33 Pruyn JFA Coping with stress in cancer patients. *Patient Education Counseling* 1983;5,2:57-62.

34 Borne HW van den, Pruyn JFA. *Contacts between fellow cancer patients [Lotgenotencontact bij kankerpatiënten]*. Thesis, Van Gorcum, Assen/Maastricht, 1985.

35 Van den Borne HW, Pruyn JFA, Van den Heuvel WJA. Effects of contacts between cancer patients on their psychosocial problems. *Patient Education Counseling.* 1987;9:33-51.

36 Pruyn, JFA, Van den Borne HW, Stringer P. Theories, methods and some results on coping with cancer and contact with fellow-sufferes. In: Watson M, Greer S. *Psychosocial Issues in Malignant Disease.* Oxford: Pergamon Press, 1986:41-52.

37 Cronbach LJ. Coefficient alpha and the internal structure of tests. *Psychometrika* 1951;16:297-339.

38 de Haes JCJM, Pruyn JFA, van Knippenberg F. Klachtenlijst voor kankerpatiënten. Eerste ervaringen. (Item list for complaints in cancer patients. First experience) *Nedl Tijdschr Psychol* 1983;38:403-22.

39 de Haes JCJM, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *Br J Cancer* 1990;62:1034-8.

40 Ryckman RM, Robbins MA, Thornton B, Cantrell P. Development and validation of a Physical Self-Efficacy Scale. *J Pers Soc Psychol* 1982;42:891-900.

41 Pruyn JFA, Borne HW van den, Reuver RSM de, De Boer MF, Bosman LJ, Pelkwijk MA ter, et al. The Locus of Control Scale for Cancer Patients. [De Locus of Control-schaal voor Kankerpatiënten.] *Tijdschrift voor Sociale Gezondheidszorg* 1988;66:404-8.

42 Watson M, Greer S, Pruyn JFA, Borne HW van den. Locus of control and adjustment to cancer. *Psychosoc Reports* 1990;66:39-48.

43 Gamba A, Romano M, Grosso IM, Tamburini M, Cantú G, Molinari R, et al.

Psychosocial adjustment of patients surgically treated for head and neck cancer. *Head Neck* 1992;14:218-23.

44 Mesters I, Van den Borne H, McCormick L, Pruyn J, De Boer M, Imbos T. Openness to discuss cancer in the nuclear family scale, development and validation. *Psychosom Med* 1997;59:269-79.

45 Wallston KA Wallston BS. Development of the Multidimensional Health Locus of Control Scales (MHLC). *Health Educ Monogr* 1978;6:160-70.

46 Pruyn JFA, Van den Heuvel WJA. Anxiety, control and information-seeking behavior in screening for cancer. In CD Spielberger, IG Sarason, PB Defares. *Stress and Anxiety.* Whashington, DC: Hemisphere Publishing Corporation, 1988;14:183-95.

47 Kaplan EL, Meier P. Non parametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457-81.

48 Cox DR. Regression models and life tables. *J R Stat Soc* 1972; B34:269-79.

49 SAS Institute Inc. SA Technical Report P-217. *SAS/STAT Software: The PHREG Procedure, Version 6.* Cary, NC: SAS Institute Inc; 1991.

50 Hall SF, Groome PA, Dixon PE. Does N stage predict survival? *J Otolaryngol* 1996;25:296-9.

51 Wolfensberger M. Using Cox's proportional hazards model for the prognostication in carcinoma of the upper aero-digestive tract. *Acta otolaryngol (Stokh)* 1992;112:376-82.

52 Platz H, Fries R, Hudec M, Tjoa AM, Wagner RR. The prognostic relevance of various factors at the time of first admission of the patient. *J Maxillofac Surg* 1983;11:3-12.

53 Thornton B, Ryckman RM, Robbins MA, Donolli J. Relationship between perceived physical ability and indices of actual physical fitness. *J Sport Psychol* 1987;9:295-300.

54 Morrow GR. Behavioural factors influencing the development and expression of chemotherapy induced side effects. *Br J Cancer* 1992;66:54-61.

55 Bandura A. *Social foundations of thought and action.* New York: Englewood Cliffs, Prentice-Hall, 1985:p.390.

56 Steptoe A. The links between stress and illness. *J Psychosom Res*, 1991;35:633-44.

57 Kaplan RM, Ries AL, Prewitt LM, Eakin E. Self- efficacy expectations predict survival for patients with chronic obstructive pulmonary disease. *Health Psychol* 1994;13:366-8.

58 Bandura A. *Social foundations of thought and action.* New York: Englewood Cliffs, Prentice-Hall, 1985:p.394.

59 Jerusalem M, Schwarzer R. Self-efficacy as a resource factor in stress appraisal

processes. In: Schwarzer R. *Self-efficacy: Thought control of action* Washington, D.C.: Hemisphere Publishing, 1992:195-213.

60 Pedhazur EJ. *Multiple regression in behavioral research* (2^{nd} ed.) New York: Holt, Rinehart and Winston, 1982:636-43.

61 Cox T, Mackay C. Psychosocial factors and psychophysiological mechanisms in the aetiology and development of cancers. *Soc Sci Med* 1982;16:381-96.

62 Derogatis LR, Abeloff MD, Melisaratos N. Psychological coping mechanisms and survival time in metastatic breast cancer. *J Am Med Assoc* 1979;242:1504-8.

63 DiClemente RJ, Temoshok L. Psychological adjustment to having cutaneous malignant melanoma as a predictor of follow-up clinical status. *Psychosom Med* 1985;47:81.

64 Greer S, Watson M. Towards a psychobiological model of cancer: psychological considerations. *Soc Sci Med* 1985;20:773-7.

65 Pettingale K, Watson M, Greer S. The validity of emotional control as a trait in breast cancer patients. *J Psychosoc Oncol* 1984;2:21-30.

66 Rodin J, Salovey P. Health psychology. *Ann Rev Psychol* 1989;40: 553-79.

67 Temoshok L. Biopsychosocial studies on cutaneous malignant melanoma: psychosocial factors associated with prognostic indicators, progression, psychophysiology, and tumor-host response. *Soc Sci Med* 1985; 20:833-40.

68 Temoshok L. Personality, coping style, emotion, and cancer: toward an integrative models. *Cancer Surv* 1987;6:545-67.

69 Temoshok L, Heller B. On comparison between apples and oranges and fruit salad: a methodological overview of medical outcome in psychosocial oncology. In Cooper CL. *Psychosocial Stress and Cancer.* London: Wiley, 1984:231-60

70 Jensen MR. Psychobiological factors predicting the course of breast cancer. *J Pers* 1987;55:317-42.

71 Fox BH. A psychological measure as a predictor of cancer. In: Cohen J, Cullen JW, Martin LR. *Psychosocial aspects of cancer,* New York: Raven Press, 1982:275-95.

72 Kiecolt-Glaser J, Glaser R. Psychological influences on immunity. *Psychosomatics* 1980;27:621-4.

73 Gross J. Emotional expression in cancer onset and progression. *Soc Sci Med* 1989;28:1239-48.

74 Stevens MH, Gardner JW, Parkin JL, Johnson LP. Head and neck cancer survival and life-style change. *Arch Otolaryngol* 1983;109:746-9.

75 Browman GP, Wong G, Hodson I, Sathya J, Russell, McAlpine L, et al. Influence of cigarette smoking on the efficacy of radiation therapy in head and

neck cancer. *N Engl J* 1993;328:159-63.

76 Gritz ER, Carr Cr, Rapkin DA, Chang C, Beumer J, Ward PH. A smoking cessation intervention for head and neck cancer patients: trial design, patients accrual, and characteristics. *Cancer Epidem Biomarkers Prev* 1991;1:67-73.

77 Gritz ER, Carr Cr, Rapkin DA, Abemayor E, Li-Jui C, Chang C, Wong WK, Belin TR, Calcaterra T, Robbins KT, Chonkick G, Beumer J, Ward PH. Predictors of longterm smoking cessation in head and neck cancer patients. *Cancer Epidem Biomarkers Prev* 1993;2:261-70.

78 Vander Ark W, Dinardo LJ, Oliver DS. Factors affecting smoking cessation in patients with head and neck cancer. *Laryngoscope* 1997;107:888-92.

Chapter 7

SUMMARY AND RECOMMENDATIONS

The purpose of this study can be summarized as follows:

A. To describe the process and outcomes of rehabilitation in long-term head and neck cancer survivors (chapter 2,3),

B. To identify predictors of rehabilitation outcomes (chapter 2,3),

C. To identify medical, psychosocial,behavioral and sociodemographic predictors of tumor relapse and time of survival of head and neck cancer patients (chapter 4,5,6), and

D. To formulate recommendations and to identify topics for future research and improvement of care.

The preceeding chapters present a review of relevant literature and a descriptive and a prospective study on samples of head and neck cancer patients.

A. REHABILITATION OUTCOMES IN LONG-TERM SURVIVORS

Literature: 1984-1996 A review of 50 studies, concerning physical and psychosocial correlates of head and neck cancer is described in chapter 2. It is evident that head and neck cancer has a severe impact on rehabilitation and quality of life outcomes of the patients. Prominent physical complaints concerned speech problems, dry mouth and throat, swallowing problems, and pain. Disturbances in psychosocial functioning and psychological distress were reported in various studies by a considerable number of patients, worry, anxiety, mood disorder, fatigue and depression being the main symptoms. These psychological disorders might be responsible for the higher suicide rate in head and neck cancer patients than in other cancer patients. Damage to body image/self-esteem was reported as a result of the disease and/or disfiguring treatment. With respect to addictive behaviors, the review reveals a decline in use of tobacco following treatment. In general, head and neck cancer appeared to have a negative effect on social, recreational and sexual functioning.

In order to verify the above findings of the literature we conducted a descriptive study on the rehabilitation outcomes of head and neck cancer patients from the Southwest of the Netherlands. In such a study we had to improve several shortcomings that came to the fore from the review study.

A theoretical model on coping with cancer should be the basis of the choice of factors to be studied. This is fundamental for a framework in which the most important problems and coping mechanisms of cancer patients fit. It is also necessary for defining concepts and making these measurable. For instance, in defining multidimensional domains the term "quality of life" becomes less vague. Following this procedure it is possible to come to a reduction of the innumerable variables used in literature.

Patients with a T1 vocal cord carcinoma were not included in the reviewed studies. Although patients of this treatment group have a favorable prognosis and are expected to suffer little physical (and psychosocial) problems, these patients are confronted with the problem of having cancer and the impending possiblity of a relapse. By including this patient group in our study comparison between several treatment groups differing in their expected impact on quality of life was made possible.

From the review it can be concluded that still little is known about the rehabilitation outcomes of long-term survivors. Such an insight is indispensable because change processes in psychosocial problems in cancer patients over time are conceivable in terms of both diminishing and deteriorating of problems.

Results of the Descriptive Study in Rotterdam In chapter 3 rehabilitation outcomes are described of 110 patients treated for head and neck cancer between 2 and 6 years previously. The patient groups in this study were (1) T1 glottic cancer patients treated with irradiation, (2) laryngectomy patients, and (3) those who had surgery for cancer in the oral cavity and/or oropharynx (all commando procedures).

It was demonstrated that T1 larynx patients treated with radiation therapy experienced a considerable number of physical complaints, such as sore muscles, fatigue, phlegm, frequent colds, as well as hoarseness, coughing and choking, even after several years had elapsed since treatment.

Laryngectomy patients and commando procedure patients experienced severe psychosocial distress. The problems of the laryngectomy patients were often related to abnormal speech. Commando procedure patients in particular had food intake problems and felt hindered by their disfigurement and the physical and social consequences. More than half of both the laryngectomy and commando procedure group felt that their appearance was damaged by the treatment. Especially laryngectomy patients were feeling uncertain with regard to the possibility of getting help in handling problems and/or questions concerning the illness and its treatment, and were feeling uncertain with regard to handling their own emotions. They also suffered from low self-esteem with regard to social functioning.

In making a comparison between the results of our study and the most prominent findings of the literature there are many similarities, such as many patients experience psychosocial complaints, have speech, food intake and disfigurement problems, and experience a damaged in body image and a threatened self-esteem.

It is notable that we found many head and neck cancer patients still being troubled after years by feelings of uncertainty. Therefore we feel that the concept uncertainty should be included in future quality of life studies.

The many physical complaints experienced by the T1 larynx carcinoma patients in our research justifies the attention to this treatment group in future quality of life studies.

It is vital to study quality of life in future studies over a longer period after treatment because the results of our research showed that even after several years of treatment patients still experience severe physical and psychosocial problems.

B PREDICTORS OF REHABILITATION OUTCOMES

Literature: 1984-1996 The quantity and quality of physical problems of the patients are related to the extent of surgery and the target site of irradiation. Patients exclusively treated with radiotherapy seemed to be better off with respect to quality of life impairment. The combination of treatment modalities – surgery, radiotherapy, chemotherapy – increased the severity of their physical and psychosocial symptoms.

Factors that clearly have a positive influence on the rehabilitation results are adequate patient information and social support.

Finally, it may be added that many studies use only descriptive or correlational analyses.

The goal of our descriptive study was to verify the above mentioned findings from the literature. In constrast with many other studies we applied a multivariate model of analysis.

Results of the Descriptive Study in Rotterdam In chapter 3 some correlations between rehabilitation process and outcomes are described of the 110 patients treated for head and neck cancer between 2 and 6 years previously. Results indicate that undergoing a laryngectomy is related with reporting decreased perceived abilities with respect to food intake, psychosocial complaints (specific to the head and neck tumor) and uncertainty. We did not observe so in the commando and T1 larynx group. With respect to the changes over time it was found that the more time elapsed since treatment the fewer head and neck specific complaints were experienced. The possibility of discussing illness related matters in the family, getting social support from the specialist and adequate information from the specialist were found the most important predictors of positive rehabilitation outcomes. Patients with a high internal locus of control with respect to the course of the disease, ie, the perception that the course of the disease may be attributed to personal elements, indicate a better rehabilitation, eg, experience less anxiety and have better speech abilities than patients with low internal locus of control.

As expected from our findings in the literature concerning the intensity of medical treatment modalities proportionating to the decline in quality of life, our study demonstrates that in case of laryngectomy patients the treatment is a negative predictor of rehabilitation outcomes. A second similar finding is the relationship between social support and positive rehabilitation outcomes.

The positive effect on rehabilitation of the patients' perception that the course of the illness can be influenced by personal efforts (internal locus of control), seems to be an important finding, not in the least for the patients themselves; more research is therefore needed to confirm this relationship.

C PREDICTORS OF SURVIVAL

Literature of Medical Prognostic Factors: 1990-1995 Traditionally, in treating head and neck cancer patients, the focus has been on tumor free survival and medical prognostic factors. In order to get insight into the recent developments with respect to medical prognostic factors of survival and tumor relapse, a review study was performed in which 55 studies were included (chapter 4). For this purpose a model for scoring the significance of potential prognostic factors was introduced. The formula of the "significance score" applied in this model is based on the number of patients in studies in which the correlation between the factor and prognosis reached statistical significance, and on the total number of patients included in studies in which the factor has been evaluated, as measures of reliability. The significance score was calculated in factors included in studies using a multivariate analysis model, ie, in 39 studies (70%). This percentage means an improvement in comparison with the preceding two decades in which the majority of studies had a non-multifactorial analysis design.[2]

Significance score (ss) in >3000 patients

Factor	Overall Survival (OS)	Occurrence of relapse
T classification	.22	.39
N classification	.83	.22
Site	.47	.55
Histological diff. grade	.24	.44
Age	.42	0
Sex	0	0

It appeared that in 55 reviewed studies all together 97 factors were studied in relation to prognosis. Only 6 factors were evaluated by means of multivariate analysis in a population of more than 3000 patients (see table below). Of these 6 factors, only one, the N classification, has reached a high significance score (.83) with respect to overall survival. The special influence of the T classification on survival appeared to be relatively low, and was found to be inconsistent concerning relapse, which might have to do with difficulty of exact clinical assessment of local tumor extent, eg, in laryngeal carcinomas. The results for tumor site were inconsistent, with a significance score of approximately .50 for both suvival and relapse, reflecting the conclusions of earlier reports/reviewers. Patients' sex was not reported as a predictor of prognosis.

For stage of disease (composed of categories of TNM classification) the calculated significance score in 2800 patients was .57 in survival, and .74 in tumor relapse. The figure concerning survival was less than expected given the results found regarding the N classification. Although the treatment related histological tumor factors, positive tumor margins and extra nodal spread showed correlations with prognosis in only small patient samples in our material, one might conclude, from reports beyond the scope of our review, that these factors may provide prognostic information.

It can be concluded that large scale studies need to be conducted to estimate the predictive value of most of claimed 'medical' prognostic factors mentioned in the literature, such as (radio-) therapy related factors, histological and biological tumor factors. Given the relatively rare incidence of head and neck malignancies, multi center studies are mandatory.

The course of malignant disease is probably not merely influenced by medical factors but by a complex of interacting medical, sociodemographic and psychosocial factors.

Correlations between OS/RFP and frequently studied psychosocial factors in 33 studies

factor	number of studies	positive correlation with OS/RFP	no correlation with OS/RFP	negative correlation with OS/RFP
depression	10	2	8	–
state-anxiety	6	2	4	–
hopelessness/helplessness	7	–	2	5
hostility	7	1	6	–
marital status	8	2	2	4
social involvement/ social support	15	7	8	–

Literature of Psychosocial Prognostic Factors: 1979-1995 The possible role of psychological, social and behavior influences in cancer risk and survival has intrigued researchers for centuries.[1] In the last three decades there has been an enormous increase in the field of psychosocial prognostic research. However, no studies analyzing the relation between psychosocial factors and survival or relapse in head and neck cancer patients were found. Therefore, the study of the literature was extended to all cancer sites. In reviewing 33 studies (chapter 5), we choose to present the "state of affairs" concerning psychosocial prognostic factors rather that to give an estimation of their prognostic value by means of patient population, study design, and statistical model.

Factors most frequently evaluated with respect to their association with overall survival (OS) and/or relapse free period (RFP) were depression, anxiety, hopelessness/ helplessness, hostility, marital status and social involvement (see table below). Results with respect to the relationship with prognosis were inconsistent, with the exception of social support. In 7 of 15 studies a *positive* relationship between psychosocial variables and OS/RFP was found for social involvement/social support, whereas no *negative* relationship was reported.

We also found inconclusive results with respect to less frequently studied variables, eg, mood, pain, functional status/every-day activities, severe/stressful life events, psychotism, day dreaming, experience of joy, locus of control, trait anxiety, and coping mechanisms, such as fighting spirit and stoic acceptance.

A number of factors were described as related with OS/RFP in only one study, eg, social class, and the "container concepts", quality of life, physical and psychological well being, and several stress variables.

Finally, multidimensional health locus of control, neurotism and somatisation showed no correlation with the outcome variables in two studies.

Results of the Prospective Study in Rotterdam The mainly inconclusive results in the literature with respect to both medical prognostic factors in head and neck cancer and psychosocial prognostic factors in all cancer patients, and the absence of such studies in head and neck cancer patients were the motive for the prospective research on prognostic factors. In this study of 133 head and neck cancer patients the medical, psychosocial, behavioral and demographic factors, as they related to survival and relapse of disease, were explored. Pretreatment scores on these factors were analyzed in their relation to overall survival and an occurrence of relapse, measured at 6-years of follow-up. Analogous to the descriptive study, the patient groups in the prospective study were (1) T1 glottic cancer patients treated with irradiation, (2) laryngectomy patients, and (3) those who had surgery for cancer in the oral cavity and/or oropharynx.

Overall Survival. Results of the Cox regression analyses, described in chapter 6, showed that from the medical variables N classification and T classification were found to be significantly ($p<.05$) associated with overall survival. Most significantly, patients with no neck metastases (N0) had a better survival prognosis than patients with N-classifications of 1, 2, or 3. Smoking at pretreatment and older age were also found to have a significant negative prognostic value. Radiotherapy given prior to the first measurement was not predictive of survival.

From the psychosocial factors three variables were significant predictors for overall survival, ie, physical self-efficacy, uncertainty about handling practical consequences of the illness, and psychosocial complaints. Patients with a high level of self-efficacy at pretreatment have a higher chance for survival. Patients with a higher score on uncertainty on how to handle practical consequences of their illness have lower chances for survival. Notably, patients with more psychosocial complaints were found to have significantly higher chances for survival.

Tumor Relapse. Patients without neck metastases (N0) had a lower chance of relapse of tumor than patients with N-classifications of 1, 2, or 3. T-classification was not found to be predictive for this outcome. Neither age at pretreatment, nor smoking, could be demonstrated to have prognostic value for relapse. Radiotherapy given prior to the first measurement was not predictive of relapse.

From the psychosocial factors three variables were significant predictors for tumor relapse, ie, Physical Self-Efficacy, psychosocial complaints, and loss of control. Patients with a high level of self-efficacy at pretreatment had a lower chance for relapse. Also, patients with more loss of control at pretreatment had a higher chance for relapse. Again, patients with more psychosocial complaints were found to have a significant lower chance for tumor relapse.

There was only one similarity between the results of our study and the findings from the literature: multi dimensional health locus of control is not a predictor of prognosis. We could not confirm the indication from literature results that social support has a predictive value with respect to survival and relapse. On the other hand the variables we found to be predictive were not evaluated or were found to have an inconclusive predictive value in other studies. Therefore in future research, it is necessary to include the variables (scales), physical self-efficacy, psychosocial complaints, uncertainty and loss of control.

Physical self-efficacy being a strong predictor for relapse of tumor as well as for overall survival in our study, if confirmed in similar studies to be done, advocates for well designed clinical trials in which exercise activity levels of patients are systematically varied to assess more precisely their differential impact on survival and relapse free period. An experimental group of patients who vary in exercise activity can be compared with patients who do not perform exercise activities (control group). Together with other variables physical self-efficacy is measured before and during the exercise activity period. All patients are followed for a longer period of time with respect to the occurrence of a relapse and overall survival. It seems possible that the recently developed health promoting program for cancer patients, 'Recovery and Balance' [3] can be used as experimental intervention. Sport training in groups of fellow-patients is an essential part of this program.

D. RECOMMENDATIONS

In this paragraph further recommendations for future research and recommendations for improvement of daily care, based on our research, are formulated.

Future Research

1. Theoretical models with respect to integrated care[4] and coping with

cancer should be developed and applied in future studies (chapter 2).

2. It is necessary to come to consensus about the further development and use of instruments to measure physical and psychosocial functioning in head and neck cancer patients (chapter 2).
3. Newly developed scales specific to head and neck cancer (head and neck specific quality of life modules) need to be validated (chapter 3).
4. Only measures with well established levels of reliability and validity should be used (chapter 5).
5. Only homogeneous patient groups of sufficient numbers should be included in such a study. The advantage of different treatment groups of head and neck cancer patients is that these are quite homogeneous. Finding a sufficient number of patients still remains to be a problem due to the relative rare incidence of this tumor. Multicenter studies are mandatory for that reason (chapter 5, 6).

Daily Practice

Recommendations for the daily practice with the aim to improve quality of life resulting from the study described in chapter 3 are:

1. Medical specialists should optimize information and social support.
2. In particular, the laryngectomy patient needs psychosocial guidance for a longer posttreatment period.
3. If appreciated by the patient, health care professionals should involve the partner as much as possible in all communications and should encourage the patient to talk at home about problems.
4. Problems of the partner, in relation to the patient and the disease, should also be open to discussion.

With respect to the *quantity of life*, from the results described in chapter 6, the following recommendations are given:

5. Given the finding of our study that expression of negative emotions might increase the time of survival, care givers should stimulate the expression of psychosocial complaints in their patients.
6. When future studies yield positive effects of exercise activity on survival and relapse free period, patients must be stimulated to do physical activities, do exercises in a group, in order to increase physical self-efficacy.
7. Physicians should intervene early and decisively in their patients' smoking behavior.

In the first 4 recommendations concerning the daily practice patient information and social support are the main issues. The medical specialist and other health care professionals as well as the family members can play an important role by providing information and support. An important condition is that the information and support of the various health care providers is well-attuned. Continuity of information (after discharge of the hospital) should be pursued as much as possible. In case of head and neck cancer patients about 20 care givers are involved.[5] One means of achieving continuity of information and care is by using a 'logbook'. The logbook, or patient-dossier, developed by our Rehabilitation-Research-Group, is defined as an instrument for giving and exchanging information. It contains both a 'communication' and an 'information' section, in a loose-leaf bound format. It also includes a sort of diary in which the patient expresses his/her feelings and psychosocial complaints. The logbook is the property of the patient, who may ultimately decide who has access to its content. It stays with the patient, but is intended to be available at all consultations and, in the domestic context, to any home-help, voluntary worker, informal carer or next of kin. It appears that patients who used a logbook proved to be better informed, to receive more support, and to experience fewer psychosocial problems. It can be concluded that the use of the logbook appeared to be effective with respect to the above mentioned recommendations.[6]

With respect to stimulating the expression of psychosocial complaints (recommendation 5) the medical specialist can play an important role. Before and during the (burdening) treatment as well as in the regular check-up visits patients are confronted with heightened uncertainty and anxiety. Thus the contact between medical specialist and patients in the out-patient department offers a good opportunity to stimulate the expression of psychosocial complaints. This should be done in a systematic and efficient way. One means of doing so is by using the Integral Checklist [7], which is an adapted version of the Rotterdam Symptom Checklist. Patients can thus express their physical and psychosocial complaints during their stay in the waiting room. It appears that, when using the checklist, specialists more often take the initiative to discuss psychosocial problems with their patients. In a recent study, conducted by our group, we found that by far the majority of the patients appreciate a discussion of the checklist with their specialist. The instrument appears to fit well in the daily hospital procedure, and using the checklist does not take the specialist any extra time.[7]

Finally, with respect to encouraging physical activities in order to increase physical self-efficacy (recommendation 6), examples could be arm raising exercises for neck dissection patients, relaxation exercises to improve the link between breathing and speech abilities in laryngectomy patients and swimming activities for groups of laryngectomees. Physical exercise should be encouraged regularly to improve strength and stamina especially in those patients low in self-efficacy.

REFERENCES

1 Holland JC. Behavioral and psychosocial risk factors in cancer: human studies. In: Holland JC, Rowland JH. *Handbook of psychooncology.* New York, Oxford: University Press, 1989: 705-26.

2 Wolfensberger M. Using Cox's proportional hazards model for the prognostication of the upper aero-digestive tract. *Acta Otolaryngol (Stokh)* 1992; 112:376-82.

3 Koppejan-Rensebrink AG, Heemskerk P. 'Recovery and Balance', health promotion and revalidation for cancer patients. A new concept for after care programs. ['Herstel en Balans", gezondheidsbevordering en revalidatie voor kankerpatienten. Een nieuw concept voor nazorg programma's.] *Medisch Contact* 1997;52:1459-60.

4 Pruyn JFA, De Boer MF , Heerema NC, Kiezebrink ML, Wiggers Th. Supportive Care [Ondersteunende Zorg]. *Ned Tijdschr Geneeskd* 1995;139:342-6.

5 Wouterlood-van Cleef IE, De Boer MF, Molendijk LW, De Jong PC, Knegt PP, Pruyn JFA, et al. Grappling with after-care: a study of the constraints experienced by care-professionals in the after-care of patients being treated for head-and-neck cancer in the Rotterdam region [Nazorg... Hoofd of halszaak? Een onderzoek naar knelpunten die hulpverleners ervaren bij de nazorg voor patienten die behandeld zijn voor een hoofd-halstumor in de regio van het IKR.] (abstract). *Tijdschrift voor Sociale Gezonheidszorg*, 1989;11: 43.

6 Van Wersch A, De Boer MF, Van der Does E, De Jong P, Knegt P, Meeuwis CA, Stringer P, Pruyn JFA. Continuity of information in cancer care: evaluation of a logbook. *Patient Education Counseling* 1997;31:223-36.

7 Pruyn JFA, Mosterd FR, Van Hest MAG, De Boer MF, Sinnige HAM, Pruyn ATH, Knegt PP. In pursuance of efficient integral care in outpatient departments: screening and referral [Op weg naar efficiënte integrale zorg voor kankerpatiënten op de polikliniek: screening en verwijzing]. Submitted for publication.

SAMENVATTING

Het doel van deze studie kan als volgt worden samengevat:

A. Het beschrijven van het rehabilitatie proces en de rehabilitatieuitkomsten van van hoofd-halskankerpatiënten die langere tijd na de behandeling overleven .

B. Het identificeren van voorspellers van rehabilitatie-uitkomsten.

C. Het identificeren van medische, psychosociale, gedragsmatige en sociodemografische voorspellende faktoren van overleving en van het optreden van een tumor recidief bij patiënten met hoofd-halskanker.

D. Het formuleren van aanbevelingen en identificeren van speerpunten voor toekomstig onderzoek en verbetering van de zorg.

In de voorgaande hoofdstukken worden overzichten van de relevante literatuur, een descriptieve - en een prospectieve studie bij cohorten hoofd-halskankerpatiënten gepresenteerd.

A. REHABILITATIE UITKOMSTEN VAN LANGE-TERMIJN OVERLEVERS

Literatuur: 1984-1996 Een overzicht van 50 studies met betrekking tot het psycho-sociaal functioneren van hoofd-halskankerpatiënten wordt beschreven in **hoofdstuk 2**. Het is duidelijk dat hoofd-halskanker een grote invloed heeft op de rehabilitatie- uitkomsten en kwaliteit van leven van deze patiënten. Belangrijke lichamelijke klachten zijn problemen met het spreken, droge mond en keel, slikproblemen en pijn. Veranderingen in het psychosociaal functioneren en psychologische klachten werden gerapporteerd in diverse studies door een aanzienlijk aantal patiënten. De belangrijkste symptomen hierbij zijn: het zich zorgen maken, angst, stemmingsveranderingen, vermoeidheid en gevoelens van neerslachtigheid. Deze ervaren psychologische problemen zouden verantwoordelijk kunnen zijn voor het verhoogde zelfmoordpercentage dat wordt gevonden bij patiënten met hoofd-halskanker in vergelijking met andere kanker-patiënten. Ook werd aantasting van het zelf/lichaams-beeld en een verminderd gevoel van eigenwaarde als gevolg van de ziekte en/of de mutilerende behandeling, vermeld. Met betrekking tot het verslavingsgedrag na de behandeling, komt uit het literatuuroverzicht naar voren dat het tabaksgebruik afneemt. Over het geheel genomen blijkt dat het hebben/gehad hebben van hoofd-halskanker een negatief effect heeft op het sociaal -, recreatief - en sexueel functioneren.

Om bovenbeschreven literatuurbevindingen te verifiëren deden wij een studie met als doel om de rehabilitatie-uitkomsten te beschrijven van hoofd-halskankerpatiënten uit zuid-west Nederland, die behandeld werden in Rotterdam.

Het was van belang om in deze studie bijzondere aandacht te besteden aan de knelpunten die werden geconstateerd in de literatuur. Zo zou een theoretisch model met betrekking tot het omgaan met levensbedreigende ziekten ten grondslag moeten liggen aan de keuze van het pakket van vragen die we aan de deelnemers aan het onderzoek zouden voorleggen. Een dergelijk model is fundamenteel voor een raamwerk waarin de belangrijkste problemen en verwerkingsstrategiën moeten passen. Een theoretisch model is ook noodzakelijk voor het definiëren van begrippen en het meetbaar maken hiervan. Zo wordt het begrip "kwaliteit van leven" minder vaag door de multidimensionele gebieden van dit concept te benoemen. Ook maakt een dergelijke werkwijze het mogelijk om te komen tot een reductie van de talloze factoren die worden gebruikt in de literatuur.

In de studies van ons literatuur-overzicht waren patiënten met een klein stembandcarcinoom, die alleen met uitwendige bestraling werden behandeld, niet betrokken. Hoewel deze patiëntengroep een goede prognose heeft en verwacht wordt dat ze weinig lichamelijke en psychosociale problemen ervaren, worden ze toch ook geconfronteerd met het probleem "kanker" en de mogelijkheid dat de ziekte na de behandeling kan terugkomen. Door deze behandelingsgroep bij onze studie te betrekken, werd het mogelijk een vergelijking te maken tussen behandelingsgroepen, die mogelijk verschillen in de ervaren problemen ten gevolge van de tumor en de behandeling.

Uit de literatuur blijkt dat er nog steeds weinig bekend is over de rehabilitatie-uitkomsten van patiënten die lange tijd overleven. Een inzicht hierin is onontbeerlijk omdat er in de tijd veranderingsprocessen – zowel ten goede en als ten slechte – kunnen optreden in de (ervaren) psychosociale problemen.

Resultaten van de descriptieve studie in Rotterdam In hoofdstuk 3 worden de rehabilitatie-uitkomsten beschreven van 110 patiënten die 2 tot 6 jaar tevoren werden behandeld voor een carcinoom in het hoofd-halsgebied. De patiëntengroepen waarmee de studie werd uitgevoerd zijn: 1) patiënten met een stembandcarcinoom, beperkt tot de stembanden (T1), uitsluitend behandeld met uitwendige bestraling, 2) laryngectomie-patiënten en 3) patiënten die een commando-operatie hebben ondergaan wegens een carcinoom in de mond-, mond/keelholte.

De T1-larynxpatiënten bleken, zelfs nog jaren na de behandeling, een aanzienlijk aantal lichamelijke klachten te hebben, zoals pijnlijke spieren, vermoeidheid, hoesten en verslikken.

De laryngectomiepatiënten en commando-operatiepatiënten bleken ernstige psychosociale klachten te ervaren. De problemen van de laryngectomiepatiënten waren dikwijls gekoppeld aan een verminderd spraakvermogen. Bij patiënten die een commando-operatie hadden ondergaan concentreerden de problemen zich rond de verstoorde voedselopname en het gemutileerde uiterlijk, met de psychosociale consequenties daarvan. Meer dan de helft van zowel de laryngectomiegroep als de "commando"groep vonden dat hun uiterlijk was beschadigd door de behandeling. Met name laryngectomiepatiënten voelden zich onzeker met betrekking tot het vinden van hulp bij het oplossen van problemen en het beantwoord krijgen van vragen betreffende de ziekte en het omgaan met de eigen emoties. Ook hadden zij een minder gevoel van eigenwaarde met betrekking tot sociaal functioneren.

Wanneer we de resultaten van ons eigen onderzoek vergelijken met de bevindingen uit de literatuur, dan zijn deze op vele punten identiek, zoals het door veel patiënten ervaren van psychosociale problemen na de behandeling, spraak- en eet/slikproblemen, problemen met het gemutileerde uiterlijk, het verstoorde lichaamsbeeld en het bedreigde gevoel van eigenwaarde.

Het is opvallend dat in onze studie veel patiënten na jaren nog steeds gehinderd worden door gevoelens van onzekerheid. Daarom vinden wij dat het begrip "onzekerheid" in toekomstige "kwaliteit van leven"-studies ook onderzocht dient te worden. Patiënten met een T1-stembandcarcinoom moeten, gezien de vele lichamelijke klachten na de behandeling die wij vonden, eveneens in de toekomst bij "kwaliteit van leven"-onderzoek worden betrokken.

Bij dergelijk onderzoek is een langdurige controle van de patiënten noodzakelijk, gezien de ernst van de lichamelijke en psychosociale problemen, die patiënten in ons onderzoek, na tal van jaren, nog steeds rapporteerden.

B. VOORSPELLERS VAN REHABILITATIE-UITKOMSTEN

Literatuur: 1984-1996 Uit het overzicht van 50 studies met betrekking tot het psychosociaal functioneren van hoofd-halskankerpatiënten beschreven in hoofdstuk 2 komt naar voren dat de kwantiteit en de kwaliteit van lichamelijke problemen van de patiënten zijn gerelateerd aan de uitgebreidheid van de chirurgische ingreep en het doelgebied van de bestraling. Patiënten die uitsluitend bestraald zijn, blijken een betere "kwaliteit van leven" te hebben dan patiënten met andere behandelingen. Combinatie-therapie (chirurgie, radiotherapie en chemotherapie) geeft meer lichamelijke en psychosociale klachten. Doeltreffende patiëntenvoorlichting en sociale ondersteuning hebben een duidelijk positieve invloed op het rehabilitatie resultaat. Tenslotte kan nog vermeld worden dat in veel studies uitsluitend beschrijvende (descriptieve) of correlationele analyse-technieken worden gebruikt.

Het doel van onze beschrijvende studie was het verifiëren van de bovenvermelde resultaten uit de literatuur. In tegenstelling tot wat wij bij veel andere auteurs over toegepaste statistiek vonden, gebruikten wij in deze studie een multivariate analyse techniek.

Resultaten van de descriptieve studie in Rotterdam In hoofdstuk 3 worden de correlaties beschreven tussen het rehabilitatie-proces en de rehabilitatie-uitkomsten van de 110 patiënten die tussen twee en zes jaar tevoren werden behandeld voor hoofd-halskanker. De resultaten laten zien dat het hebben ondergaan van een laryngectomie is gerelateerd aan de rapportage van het ervaren van minder goede voedselopname, meer psychosociale klachten die specifiek zijn voor patiënten met hoofd-halstumoren en meer onzekerheid. Dit werd niet waargenomen bij de "commando"groep en de T1-larynxgroep. Met betrekking tot veranderingen optredend in het tijdsverloop, werd gevonden dat naarmate meer tijd verstreek, minder "hoofd-hals specifieke" klachten werden ervaren. De belangrijkste voorspellers van een goed rehabilitatie resultaat waren de mogelijkheid om problemen met betrekking tot de ziekte te bespreken met de naaste familie, sociale ondersteuning van de specialist en doeltreffende voorlichting van de specialist. Patiënten met een hoge interne "locus of control" met betrekking tot het verloop van de ziekte (de patiënt vindt dat hij/zij zelf invloed heeft op het verloop van de ziekte) geven aan beter gerehabiliteerd te zijn - dat wil zeggen, ervaren minder angst en ervaren betere spraakmogelijkheden - dan patiënten die aangeven dat ze een lage interne "locus of control" hebben.

Overeenkomstig de bevinding uit de literatuur, dat de kwaliteit van leven lager werd gescoord naarmate de medische behandeling intensiever was, wordt in onze studie aangetoond dat het soort behandeling, met name het hebben ondergaan van een laryngectomie, een voorspeller is van het rehabilitatie resultaat. Een tweede bevinding van onze studie, die identiek is aan de conclusies van de literatuur, is het verband tussen sociale ondersteuning en positieve rehabilitatie-uitkomsten.

Het positieve effect op de rehabilitatie van het gerapporteerde gevoel van de patiënt dat hij/zij zelf invloed heeft op het verloop van zijn/haar ziekte, lijkt een belangrijke bevinding - niet het minste voor de patiënt zelf - die in toekomstig onderzoek geverifieerd dient te worden.

C. VOORSPELLERS VAN OVERLEVING

Literatuur betreffende medisch-prognostische factoren: 1990-1995 Van oudsher ligt de nadruk bij het behandelen van patiënten met hoofd-halskanker op tumorvrije overleving en medisch-prognostische factoren. Om meer inzicht te krijgen in recente ontwikkelingen met betrekking tot medisch-prognostische factoren, werd een literatuurstudie verricht, waarbij 55 relevante studies werden geanalyseerd (**hoofdstuk 4**). Hiervoor werd een model voor het scoren van de statistische betrouwbaarheid van potentiële prognostische factoren geïntroduceerd. De formule van de zogenaamde "significantie-score" is gebaseerd op het aantal patiënten in studies, waarin de correlatie tussen de desbetreffende factor en de prognose statistische significantie bereikt, en het totaal aantal patiënten, dat betrokken was bij de diverse studies, waarin de factor werd geëvalueerd. De significantie-score werd alleen berekend voor factoren die met behulp van multivariate analyes werden geëvalueerd. Dit was het geval in 70% (39 studies) van het totaal aantal studies, hetgeen een forse toename is in vergelijking tot de 20 daaraan voorafgaande jaren, toen men zich voornamelijk beperkte tot non-multifactoriële analyse-technieken.

Het bleek dat in 55 studies in totaal 97 factoren werden geanalyseerd met betrekking tot hun relatie met de overleving ("overall survival") en/of het terugkeren van de ziekte (optreden van een recidief/"relapse"). Slechts zes factoren werden (met behulp van een multivariate analyse-techniek) bestudeerd in een populatie van meer dan 3000 patiënten. Van deze zes factoren bereikte slechts de N-classificatie (aantal en localisatie van halskliermetastasen) een hoge significantie-score (83%) in relatie tot de overleving. De gevonden voorspellende waarde van de T-classificatie (grootte van het primaire tumorproces) voor de overleving was relatief laag (22%) en tamelijk inconsistent met betrekking tot het optreden van een recidief (39%); dit laatste zou verband kunnen houden met de moeilijkheid om exact de locale tumor-uitbreiding vast te stellen, zoals bijvoorbeeld bij het larynxcarcinoom. Resultaten voor de tumor-localisatie waren inconsistent zowel betreffende overleving als optreden van recidief, ca. 50%, hetgeen ook geconcludeerd werd uit artikelen en reviews van voor de periode die door ons werd bestudeerd. Het geslacht van de patiënt bleek geen voorspellende waarde voor de prognose te hebben.

Voor het stadium van de ziekte (samengesteld uit de T-, N- en M-classificatie) werd een significantie-score berekend in een patiëntenpopulatie van 2800 patiënten: 57% met betrekking tot de overleving en 74% in relatie tot het optreden van een recidief. Het percentage bij de overleving ligt lager dan verwacht zou mogen worden op grond van de gevonden waarde voor de N-classificatie. Hoewel de aan de behandeling gerelateerde histologische factoren, positief resectievlak en extra-nodale groei, in ons literatuuroverzicht bij een kleine patiëntenpopulatie, correlaties lieten zien met de prognose, mogen we mede op grond van literatuur die niet in ons overzicht is opgenomen, wellicht toch tot de conclusie komen dat deze factoren prognostisch van belang zijn.

We kunnen concluderen dat studies met grote aantallen patiënten nodig zijn om de voorspellende waarde van de meeste "medische" factoren, waarvan in studies wordt geclaimed dat ze prognostische informatie bevatten, zoals (radio)therapie gerelateerde factoren, histologische en biologische tumorfactoren, nader te evalueren. Gezien het relatief zeldzaam voorkomen van hoofd-halstumoren zijn "multi-center" studies hiervoor aangewezen.

Het verloop van een kwaadaardig ziekteproces wordt waarschijnlijk niet alleen bepaald door medische factoren maar is het resultaat van een complexe interactie van medische - , sociodemografische - en psychosociale factoren.

Literatuur betreffende psychosociale prognostische factoren: 1979-1995 De mogelijke rol die psychologische -, sociale - en gedragsmatige factoren spelen bij het ontstaan en het verloop van kanker heeft onderzoekers al eeuwen geïntrigeerd. In de afgelopen drie decennia is er sprake van een enorme toename van research-activiteiten op het gebied van psychosociale prognostische factoren. Er zijn evenwel tot nu toe geen studies gerapporteerd die de relatie tussen psychosociale factoren enerzijds en overleving en/of het optreden van een recidief anderzijds bij hoofd-halskanker hebben onderzocht. Om die reden werd een literatuurstudie over dit onderwerp uitgebreid naar alle kankerpatiënten. Bij het overzicht van 33 studies (hoofdstuk 5) hebben wij gekozen voor een overzicht van de stand van zaken betreffende psychosociale prognostische factoren, in plaats van een inschatting te geven van de prognostische waarde op basis van de grootte van de onderzochte patiëntenpopulatie, het studie "design" en de toegepaste statistische methode, zoals bij de medisch-prognostische factoren.

De factoren die het meest frequent werden geëvalueerd voor wat betreft hun relatie tot de overleving en/of het optreden van een recidief waren: neerslachtige (depressieve) gevoelens, (toestands) angst, hopeloosheid/hulpeloosheid, vijandigheid, huwelijkse staat en sociale betrokkenheid/sociale ondersteuning. De gevonden resultaten voor deze zes factoren waren met uitzondering van de laatste nogal inconsistent. In zeven van de 15 studies werd een positieve relatie gevonden tussen een sociale betrokkenheid en de aanwezigheid van sociale ondersteuning enerzijds en een goede prognose anderzijds, terwijl een *negatief* verband niet kon worden aangetoond in de onderzochte studies.

Ook bij minder frequent bestudeerde variabelen zoals bijvoorbeeld stemming, pijn, functionele status/allerdaagse bezigheden, ernstige/ingrijpende gebeurtenissen, psychotisch gedrag, dagdromen, vreugde, “locus of control”, persoonsgebonden angst en verwerkingsstrategiën, zoals strijdlust en acceptatie, werden geen overtuigende resultaten gevonden.

Een aantal factoren, zoals bijvoorbeeld sociale klasse en de “container begrippen”, kwaliteit van leven, lichamelijk - en psychologisch welzijn en een aantal “stress”-variabelen, vertoonden slechts in één studie een relatie met overleving en/of recidief.

Tenslotte werd er voor de variabelen multi-dimensionele “health locus of control” (relatie aangeven tussen oorzaak en gevolg voor de gezondheid in het algemeen), neuroticisme en somatisatie, voor elke variabele in twee studies, *geen* verband gevonden met de uitkomst-variabelen (prognose).

Resultaten van de prospectieve studie in Rotterdam Aanleiding tot een prospectieve studie was het vrijwel geheel ontbreken van overtuigende resultaten in de literatuur met betrekking tot zowel medisch-prognostische factoren bij hoofd-halskanker, als psychosociale-prognostische factoren bij kanker in bredere zin. Bovendien zijn er geen rapportages te vinden over psychosociale-prognostische studies toegespitst op patiënten met hoofd-halskanker. In deze studie met 133 hoofd-halskankerpatiënten werden medische -, psychosociale -, gedragsmatige - en demografische factoren in hun relatie tot overleving en het optreden van een recidief bestudeerd. Scores van deze factoren gemeten vlak vóór de behandeling werden geanalyseerd met betrekking tot de “overall” overleving en het recidief met een pijldatum van zes jaar nadien. De onderzoeksgroepen van deze prospectieve studie waren analoog aan die van de descriptieve studie: 1) patiënten met een T1 stembandcarcinoom alleen behandeld met uitwendige bestraling, 2) laryngectomie-patiënten en 3) patiënten die geopereerd waren aan een carcinoom in de mond/mond-keelholte.

Overleving De resultaten van de Cox regressie analyses, beschreven in

hoofdstuk 6, laten zien dat van de medische variabelen, de N-classificatie en de T-classificatie, een significant ($p < 0{,}05$) verband tonen met de "overall" overleving. Duidelijk komt naar voren dat patiënten zonder halskliermetastasen (N0) een betere overlevingsprognose hebben dan patiënten met één of meer halskliermetastasen (N1, 2 of 3). Het roken, geëvalueerd vlak voor de behandeling, en gevorderde leeftijd waren significante voorspellers van een slechtere overleving. Het eerder bestraald zijn voor hetzelfde tumorproces voorafgaand aan de eerste meting bleek geen invloed te hebben op de levensduur.

Drie psychosociale factoren, te weten "physical self-efficacy" (het vertrouwen in het eigen lichamelijk functioneren), onzekerheid over het omgaan met de praktische gevolgen van de ziekte en de behandeling, en het uiten van psychosociale klachten, bleken significante voorspellers van de overlevingsduur te zijn. Patiënten met een hoog niveau van "self-efficacy" bij de meting vóór de behandeling hebben een grotere kans langer te overleven. Een hoge score op het item "onzekerheid over het omgaan met de praktische gevolgen van de ziekte en de behandeling" hangt samen met minder kans om te overleven. Opvallend is dat patiënten die aangeven meer psychosociale klachten te hebben significant meer kans hebben langer te overleven.

Optreden van tumor-recidief. Patiënten zonder halskliermetastasen bleken een geringere kans op een tumor-recidief te hebben dan patiënten met N1, 2 of 3. De T-classificatie had geen voorspellende waarde voor wat betreft het optreden van een recidief. Van de leeftijd bij de eerste meting en het rookgedrag kon eveneens niet worden aangetoond dat deze het ontstaan van een tumor-recidief zouden kunnen voorspellen. Ook bij het recidief bleek eerdere bestraling van het tumorproces geen voorspellende waarde te hebben.

Betreffende de psychosociale factoren, werd gevonden dat "physical self-efficacy", psychosociale klachten en verlies van controle, significant gecorreleerd waren met het optreden van een tumor-recidief. Patiënten met een hoog niveau van "self-efficacy" vlak voor de behandeling hadden minder kans om een recidief te krijgen. Als er veel controle-verlies wordt ervaren voor de behandeling blijkt dit samen te gaan met een grotere kans op een recidief. Mensen die zeggen veel psychosociale klachten te ervaren blijken, net zoals dat het geval was bij de overleving, ook minder kans op een tumor-recidief te hebben.

De enige overeenkomst tussen de resultaten van deze studie en de bevindingen in de literatuur is dat de "multi-dimensional health locus of control"-schaal geen voorspeller is van overleving en de kans om een tumor-recidief te krijgen. In onze studie konden wij de bevinding dat sociale ondersteuning mogelijk gecorreleerd is met de prognose betreffende overleving en kans op recidief, niet bevestigen. Daarentegen vonden wij factoren als voorspellers van prognose, die in de literatuur niet waren onderzocht of geen overtuigende resultaten lieten zien. Dit leidt tot de conclusie dat het noodzakelijk is om in toekomstig onderzoek, variabelen (schalen) zoals "physical self-efficacy", psychosociale klachten, onzekerheid en controleverlies toe te voegen aan de reeks van mogelijke psychosociale voorspellers.

Nadat in identieke vervolgstudies wordt bevestigd dat "physical self-efficacy" een duidelijke voorspeller is van de prognose, kan worden gedacht aan goed opgezette studies waarin de intensiteit van lichamelijke oefening systematisch wordt gevarieerd om nauwkeurig de gedifferentieerde invloed van deze, in intensiteit verschillende, trainingsprogramma's op de prognose te kunnen vaststellen. In een dergelijke studie zou de experimentele groep moeten bestaan uit patiënten die men de verschillende lichamelijke trainingsactiviteiten laat verrichten en een controle-groep die het zonder een programma van oefeningen doet. Samen met andere relevante variabelen wordt dan de "physical self-efficacy" gemeten vóór en gedurende de periode van lichamelijke oefeningen. Alle patiënten zullen een ruime periode van tenminste vijf jaar moeten worden gevolgd, waarin het optreden van een eventueel recidief en de overleving worden vastgesteld. Een recent ontwikkeld gezondheidsbevorderend revalidatieprogramma, "herstel en balans", zou hierbij als experimentele interventie kunnen worden gebruikt; sport en training van lotgenoten zijn essentiële onderdelen van dit programma.

D. AANBEVELINGEN

In de paragraaf "Aanbevelingen" van **hoofdstuk** 7 worden nog een aantal speerpunten voor toekomstig onderzoek naar voren gebracht en worden aanbevelingen gedaan voor verbetering van de zorg.

Ten behoeve van toekomstig onderzoek worden genoemd: het belang van een theoretisch model betreffende integrale zorg en het omgaan met kanker, de noodzakelijke consensus over het te ontwikkelen hoofd-hals specifiek psychosociaal meetinstrumentarium, de onontbeerlijke validatie van dat instrumentarium en de vereiste om homogene patiënten-populaties van voldoende omvang te onderzoeken.

Met betrekking tot de aanbevelingen voor de dagelijkse praktijk worden genoemd: de noodzaak om voorlichting aan en ondersteuning van patiënten te optimaliseren, het intensief begeleiden van met name laryngectomie patiënten voor langere tijd post-operatief, het bevorderen van het bespreken van aan de ziekte gerelateerde problemen in het gezin, het openstaan voor de problemen van de partner van de patiënt, het stimuleren van het uiten van psychosociale klachten, het doen van lichamelijke oefeningen in groepsverband (bijvoorbeeld het groepszwemmen voor gelaryngectomeerden) en het advies om hoofd-halskankerpatiënten in een vroeg stadium regelmatig en beslist te wijzen op de gevaren van het roken, bijvoorbeeld door de behandelend artsen.

Tenslotte wordt er gerefereerd aan twee succesvol afgesloten projecten, te weten het "logboek-project" en het project "Op weg naar een efficiënte polikliniek", die zijn voortgekomen uit het in dit proefschrift gerapporteerde onderzoek.

APPENDIX I

Table 1 Medical prognostic factors for survival/relapse (univariate analysis)

Article (ref No.)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	No. pat surv	No. pat rel
Number of patients	244	47	100	105	28	199	58	330	134	53	52	104	65	65	67	763		
Retro/prospective	r	r	r	p	r	p	r	r	r	p	r	r	r	r	r	p		
Host factors																		
Age							0/0									0/	821	58
Sex												/0				0/	763	104
Performance status						/0										1/	763	199
Nutritional status/score															1/1		67	67
Tobacco consumption		/0															–	94
Alcohol consumption		/0															–	94
Prostaglandine E concentration										0/1							–	53
Treatment factors																		
Treatment modality												/0					–	104
Postoperative wound infection									1/1								134	134
Post-operative radiotherapy	/0																–	244
Total given dose RT			/0			/1							/0				–	364
RT field size								0/0					/0				330	395
Tumorresponse evaluation at 40 Gy			/1					0/1									330	430
RT delay po>6 weeks						/0							/0				–	264
Dose fraction								/1					/0				–	395
Clinical tumor factors																		
Site	/0		/1			/0						/0		0/			65	647
T classification	/1											/0		0/			65	348
N classification												/0		0/			65	104
Tumor thickness							1/1										58	58
Stage of disease									1/1								134	134
Vocal cord tumor extension													/1				–	65

Table 1 Continued

Article (ref No.)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	No.	No.
Number of patients	244	47	100	105	28	199	58	330	134	53	52	104	65	65	67	763	pat	pat
Retro/prospective	r	r	r	p	r	p	r	r	r	p	r	r	r	r	r	p	surv	rel
Histological tumor factors																		
P -N stage	/1					/0								1/1			65	508
Extra nodal spread	/0					/1											–	443
Tumor positive resection margins						/0											–	199
Histologic differentiation grade		/1			/0		0/0					/0		0/			123	284
Histological grading (Broders)											0/						52	–
Growth pattern		/1												0/			65	47
Nuclear differentiation		/0															–	94
Mode of invasion		/1															–	47
Vascular invasion		/0				/0								0/			65	293
Cellular response		/0															–	47
Neural invasion						/0											–	199
Invasion muscle/bone/ skin/cartilage						/0											–	199
Tumor associated tissue eosinophilia												/1					–	104
Lymphocytosis												/0					–	104
Plasma cells												/0					–	104

Table 1 Continued

Article (ref No.)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	No. pat surv	No. pat rel
Number of patients	244	47	100	105	28	199	58	330	134	53	52	104	65	65	67	763		
Retro/prospective	r	r	r	p	r	p	r	r	r	p	r	r	r	r	r	p		
Biological tumor factors											0/							
Epidermal growth factor											0/			0/			–	117
Insulin-like growth factor																	52	–
P 53E														0/			65	–
Catepsin immuno reactivity														0/			65	–
Tissue polipeptide-specific antigen											0/						52	–
Median labeling index (LI)				0/													105	–
Duration of S-phase (Ts)				0/													105	–
Potential doubling time (Tpot)				0/													105	–
Total labeling index (TLI)				0/													105	–
Synthesis phase fraction														0/			65	–
Proliferating cell nuclear antigen					/1												–	28
Degree in nuclear DNA aberation					/1												–	28
DNA ploidy (index)														0/			65	–
Circulating prolactin level											1/						52	–

No. pat surv = Number of patients in which the factor has been studied in relation to overall survival.
No. pat rel = Number of patients in which the factor has been studied in relation to relapse.

Table 2 Medical prognostic factors for survival/relapse (multivariate analysis)

Article	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Number of patients	511	91	145	109	165	230	296	306	378	171	189	111	72	55	1315	194	74	88	492
Retro/prospective	r	r	r	r	r	r	r	r	r	p	r	r	r	r	r	r	p	p	r
Host factors																			
Age	0/	0/0	0/0		0/	0/0	0/			0/0		0/0	/0		1/0	/0	/0	/0	
Sex	0/	0/0	0/0		0/	0/0		/0		0/0		0/0		/0	0/0	/0			
Performance status								/0											
Tobacco consumption	0/				0/		0/											/0	
Alcohol consumption	0/				0/	1/1	1/											/0	
Continuing smoking/alc.					0/											/1			
Sedimentation rate											0/								
Immune globulin A																			
Serum C1q-binding molecules																			
Hemoglobin												1/1							
Rhesus bloodgroup												1/1							

(continued)

36 103 r	37 47 r	38 172 r/p	39 110 r	40 80 r	41 265 r	42 49 r	43 66 r	44 947 p	45 148 r	46 207 r	47 512 p	48 221 r	49 66 r	50 48 r	51 278 r	52 161 p	53 109 r	54 83 p	55 765 p	score sign surv	score sign rec	No. pat surv	No. pat rel
0/0		0/0	/0		0/0		/0		0/0	0/	1/0	0/0		0/0	1/1	/0				.42*	0	4989	4354
0/0	/0	0/0	/0					0/	0/0	0/	0/0	0/0	0/0	0/0		/0	0/0			0	0	5270	4094
			/0					0/			1/0		1/0							.38	0	1525	994
												0/0	1/0			/1	0/0			.05	.24	1368	645
																/0				.44	0	1202	479
																				0	1	165	194
																				0	–	189	–
					0/0															0	0	103	103
					0/1															0	1	103	103
																	1/1			1	1	220	220
																				1	1	111	111

Table 2 (continued)

Article	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Number of patients	511	91	145	109	165	230	296	306	378	171	189	111	72	55	1315	194	74	88	492
Retro/prospective	r	r	r	r	r	r	r	r	r	p	r	r	r	r	r	r	p	p	r
Treatment factors																			
Treatment modality						1/0				0/0			/0						0/0
Type of surgery																	/0		
(Type of) neck dissection																			0/0
Para-tracheal node dissection																			
Pretreatment tracheostomy	1/						0/												
Salvage surgical procedure																			
Postoperative radiotherapy																			
Total given dose RT		0/0														/0			0/0
RT field size																/0			0/1
Overall treatment time RT (days)		1/1						/0											
Response to radiotherapy																			
Dose fraction																			
Voice quality after radiotherapy								/0											
Response to chemothearpy				0/0		1/0													
Hemoglobin drop								/1											
Blood transfusion units																			

In the squares, the '0' or '1' before and after the slash stand for 'yes' or 'no' significant with respect to overall survival and relapse, respectively.

(continued)

36 103 r	37 47 r	38 172 r/p	39 110 r	40 80 r	41 265 r	42 49 r	43 66 r	44 947 p	45 148 r	46 207 r	47 512 p	48 221 r	49 66 r	50 48 r	51 278 r	52 161 p	53 109 r	54 83 p	55 765 p	score sign surv	score sign rec	No. pat surv	No. pat rel
					0/0					0/		0/	0/0	0/0						.14	0	1700	1344
							/0			0/					0/0					0	0	485	418
												0/			0/0					0	0	991	770
															0/0					0	0	278	278
												1/			1/1					.77	1	1306	278
									0/0											0	0	148	148
															0/0					0	0	278	278
0/0									0/0											0	0	834	1028
0/1																	0/0			0	.66	704	898
0/0																				.47	.18	194	500
														1/0						1	0	48	48
																	0/0			0	0	109	109
									1/1											1	.33	148	454
																				.68	0	339	339
																/0				–	.66	–	467
										1/										1	–	207	–

No. pat surv = Number of patients in which the factor has been studied in relation to overall survival.
No. pat rel = Number of patients in which the factor has been studied in relation to relapse.

* example of calculation of the 'significance score' for the factor 'age' in relation to overall survival:
score = (1315 + 512 + 278) / 2105 = 2105 / 4989 = .42

Table 2 Medical prognostic factors for survival/relapse (multivariate analysis)

Article	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Number of patients	511	91	145	109	165	230	296	306	378	171	189	111	72	55	1315	194	74	88	492
Clinical tumor factors																			
Site	1/		0/0	0/0			0/		/0	0/0		0/0	/0		1/1		/1		1/1
T classification						1/0	0/	/1	/0			1/1			0/0		/0		1/1
N classification	1/					1/0	1/	/1	/1				/1		1/0		/0		1/0
Tumor thickness																			
Level lymp node																			0/1
Fixation lymph node																			1/1
Location sec. prim. tumor					1/														
Stage of disease			1/1				0/			0/0	0/1	1/1	/0	/0	1/1				
Exophytic growth pattern																			
Dyspnea	0/																		
Vocal cord mobility			0/0				1/												
Vocal cord tumor extension																/0			
Duration of symptoms	0/											0/0							

(continued)

36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	score sign surv	score sign rec	No. pat surv	No. pat rel
103	47	172	110	80	265	49	66	947	148	207	512	221	66	48	278	161	109	83	765				
		0/0	/0	/0	0/0			0/		0/		1/		0/0	1/1	/0		/0	0/	.47	.55	60535	4064
		0/0					/0	0/		0/			1/1	0/0	1/1	/1	0/0	/0	0/	.22	.39	5342	3889
		0/0								0/		1/	0/0	0/0	0/0	/0		/0	1/	.83	.22	4601	3675
	/0																			–	0	–	47
								1/				0/			0/0					.43	.72	2168	1000
																				1	1	492	492
																				1	–	165	–
			/0		0/0		/0			0/			0/1			/1		/1		.57	.74	2765	2809
												0/								0	0	221	221
																				0	–	551	–
									1/1											.75	.51	589	293
0/0																				0	0	103	297
													0/0							0	0	688	177

Table 2 (continued)

Article	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Number of patients	511	91	145	109	165	230	296	306	378	171	189	111	72	55	1315	194	74	88	492
Histological tumor factors																			
p - T classification	0/																		
p - N classification	0/													/1				/1	
Extra nodal spread														/0					
Tumor positive resection margins	1/													/0					
Histologic differentiation grade	0/	0/0		0/0			0/			0/0			/0	/0	1/1	/0	/0	/1	
Histological score (Jacobson)													/1						
Growth pattern																		/0	
Mode of invasion																			
Depth of invasion																			
Vascular invasion																			
Neural invasion																			
Invasion muscle/bone/ skin/cartilage	0/																		
Tumor associated desmoplasia																			
Nuclear volume																			
Lymphocytosis, polimorphism																			
Biological tumor factors																			
Epidermal growth factor				0/1													/1		
Squamos cell carcinoma antigen											0/								
Serum thymidine kinase activity											0/								
Tumor angiogenesis																			
DNA ploidy (index)										0/0			/0					/0	
Proliferative activety (SPF)										1/1									

(continued)

36 103	37 47	38 172	39 110	40 80	41 265	42 49	43 66	44 947	45 148	46 207	47 512	48 221	49 66	50 48	51 278	52 161	53 109	54 83	55 765	score sign surv	score sign rec	No. pat surv	No. pat rel
				/0																0	0	511	80
								0/		0/					0/0					0	.34	1943	421
										1/					0/1					.43	.83	485	333
				/0		/1				1/					1/1					1	.79	485	413
0/0	/0		/0	/0		/0		0/	0/0	0/		0/		0/0	0/0		0/0	/0	0/	.24	.44	5446	3224
																				–	1	–	72
				/1																–	1	–	168
																/1				–	1	–	161
				/0		/1	/0									/0				–	.14	–	356
				/1		/0						0/			0/0	/0				0	.14	499	568
				/0		/0									0/0					0	0	278	407
				/0											0/0					0	0	789	356
						/0														–	0	–	49
																/1				–	1	–	161
						/0														–	0	–	153
																				0	1	109	183
																				0	–	189	–
																				0	–	189	–
							/1							0/0						0	.58	48	114
	/1	/1	/0																	0	.33	171	660
																				1	1	171	171

No. pat surv = Number of patients in which the factor has been studied in relation to overall survival.
No. pat rel = Number of patients in which the factor has been studied in relation to relapse.

Tabel 3 Selection criteria for patient inclusion: tumor site and treatment regime

Author, year	Tumor site / treatment regime
1[a] Leemans, '94	Primary scc[b] in the head and neck / surgery with 'en bloc with neck' resection, surgical margins free of tumor
2 Odell, '94	Scc of the lateral tongue, <2 cm. / implant radiotherapy and salvage loco-regional surgery
3 Inoue, '93	T 1-2 supraglottic larynx carcinoma (N0) / radiotherapy
4 Cooke, '94	Scc of the head and neck
5 Munck-Wikland, '92	T1N0M0 glottic larynx carcinoma
6 Peters, '93	Oral cavity,, orofarynx, hypofarynx, larynx, (92% stadium II en IV) / combined surgery and radiotherapy
7 Nathanson, '89	Primary scc of the mobile tongue (T1N0M0) / surgery, partial glossectomy
8 Inoue, '92	T1-2 glottic larynx carcinoma / radiotherapy
9 Grandis, '92	Scc of the head and neck / surgery
10 Kaplan, '92	Larynx and hypopharynx carcinoma / surgery ± chemo/radiotherapy
11 Bhatavdekar, '93	Scc of the tongue, stage III en IV
12 Thompson, '94	Scc of the larynx
13 Shim '94	T1-T2 , N0 (stage II) glottic larynx cancer / radiotherapy
14 Resnick, '95	Carcinoma of the larynx / laryngectomy with neck dissection
15 Lopez, '94	(Malnourished patients) treated for scc of the head and neck / nutritional support
16 Stell '90	Laryngeal carcinoma
17 Manni, '92	T3 N0-3 M0 Laryngeal carcinoma
18 Rudoltz, '93	T1-Glottic larynx carcinoma
19 Kowalski, '93	T1-Glottic larynx carcinoma stage I and II
20 Dassonville, '93	Head and neck carinoma
21 Schwartz, '94	Scc of the larynx, pyriform sinus, oral cavity, mobille tongue and base of tongue
22 Nyman, '92	Scc of the oral tongue
23 Pradier, '92	Scc of the larynx (male)
24 Van Acht, '92	Glottic and supraglotticcarcinoma / primary radiotherapy
25 Krishnan, '92	Oral cancer / radical radiotherapy
26 Fietkau, '94	Primary scc of the head and neck
27 Fontana, '93	Scc of the head and neck, oral cavity, orpfarynx, hypofarynx
28 Bryne, '91	Oral scc (buccal and maxillary alveolar mucosa)
29 Zätterström, '91	Scc of the head and neck without prior therapy
30 Foote, '93	Scc of base of tongue / curative surgery
31 Wiernik, '91	Scc of the larynx and hypopharynx / initial treatment: radiotherapy
32 Terhaard, '91	T1-larynx carcinoma (glottic, supra-glottic and sub-glottic) / radiotherapy
33 Maurizi, '92	Primary laryngeal carcer / primary treatment surgery
34 Truelson, '92	Advanced scc of the larynx (T3-T4) / laryngectomy with po. radiotherapy
35 Cerezo, '92	Primary scc of the head and neck with positive neck nodes at diagnosis
36 Small, '92	T1 glottic larynxcarcinoma, treated with radiotherapy
37 Munck-Wikland, '92	Scc of the mobile tongue (T1N0M0) / surgery local excision
38 Kearsley, '91	Scc of the head and neck

Table 3 Continued

Author, year	Tumor site / treatment regime
39 Cooke, '91	Primary scc of the larynx / surgery
40 Ravasz, '91	Scc of the oaral cavity, oropharynx, laryngo-hypopharynx / surgery
41 Lydiatt, '93	Primary scc of the head and neck
42 Jones, '92	Primary scc of the oral cavity, stage I en II / surgery
43 Williams, '94	Scc of the oral cavity (T1-3, N0) / surgery
44 Jones, '94	Lymph node metastasis of scc in the head and neck
45 Kersh, '90	Scc of the glottic larynx, stage I en II / radiotherapy
46 Barra, '94	Scc in the H&N (larynx, oropharynx, hypopharynx, cavum oris) surgically treated
47 Stell '92	Primary scc of the oral cavity
48 Kowalski, '96	Stage III glottic and transglottic scc / primary treatment surgery or radiotherapy
49 Mak-Kregar, '92	Carcinoma of the base of tonque
50 Zätterström, '95	Squamous cell carcinoma of the head and neck
51 Kowalski, '91	Primary laryngeal cancer / surgery
52 Bundgaard, '96	Intra-oral squamous cell carcinoma
53 Douglas, '95	T1-2 N0 glottic larynx squamous cell carcinoma / definitive radiotherapy
54 Corvo, '95	Scc of the head and neck, stage II-IV (oral cavity, pharynx or larynx / radiotherapy: conventional vs. accelerated)
55 Stell '90	Laryngeal carcinoma

[a] reference number
[b] Scc = squamous cell carcinoma

APPENDIX II

Questionnaire with respect to scales described in the retrospective and prospective study

		page
Uncertainty		204
subscale 1: about the prospects of the illness and treatment	items 1-9	
subscale 2: about possibilities of access to help and about getting solutions to problems related to the illness and treatment	items 10-17	
subscale 3: about how to handle practical consequences of the illness	items 18-28	
subscale 4: uncertainty about how to cope with own emotions	items 29-35	
Loss of Control	8 items	206
Complaints Checklist for Cancer Patients (RSCL)		206
subscale 1: psychosocial complaints	items 1-8	
subscale 2: physical complaints	items 9-15	
subscale 3: head and neck specific complaint	items 16-36	
Openness to discussion of the illness in the family	8 items	208
Feelings of depression	10 items	209
Self-esteem		210
subscale 1: with respect to the ability to perform	items 1-6	
subscale 2: with respect to social functioning	items 7-11	
Cancer Locus of Control/attribution style		211
subscale 1: with respect to the cause of the illness	items 1-3	
subscale 2: with respect to the course of the illness	items 4-10	
subscale 3: with respect to religious control	items 11-13	
Self Efficacy Scale (Ryckman)		212
subscale: physical self-efficacy	7 items	
Self-efficacy with respect to head and neck tumors		213
subscale: self-confidence in oral presentation	items 1-9	
subscale: perceived abilities in swallowing and food intake	items 10-18	
subscale: perceived speech abilities	items 19-23	
Multidimensional Health Locus of Control - internal (Wallston and Wallston)	6 items	214
*State anxiety (Spielberger)**	18 items	215
Loneliness	5 items	216
Appreciation of information from the specialist	3 items	216

* Dutch version in which we excluded 2 items on basis of factor-analysis in several studies.

Uncertainty

Now we are going to present you with some topics for which you perhaps would like to have more information, that is, things you would like to know more about. For each of these topics we want to ask you to indicate the extent to which you need more information ("not at all", "a little", "rather much", or "very much") on those topics. Please place a circle around the answer that seems best to you. Place a circle around:

1 if you would like to know "not at all" more about that subject
2 if you would like to know "a little" more about that subject
3 if you would like to know "rather much" more about that subject
4 if you would like to know "very much" more about that subject

To what extent would you like to know more about:	not at all	a little	some what	very much
1 Your present condition	1	2	3	4
2 The cause of your illness	1	2	3	4
3 The possible course of your illness	1	2	3	4
4 Survival rates of your illness	1	2	3	4
5 Possible consequences of your illness	1	2	3	4
6 The benefit or goal of the treatment	1	2	3	4
7 Possible side-effects of the treatment such as tiredness, an increase in your burden, etc.	1	2	3	4
8 Possible results of the treatment	1	2	3	4
9 The course of things around the treatment (procedure, duration)	1	2	3	4
10 What you can (or are allowed to) do in your situation e.g., working, hobbies, eating, drinking, etc.	1	2	3	4
11 How to find your way (the best way) around a hospital	1	2	3	4
12 What is the best way to talk or interact with a physician	1	2	3	4
13 How to talk with people, who are intimate, about eventual problems related to your illness	1	2	3	4
14 Possibility of getting immediate help if you experience problems and have questions about your illness	1	2	3	4
15 Where to get (good) educational material or literature about your illness and treatment	1	2	3	4
16 Protheses (like wigs etc.)	1	2	3	4
17 How to keep or get psysically fit (exercises and diet)	1	2	3	4
18 How other people, who are in the same circumstances as you, react to their illness and treatment	1	2	3	4
19 Hygienic practices related to your illness	1	2	3	4
20 The best way to dress so that you minimize the chances that others will notice your handicap	1	2	3	4
21 How (and where) to get contact with patients or ex-patients who have (had) the same illness	1	2	3	4
22 How to learn to talk better	1	2	3	4
23 The equipment to make yourself more understandable	1	2	3	4
24 How to function better in general	1	2	3	4

(continued)

To what extent would you like to know more about:	not at all	a little	some what	very much
25 How to increase your self-confidence	1	2	3	4
26 How to enjoy life	1	2	3	4
27 How to make yourself better understood	1	2	3	4
28 The functioning of other patients who have (had) the same illness	1	2	3	4
29 How to act so that others perceive you as more self-assured	1	2	3	4
30 How to learn to control yourself	1	2	3	4
31 How to deal with the problems of the handicap	1	2	3	4
32 How to make yourself more socially useful	1	2	3	4
33 Relaxation-exersices (eg, yoga, respiratory exercises)	1	2	3	4
34 Possibilities of the therapies to understand and accept the illness better	1	2	3	4
35 How to present yourself to other people and how to interact with them	1	2	3	4

Loss of control

We know that in patients sometimes certain reactions can occur as a result of their illness and the treatment it. Below you find some of such possible results. We would like to know if some of them occurred to you.

Please indicate, by marking the squares, at the end of the lines which of these results also occurred in you as a result of your illness and the treatment.

By/since my illness and/or treatment for it:

1 I'm not or only partly able to work or do the house-keeping ☐
2 I had a loss in financial income ☐
3 I have less sexual contact with my partner ☐
4 I can't do in my leisure time what I did formerly ☐
(also think of holidays, sports, hobbies) ☐
5 I became more dependent on others ☐
6 I can control my emotions less ☐
7 I am not quite my usual (old) self again ☐
8 More things bother me ☐

Complaints checklist for cancer patients

In this questionnaire you will be asked about your symptoms. For each symptom mentioned below we would like you to indicate to what extent you suffer, by encircling the answer most applicable to you. For each question please indicate how you have been feeling the past three days.

Example:
If, during the past three days, you suffered "a little" from coughing, you encircle like this:

	not at all	a little	somewhat	very much
coughing	1	[✓ 2]	3	4

	not at all	a little	somewhat	very much
1 Irritability	1	2	3	4
2 Worrying	1	2	3	4
3 Depressed	1	2	3	4
4 Nervousness	1	2	3	4
5 Feel desperate about the future	1	2	3	4
6 Feel lonely	1	2	3	4
7 Feel tense	1	2	3	4
8 Anxious	1	2	3	4
9 Tiredness	1	2	3	4
10 Sore muscles	1	2	3	4
11 Low back pain	1	2	3	4
12 Headache	1	2	3	4

continued

		not at all	a little	somewhat	very much
13	Dizziness	1	2	3	4
14	Tingling hands/feet	1	2	3	4
15	Short of breath	1	2	3	4
16	Feelings of shame during eating	1	2	3	4
17	Difficulty with chewing	1	2	3	4
18	Difficulty with swallowing	1	2	3	4
19	Forming of phlegm	1	2	3	4
20	Coughing	1	2	3	4
21	Problems with dentures	1	2	3	4
22	Not to be able to make yourself intelligible	1	2	3	4
23	The feeling that others don't understand you	1	2	3	4
24	Tickling in the throat	1	2	3	4
25	Difficulty in accepting yourself as you are	1	2	3	4
26	Loss of taste	1	2	3	4
27	Difficulty in controlling yourself	1	2	3	4
28	Difficulty in breathing	1	2	3	4
29	Pain in the body	1	2	3	4
30	Difficulty in keeping patience	1	2	3	4
31	Feeling of restlessness	1	2	3	4
32	Anger	1	2	3	4
33	The feeling of standing all alone	1	2	3	4
34	Difficulty in falling asleep	1	2	3	4
35	Feelings of worthlessness	1	2	3	4
36	Runny nose	1	2	3	4

Openness of discussing the illness in the family

The following eight sentences are about the openness of discussing your illness and its consequences with your partner and/or child(ren). (If you have no partner and also no child(ren) you can omit this question).
Please indicate for each sentence whether you agree or disagree. Following each sentence there are four possibilities for an answer. Pleas encircle the answer that is closest to your opinion. Encircle:

1 if you agree very much with the sentence ("very much")
2 if you agree with the sentence ("agree")
3 if you don't agree with the sentence ("not agree")
4 if you don't agree with the sentence at all ("not agree at all")

	agree very much	agree	not agree	not agree at all
1 I talk as little as possible about my illness because I don't want to make my family uneasy	1	2	3	4
2 My partner doesn't like me to talk about my problems	1	2	3	4
3 My children don't like me to talk about my problems	1	2	3	4
4 If I talk about my illness, others gloss over it	1	2	3	4
5 My family always want to hear from me that I'm doing well	1	2	3	4
6 Talking about emotions related to my illness upsets my family	1	2	3	4
7 My partner often doesn't know what to say or to do when I'm feeling down	1	2	3	4
8 My children often don't know what to say or to do when I'm feeling down	1	2	3	4

Depression (Zung)

Below are some sentences which possibly have to do with how you felt the last few days. We would like to know to what extent these sentences apply to you. For each sentence there are four possibilities for an answer, namely

1 = "seldom or never"
2 = "sometimes"
3 = "often"
4 = "very often or always"

Please read these sentences one by one and each tome encircle the answer that fits best how you felt the last few days.

		seldom or never	sometimes	often	very often or always
1	I feel gloomy and dow	1	2	3	4
2	I have fits of weeping or would like to cry	1	2	3	4
3	I feel tired all the time	1	2	3	4
4	I look forward to the future with confidence	1	2	3	4
5	My mind is just as clear as ever	1	2	3	4
6	I have the feeling that everything I do well as smoothly as ever	1	2	3	4
7	I am more irritable than ever	1	2	3	4
8	I have just as much pleasure as I always had	1	2	3	4
9	I feel spiritless or lifeless	1	2	3	4
10	I don't see the use of many things anymore	1	2	3	4

Self-esteem

Below are some sentences. There are three possible answers for each sentence, namely correct ? incorrect

If you think that at this moment the sentence applies to you, then encircle “correct”, so: [✓ correct] ? incorrect

If you think that at this moment the sentence does not apply to you, then encircle “incorrect”, so: correct ? [✓ incorrect]

only if you are **absolutely not able** to answer with “incorrect” then encircle “?”, so: correct [✓ ?] incorrect

There are no right or wrong answers, so please give your own opinion. Please do not omit a sentence.

1	I feel cheerful	correct	?	incorrect
2	I can handle my problems myself	correct	?	incorrect
3	I can cope with a setback only with great difficulty	correct	?	incorrect
4	I have a lack of self confidence	correct	?	incorrect
5	I am not able to do a lot of work in a short time	correct	?	incorrect
6	Until now I succeeded in getting almost everything I wanted	correct	?	incorrect
7	I think I look good	correct	?	incorrect
8	Others don’t perceive me as attractive	correct	?	incorrect
9	Others find it pleasant to associate with me	correct	?	incorrect
10	Dealing with people is not my strongest point	correct	?	incorrect
11	I can deal better with people than others can	correct	?	incorrect

Cancer Locus of Control/attribution style

Below are some sentences. Some are about possible causes of your illness; others are about (or to what extent) certain persons or things that influence the course of the illness in the future. We are interested in your opinion about these sentences. Following each sentence are four possibilities for an answer. Following each sentence are four possibilities for an answer. Please encircle the answer that reflect your opinion about these sentences most accurately. Encircle:

1 if you "completely agree" with that sentence
2 if you "slightly agree" with that sentence
3 if you "slightly disagree" with that sentence
4 if you "completely disagree" with that sentence

		completely agree	slightly agree	slightly disagree	completely disagree
1	That I became ill has to do with my life-style	1	2	3	4
2	That I became ill is partly my fault	1	2	3	4
3	That I became ill is especially due to myself	1	2	3	4
4	I myself strongly exercise influence upon the course of my illness	1	2	3	4
5	My physician strongly exercises influence upon the course of my illness	1	2	3	4
6	My partner strongly exercises influence upon the course of my illness	1	2	3	4
7	Friends, acquaintances or relatives strongly exercise influence upon the course of my illness	1	2	3	4
8	By living healthily I exercise influence upon the course of my illness	1	2	3	4
9	If I follow the prescriptions of my doctor then I strongly influence the course of my illness	1	2	3	4
10	By fighting against my illness I can influence the course	1	2	3	4
11	That I fell ill is partly because God decided	1	2	3	4
12	God exercises a strong influence upon the course of the illness	1	2	3	4
13	My religion has an influence upon the course of my illness	1	2	3	4

Self Efficacy Scale (Ryckman)

Below are some sentences which are attitude statements about you. We are interested in the extent to which you agree or disagree. Please read each statement carefully. Then indicate the extent to which you agree or disagree by encircling the appropriate number. The numbers and their meaning are as follow:

1 means that you "strongly agree" with the sentence
2 means that you "somewhat agree" with the sentence
3 means that you "slightly agree" with the sentence
4 means that you "slightly disagree" with the sentence
5 means that you "somewhat disagree" with the sentence
6 means that you "strongly disagree" with the sentence

If you find that the numbers to be used in answering do not adequately indicate your opinion, please use the one which is closest to the way you feel.

	strongly agree	somewhat agree	slightly agree	slightly disagree	somewhat disagree	strongly disagree
1 I am not agile and graceful	1	2	3	4	5	6
2 Sometimes I don't hold up well under stress	1	2	3	4	5	6
3 I can't run fast	1	2	3	4	5	6
4 I have physical defects that some times bother me	1	2	3	4	5	6
5 I don't feel in control when I take tests involving physical dexterity	1	2	3	4	5	6
6 I have poor muscle tone	1	2	3	4	5	6
7 I am sometimes envious of those better looking than myself	1	2	3	4	5	6

Head and Neck self efficacy

Below are some sentences which are attitude statements about you. We are interested in the extent to which you agree or disagree with them. Please read each statement carefully. Then indicate the extent to which you agree or disagree by encircling the appropriate number.
The numbers and their meaning are as follows:

1 means that you "strongly agree" with the sentence
2 means that you "somewhat agree" with the sentence
3 means that you "slightly agree" with the sentence
4 means that you "slightly disagree" with the sentence
5 means that you "somewhat disagree" with the sentence
6 means that you "strongly disagree" with the sentence

If you find that the numbers to be used in answering do not adequately indicate your opinion, please use the one which is closest to the way you feel.

		strongly agree	somewhat agree	slightly agree	slightly disagree	somewhat disagree	strongly disagree
1	People usually can't hear me when I speak	1	2	3	4	5	6
2	My pronunciation of words is sometimes poor	1	2	3	4	5	6
3	People do not like the sound of my voice	1	2	3	4	5	6
4	My voice is pleasant	1	2	3	4	5	6
5	Unfortunately, my voice is boring to people	1	2	3	4	5	6
6	My sense of smell is normal	1	2	3	4	5	6
7	My laugh is loud	1	2	3	4	5	6
8	I am sometimes unable to do things because of my physical handicap	1	2	3	4	5	6
9	When I speak, there are many other sounds	1	2	3	4	5	6
10	Speaking tires me	1	2	3	4	5	6
11	I have difficulty sometimes with breathing	1	2	3	4	5	6
12	My face is attractive	1	2	3	4	5	6
13	My appetite is good	1	2	3	4	5	6
14	I have no problems with inhaling air	1	2	3	4	5	6
15	I can swallow well	1	2	3	4	5	6
16	Often I am reluctant to make contacts with strangers	1	2	3	4	5	6
17	I have troubles with eating and drinking	1	2	3	4	5	6
18	I never choke	1	2	3	4	5	6
19	I speak very well	1	2	3	4	5	6
20	I am relaxed when speaking to others	1	2	3	4	5	6
21	People can understand my speach	1	2	3	4	5	6

(continued)

	strongly agree	somewhat agree	slightly agree	slightly disagree	somewhat disagree	strongly disagree
22 I am definitely able to speak long sentences	1	2	3	4	5	6
23 I have good posture	1	2	3	4	5	6

Multi Dimensional Health Locus of Control - Internal

In the following sentences you can indicate how you feel about your health. Please read each sentence and then indicate the answer that applies best to you. With these answers you can indicate how you **think in general about your health.** There are no good or bad answers. Don;t spend too much time to one sentence but give the answer that reflects best to how you perceive your health. You can do that by encircling:

1 which means that you "strongly agree" with the sentence
2 which means that you "somewhat agree" with the sentence
3 which means that you "slightly agree" with the sentence
4 which means that you "slightly disagree" with the sentence
5 which means that you "somewhat disagree" with the sentence
6 which means that you "strongly disagree" with the sentence

	strongly agree	somewhat agree	slightly agree	slightly disagree	somewhat disagree	strongly disagree
1 If I get sick, it is my own behavior which determines how soon I get well again	1	2	3	4	5	6
2 I am in control of my health	1	2	3	4	5	6
3 When I get sick I am to blame	1	2	3	4	5	6
4 The main thing which affects my health is what I do myself	1	2	3	4	5	6
5 If I take care of myself, I can avoid illness	1	2	3	4	5	6
6 If I take the right actions, I can stay healthy	1	2	3	4	5	6

State Anxiety

A number of statements which people have used to describe themselves are given below. Read each statement and then encircle the appropriate answer to indicate how you feel right now, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

		not at all	somewhat	moderately	very much so
1	I feel calm	1	2	3	4
2	I feel secure	1	2	3	4
3	I am tense	1	2	3	4
4	I feel strained	1	2	3	4
5	I feel at ease	1	2	3	4
6	I am presently worrying about possible misfortunes	1	2	3	4
7	I feel satisfied	1	2	3	4
8	I feel frightened	1	2	3	4
9	I feel comfortable	1	2	3	4
10	I feel self-confident	1	2	3	4
11	I feel nervous	1	2	3	4
12	I am jittery	1	2	3	4
13	I am relaxed	1	2	3	4
14	I feel content	1	2	3	4
15	I am worried	1	2	3	4
16	I feel confused	1	2	3	4
17	I feel steady	1	2	3	4
18	I feel pleasant	1	2	3	4

Loneliness

We would like to ask you some questions about how you feel presently. Please indicate whether you agree or disagree with the following sentences.

If you agree with the sentence, then encircle "agree".
If you disagree with the sentence, then encircle "disagree".

1	Real friends are hard to find	agree	disagree
2	When all is said and done, almost nobody cares about you	agree	disagree
3	Sometimes it is very difficult to make lasting contacts	agree	disagree
4	I sometimes feel very lonely	agree	disagree
5	Sometimes I have the feeling that, in the final analysis, you are alone in the world	agree	disagree

Evaluation of information from physician

The following 3 questions are about the information you received from the physician(s) about your illness and treatment.
Please answer with a "yes" or "no".

Did you think this information was:

1	Given frankly?	yes	no
2	Given too hastily?	yes	no
3	Given completely?	yes	no

DANKWOORD

Ere wie ere toekomt...

Prof.dr H.W. Van den Borne, Dr J.F.A. Pruyn, Prof. R.M. Ryckman, the "research team", that made it all possible to happen! (elke poging tot het aanbrengen van een volgorde anders dan alphabetisch, zou iemand te kort doen)

Dr C.A. Meeuwis, de collega op de werkvloer, die bergen patiëntenwerk verzette om de auteur van dit geschrift "uit de wind te houden".

Prof.dr C.D.A. Verwoerd, de grote stimulator als het er op aan komt, die ook in de details sterk is.

Prof.dr P.C. De Jong, de geestelijke vader van het concept dat de hoofd-hals-patient meer zorg behoeft dan de behandeling van zijn tumorproces.

Dr P.P. Knegt, met waardevolle opmerkingen over het werk als geheel en intensieve bemoeienis met hoofdstuk 4.

Prof.dr S.E.R. Hovius, Prof.dr J. Passchier en Prof.dr G. Stoter, leden van de "kleine commissie", die de moeite hebben genomen het manuscript op de wetenschappelijke waarde te beoordelen.

Dr W.M.H. Eijkenboom las het manuscript kritisch door.

De leden van de Werkgroep Hoofd-HalsTumoren Rotterdam van toen en nu (huidige voorzitter S.J.M. Wijthoff) die, bewust of onbewust, hebben deelgenomen aan dit project, al was het maar door de deelnemende patiënten multidisciplinair te begeleiden.

M.A. Smit Jongbloed-Ter Pelkwijk, drs. R.S.M. De Reuver en drs. L.J. Bosman, destijds leden van de projectgroep en in een latere fase dr I. Mesters, die zich o.a. intensief met datamanagement en dataverwerking hebben beziggehouden.

Alle medewerkers van het AZR Dijkzigt en Daniel den Hoed, die direct of indirect bij het tot stand komen van dit werk betrokken zijn geweest.

De patiënten die – aan beide zijden van de Maas – hebben meegewerkt aan de onderzoeksprojecten.

En als eerste....
Drs. Carien C. Van Hoogevest, die met mij huwde terwijl bekend was dat deze "scriptie" nog afgemaakt moest worden en de soms ondankbare ondersteuning op het thuisfront verzorgde.

PUBLICATIONS CONCERNING THE HEAD AND NECK REHABILITATION RESEARCH

1. De Boer, MF, Bosman LJ, Schmit-Jongbloed-ter Pelkwijk MA, De Reuver RSM, Van den Borne HW, Knegt PP, Pruyn JFA, De Jong PC. Medische en psychosociale rehabilitatie van patiënten behandeld vanwege een carcinoom in het hoofd-halsgebied. Een verslag van de voorbereidingsfase van een longitudinale studie, 304 blz. Werkgroep Hoofd- halstumoren/IVA, Rotterdam/Tilburg, februari 1988.

2. Pruyn JFA, Van den Borne HW, De Reuver RSM, De Boer MF, Bosman LJ, Ter Pelkwijk MA, De Jong PC. De Locus of Control-schaal voor kankerpatiënten. *Tijdschrift voor Sociale Gezondheidszorg* 1988;66:404-8.

3. Wouterlood-van Cleeff, IE, De Boer MF, Molendijk LW, De Jong PC, Knegt P, Pruyn JFA , Visch LL. Nazorg bij Hoofd-Halstumoren. Een onderzoek naar knelpunten die hulpverleners ervaren bij de nazorg voor patiënten die behandeld zijn voor een hoofd-halstumor in de regio van het IKR. Rotterdam, april 1989.

4. Schmit Jongbloed-ter Pelkwijk MA, De Jong PC, Bosman LJ , De Boer MF, Knegt PPM, Pruyn JFA. Logopedische klachten bij patiënten met een tumor in het hoofd-halsgebied. *Logopedie en Foniatrie* 1989;61:380-5.

5. De Boer, MF, Bosman LJ, Van den Borne HW, Knegt PP, Pruyn JFA, De Jong PC. Medische en psychosociale rehabilitatie van patiënten behandeld vanwege een carcinoom in het hoofd-halsgebied. Een transversale studie, 222 blz. Werkgroep Hoofd- halstumoren/IVA, Rotterdam/Tilburg, februari 1991.

6. Wouterlood-van Cleeff, IE, De Boer MF, De Jong PC, Pruyn JFA, Molendijk LW, Visch LL, Knegt PP. Knelpunten in de zorg voor hoofd-halstumorpatiënten. Een veldonderzoek. *Medisch Contact* 1991;6:179-181.

7. Bosman LJ, Fabert JMW, Pruyn JFA, Schmit-Jongbloed-ter Pelkwijk MA, De Boer MF, Van den Borne HW, De Jong PC, Ryckman RM. Judging speech communication effectiveness in oral cancer patients. *J Commun Disord* 1991; 24:40-50.

8. Pruyn JFA, Meeuwis CA, Baak A, Brand E, Cats A, Van der Does E, Van der Graaf N, Van der Jagt T, De Jong PC, Knegt PP, Van Wersch AMEA, De Boer MF. Het logboek-project: resultaten van de pilot-studie. *IKR-bulletin* 1994; 19:37-40.

9. De Boer MF, Pruyn JFA, Van den Borne B, Knegt PP, Ryckman RM, Verwoerd CDA. Rehabilitation outcomes of long-term survivors treated for head and neck cancer. *Head Neck* 1995;17:503-515.

10. Pruyn JFA, De Boer MF, Heerema NC, Kiezebrink ML, Wiggers Th. Supportive Care [Ondersteunende Zorg]. *Ned Tijdschr Geneeskd* 1995;139:342-6.

11. Van Wersch AMEA, De Boer MF, Pruyn JFA, Meeuwis CA, Baak A, Brand E, Cats A, Van der Does E, Van der Graaf N, Van der Jagt T, De Jong PC, Knegt PP. Verbetering van continuïteit van voorlichting aan patiënten die behandeld worden voor een tumor in het hoofd-/halsgebied door coördinatie en gebruik van een logboek: de eindrapportage. IGO, Willemstad, oktober 1995.

12. De Boer MF, Meeuwis CA, Knegt PP, Van Wersch AMEA, Pruyn JFA. Een logboek voor kankerpatiënten? Dat werkt! *Tijdschrift Kanker.* februari 1997.

13. Van Wersch A, De Boer MF, Van der Does E, De Jong P, Knegt P, Meeuwis CA, Stringer P, Pruyn JFA. Continuity of information in cancer care: evaluation of a logboek. *Patient Education Counseling.* 1997;31:223-36.

14. Mesters I, Van den Borne H, McCormick L, Pruyn J, De Boer M, Imbos T. Openness to discuss cancer in the nuclear family scale, development and validation. *Psychosom Med* 1997;59:269-79.

15. De Boer MF. Voorlichting en communicatie bij de behandeling van patienten met maligne tumoren in het hoofd-halsgebied. Is het logboek een onmisbaar hulpmiddel? *Nederlands Tijdschrift voor Keel-,Neus- en Oorheelkunde* 1998; 4:p.5.

16. De Boer MF, McCormick LK, Pruyn JFA, Ryckman RM, Van den Borne HW. Physical and psychosocial correlates of head and neck cancer: a review of the literature. *Otolaryngol Head Neck Surg* in press.

17. De Boer MF, Ryckman RM, Pruyn JFA, Van den Borne HW. Psychosocial correlates of cancer relapse and survival: a review of the literature. *Patient Education and Counselling* in Press.

18. De Boer MF, Van den Borne HW, Ryckman RM, Volovics l, Knegt PP, Meeuwis CA, Mesters I, Verwoerd CDA. Psychosocial and physical correlates of survival and relapse in head and neck cancer patients: results of a 6-year longitudinal study. *Cancer* in press.

CURRICULUM VITAE

Geboren	28-02-1946
1959-1966	Gymnasium beta, Huygens Lyceum, Voorburg
1966-1973	Studie geneeskunde, Rijks Universiteit Groningen
1973-1974	Militaire Dienst (Landmacht), arts-assistent afdeling KNO Heelkunde in Militair hospitaal, Den Haag, hoofd Dr A.C.W. Derks
1974-1978	Arts-assistent KNO-Heelkunde, Academisc Ziekenhuis Rotterdam, Prof.dr W.H. Struben en Prof.dr E.H. Huizing
1978-1980	Opleiding hoofd-halschirurgie, Daniel den Hoed-kliniek hoofd Prof. dr P.C. De Jong
1979-1985	Staflid afdeling KNO/Hoofd-Halschirurgie Daniel den Hoed-Kliniek
1979-1981	part-time KNO-arts in Gasthuis, Middelburg en Bethesda/Sint Jozef Ziekenhuis, Vlissingen
1981-1986	part-time KNO-arts in Eudokia Ziekenhuis Rotterdam
1985-1996	Hoofd afdeling KNO/Hoofd-Halschirurgie Daniel den Hoed Kliniek
1984-1989	Voorzitter Werkgoep Hoofd-Halstumoren Rotterdam
1996-heden	Staflid afdeling Keel-, Neus- en Oorheelkunde Academisch Ziekenhuis Rotterdam, hoofd Prof.dr C.D.A. Verwoerd
1985-1995	Lid van het Dagelijks Bestuur van de Nederlands Werkgroep Hoofd-Halstumoren
1995-heden	Lid van het Algemeen Bestuur van de Nederlands Werkgroep Hoofd-Halstumoren