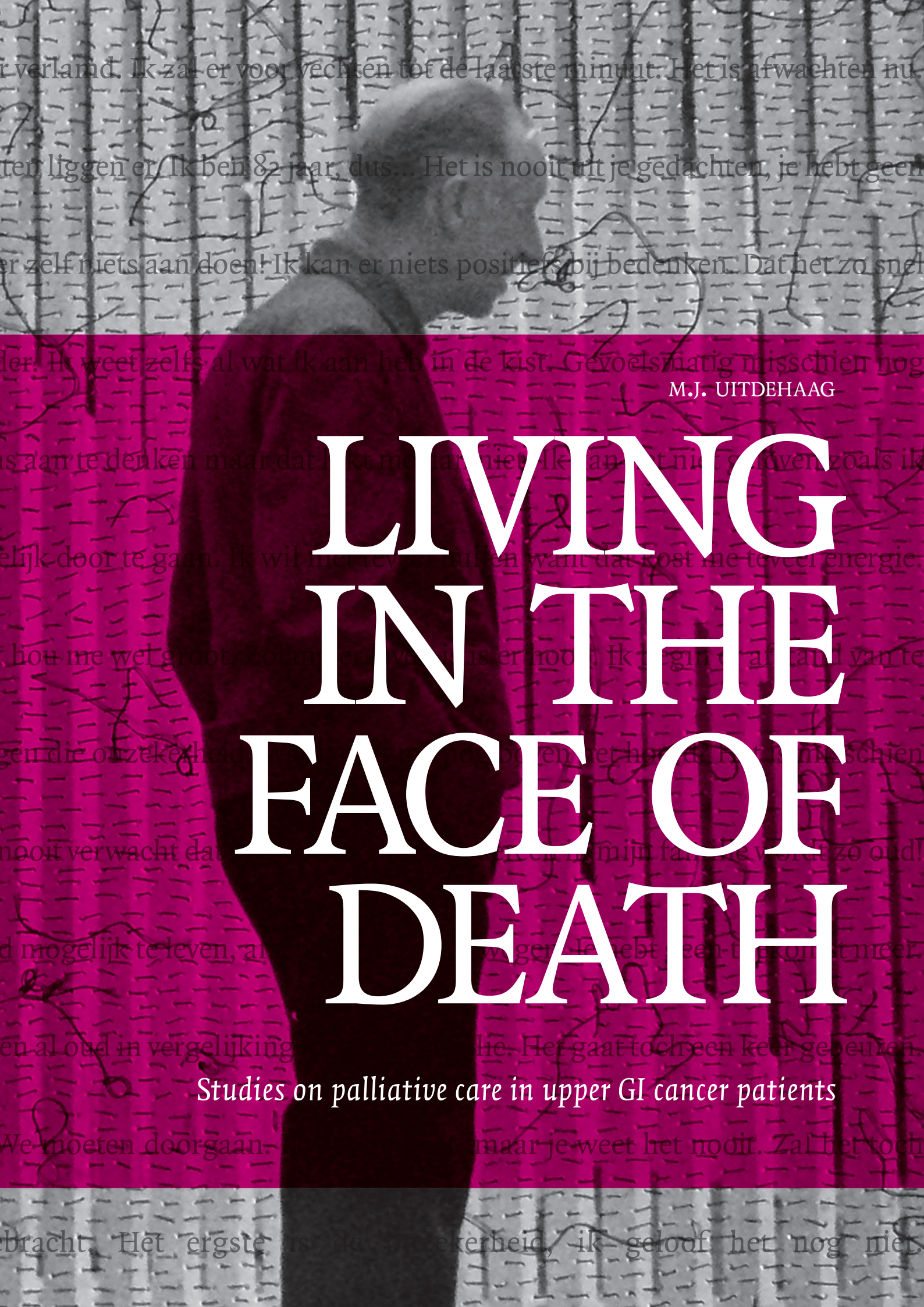


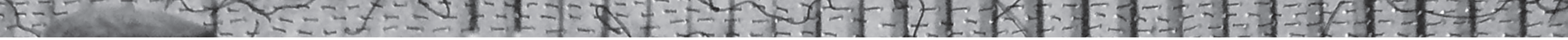
M.J. UITDEHAAG

# LIVING IN THE FACE OF DEATH

*Studies on palliative care in upper GI cancer patients*

# LIVING IN THE FACE OF DEATH

M.J. Uitdehaag 2012



# LIVING IN THE FACE OF DEATH

Studies on Palliative Care in Upper GI Cancer Patients
Leven in de wetenschap dat de dood dichtbij is
(Studies met betrekking tot de palliatieve zorg voor
patiënten met kanker in het bovenste spijsweg kanaal)

**Proefschrift**

*ter verkrijging van de graad van doctor*
*aan de Erasmus Universiteit Rotterdam*
*op gezag van de rector magnificus*
*Prof. Dr. H.G. Schmidt en volgens besluit*
*van het College voor Promoties.*

*De openbare verdediging zal plaatsvinden op*
*donderdag 14 juni 2012 om 13.30 uur*

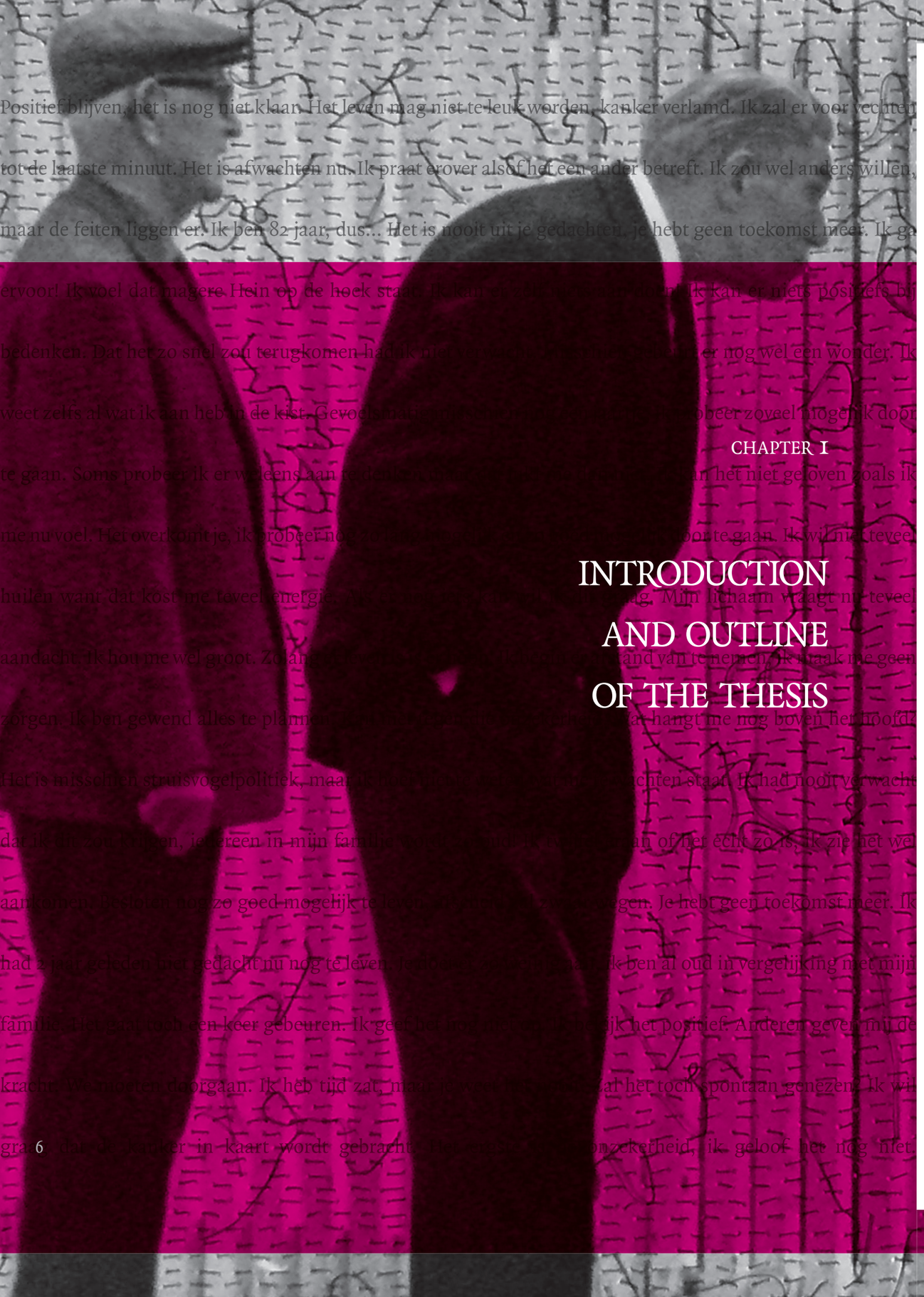
**Magdalena Joanna (Madeleen) Uitdehaag**
*Geboren te Essen (België)*

**LIVING IN THE FACE OF DEATH**



| | |
|---|---|
| **Promotoren** | Prof. dr. E.J. Kuipers<br>Prof. dr. P.D. Siersema |
| **Overige leden** | Prof. dr. H.W. Tilanus<br>Prof. dr. J. Passchier<br>Prof. dr. J.F.A. Pruijn |

*Het leven is geneigd ons de juiste richting te wijzen (Deepak Chopra)*



CHAPTER 1

# INTRODUCTION AND OUTLINE OF THE THESIS



## INTRODUCTION

In the Netherlands, more than 40.000 persons die annually due to cancer.[1] Cancers of the gastrointestinal tract account for approximately 23% of human malignancies. As result, the gastrointestinal tract is affected more often by cancer than any other tract in the human body. Among gastro intestinal (GI) cancers, the highest incidence is observed for colorectal cancer.[2-5] While colorectal cancer is associated with an approximate 45% mortality rates, the fatality rates from some other GI cancers are even worse. For example, the 5-year survival rates for esophageal, liver, gallbladder, bile ducts and pancreas cancer range between 4 and 17%.[4, 5] In the Netherlands, between 2004 and 2008 the incidences of these cancer types, except gallbladder, increased with approximately 20%. The most marked increase was noted for esophageal adencarcinoma[5], which showed an increase from 281 in 1998 to 844 in 2003.[6]

The low survival rate for these types of upper GI cancer is mainly due to the fact that presenting symptoms are often absent or non-specific and long evolving before medical attention is sought.[7-9] Consequently, these cancers are usually diagnosed at an advanced stage when curative options are limited.[8-10] Moreover, even patients who are able to undergo treatment with a curative intent often relapse.[10-12] Both patient categories require palliative care.

Palliative care is defined by World Health Organization (WHO) as an approach that improves the quality of life (QoL) of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.[13] This implies that palliative care primarily aims at improvement of QoL of patients and their families.

## QUALITY OF LIFE

Quality of life contains five types of measures of patient outcomes (Figure 1).[14] This firstly includes biological function, which describes the function of cells, organs, and organ systems. Biological function can be assessed through physical examination, laboratory tests, and further diagnostic work-up. The second domain which determines QoL includes physical, emotional, and cognitive symptoms perceived by a patient. The most common dimensions of symptoms that are measured include frequency, intensity, and distress. Functional status, the third component of QoL, is composed of physical, psychological, social, and role function. The fourth domain consists of general health perceptions, which refers to a subjective rating that includes all of the health concepts that precede it. This component is most commonly measured with a single global question to ask people to rate their health on a Likert scale ranging from poor to excellent. Fifth, overall quality of life, is described as subjective well-being, which means how happy or satisfied someone is with life as a whole. Life satisfaction can be measured through a single global question, asking how satisfied the person is with life in general, or through a series of questions about satisfaction with various aspects of life.

All these outcomes are influenced by individual characteristics (such as body composition and function, motivation, cognitive appraisal) and environment characteristics (such as family, friends and health care providers; significant others can have a strong influence over when and where health care is sought and whether treatment is adhered to). Healthcare interventions to improve or maintain quality of life of patients can therefore be directed towards individual as well as environment characteristics.

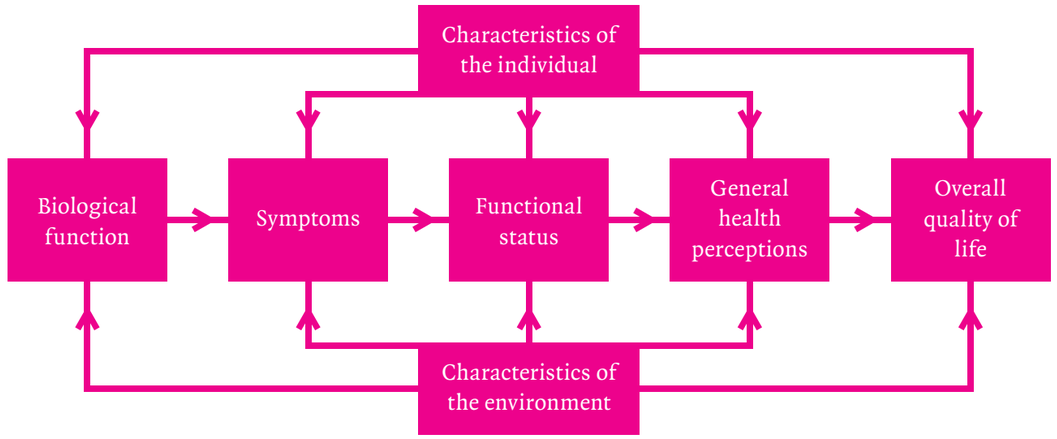



**Figure 1.** *Revised Wilson and Cleary model for health-related quality of life.*[14]

## OUR QUESTIONS

At the start of this thesis, palliative care in the hospitals began to develop. This was mainly boosted by the work of six centres for development of palliative care, divided over the Netherlands. These centres were identified by the ministry of health, welfare and sport in 1998, which carried their work on to the comprehensive cancer centres in 2004. In our hospital there was little attention for palliative care, while many people at the gastrointestinal liver ward were faced with a palliative diagnosis. Depending on the professional, the palliative phase was marked clearly for the patient which empowered them to be involved in further treatment decisions, attention was paid to more than just physical symptoms and patients were offered an opportunity to hospital based follow-up after the bad news. We wanted to develop a uniform policy for these patients where QoL was the most important outcome. Therefore it was necessary to start with the main problems these patients experienced after the transition to the palliative phase of the disease. Furthermore, the high rate of hospital based re-interventions for dysphagia or gastric outlet obstruction in this group of patients was worrying, especially when we take into account the effect of this on QoL. We want to find a new stent design with less migration, nontumoral or tumoral tissue ingrowth and overgrowth, and food-bolus obstruction, with the least possible number of complications.

## AIM

The general aim of this thesis was to explore the main problems and needs of patients with incurable upper GI cancer and to study different interventions to maintain or improve their quality of life.

## OUTLINE OF THIS THESIS

The outline of this thesis is shown graphically in Figure 2. The transition from care with curative intent to palliative care marks a drastic change in the life-expectancy of a patient, and thus drastically and negatively patient's view of her or his future and the patient has to adjust to this new situation. Several studies claimed that the provision of recordings of key consultations benefit most adults with cancer in terms of recalling and understanding the information[15, 16], receiving support[16-18], and to feel more empowered during the next consultation.[19-21] Although there is a lack of evidence about the potential value of tapes at the palliative stage of cancer care.[15] In this thesis we investigated the feasibility (in terms of technical and procedural problems) and utility (in terms of appreciation and listening), of the provision of CD recordings on consultations involving the transition to palliative care for patients with irresectable or recurrent esophageal or head or neck cancer (chapter 2).

Knowledge of symptom prevalence and intensity, and health care needs of patients with non-curable GI cancer is important in clinical practice as it enables professional caregivers to focus on these issues and achieve optimal symptom control of patients. Symptom control is paramount in order to allow the patient to achieve the best quality of life possible in the remaining time left. In this thesis, we therefore aimed to explore the specific problems and needs of patients with advanced upper GI cancer (chapter 3).

For patients with esophageal cancer as well as for patients with cancer of the periampullary area (head of the pancreas, distal bile duct, papilla of Vater), and with distal stomach or duodenal cancer, dysphagia is known as a common symptom, causing significant distress.[9, 22] Self-expandable metal stents are commonly used for the palliation of malignant obstruction because of inoperable disease. Although much progress have been made in the last ten years in stent treatment, further improvements are needed in terms of a lower rate of re-intervention mainly due to non-malignant tissue overgrowth and migration.[9] Several new developed stents were studied with focus on both safety and efficacy (chapter 4).

Nurses have provided major input in the evolution of palliative care for patients with GI cancer. The role of nursing personnel has expanded in recent years.[23] Clinical nurse specialists and nurse practitioners have established a position as physician substitutes, performing tasks and procedures previously solely performed by physicians. This phenomenon is mostly seen in follow-up of patients with chronic disorders. We recently performed a study in which patients after intentionally curative surgery for oesophageal or gastric cardia cancer were randomized to standard follow-up by surgeons at the outpatient clinic or by regular home visits of a specialist nurse.[24] We found that nurses can well perform follow-up of patients at home after upper gastrointestinal cancer surgery, and we hypothesized that this intervention could have the same positive effects for patients in the palliative stage of their disease. On the basis of the main problems experienced by patients with advanced upper GI cancer (chapter 3), we developed guidelines for nurse-led follow-up of patients with advanced upper GI cancer. In this thesis we evaluated nurse-led follow-up for palliative GI cancer patients by home visits compared with the usual medical follow-up in outpatient clinic in a randomized study (chapter 5).

In chapter 6, the main results of the thesis are summarized, followed by a reflection on the methodology, the general conclusions concerning the main objectives of the thesis and implications for further research and practice.





M.J. Uitdehaag | Living in the face of death

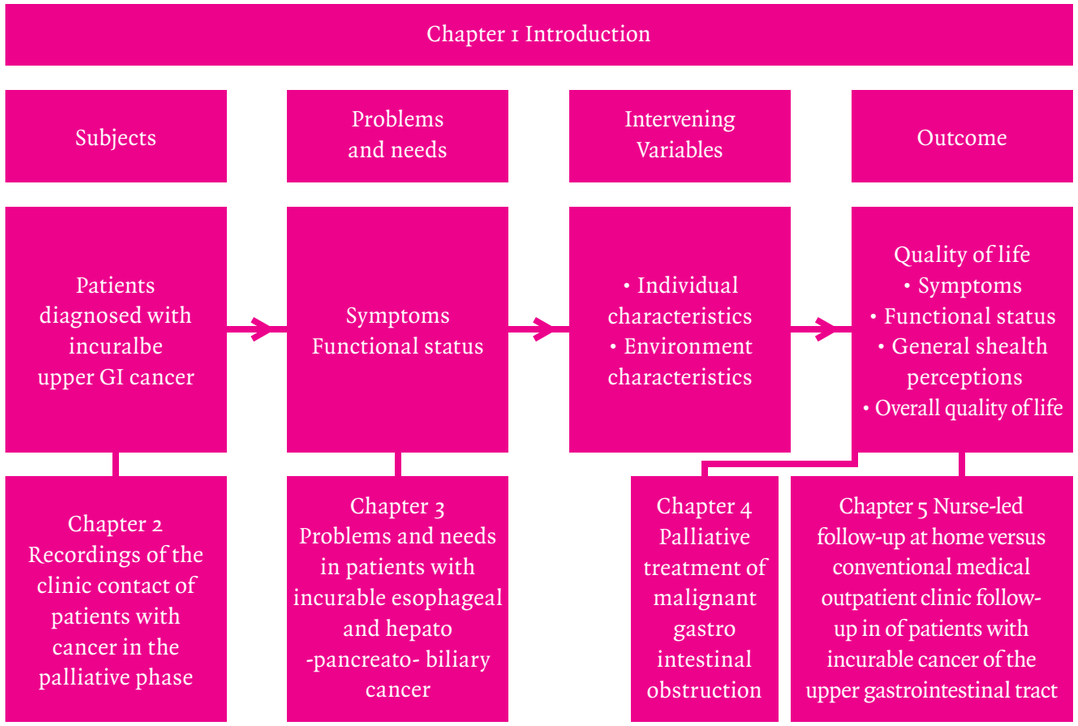



**Figure 2.** *Outline of this thesis.*

## REFERENCES

1. CBS. Centraal Bureau voor de Statistiek (Statistics Netherlands). 2012; http://statline.cbs.nl; (assessed 16-02-2012).

2. Ferlay J, Autier P, Boniol M, et al. Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol 2007;18:581-592.

3. Parkin DM, Bray F, Ferlay J, et al. Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74-108.

4. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62:10-29.

5. IKNL. Integraal Kankercentrum Nederland (Comprehensive Cancercentre the Netherlands). 2012; http://cijfersoverkanker.nl/; (assessed 18-02-2012).

6. Crane LM, Schaapveld M, Visser O, et al. Oesophageal cancer in The Netherlands: increasing incidence and mortality but improving survival. Eur J Cancer 2007;43:1445-1451.

7. Gullo L, Tomassetti P, Migliori M, et al. Do early symptoms of pancreatic cancer exist that can allow an earlier diagnosis? Pancreas 2001;22:210-213.

8. Klapman J, Malafa MP. Early detection of pancreatic cancer: why, who, and how to screen. Cancer Control 2008;15:280-287.

9. Siersema PD. New developments in palliative therapy. Best Pract Res Clin Gastroenterol 2006;20:959-978.

10. Cha CH, Saif MW, Yamane BH, et al. Hepatocellular carcinoma: current management. Curr Probl Surg 2010;47:10-67.

11. Hulscher JB, van Sandick JW, Tijssen JG, et al. The recurrence pattern of esophageal carcinoma after transhiatal resection. J Am Coll Surg 2000;191:143-148.

12. Orr RK. Outcomes in pancreatic cancer surgery. Surg Clin North Am 2010;90:219-234.

13. WHO. World Health Organisation. 2003; http://www.who.int/cancer/palliative/definition/en/; (assessed 16-2-2012).

14. Ferrans CE, Zerwic JJ, Wilbur JE, et al. Conceptual model of health-related quality of life. J Nurs Scholarsh 2005;37:336-342.

15. Scott JT, Harmsen M, Prictor MJ, et al. Recordings or summaries of consultations for people with cancer. Cochrane Database Syst Rev 2003:CD001539.

16. Ong LM, Visser MR, Lammes FB, et al. Effect of providing cancer patients with the audiotaped initial consultation on satisfaction, recall, and quality of life: a randomized, double-blind study. Journal of Clinical Oncology 2000;18:3052-3060.

17. McHugh P, Lewis S, Ford S, et al. The efficacy of audiotapes in promoting psychological well-being in cancer patients: a randomised, controlled trial. British Journal of Cancer 1995;71:388-392.

18. Knox R, Butow PN, Devine R, et al. Audiotapes of oncology consultations: only for the first consultation? Annals of Oncology 2002;13:622-627.

19. Wilkes L, White K, O'Riordan L. Empowerment through information: supporting rural families of oncology patients in palliative care. Aust J Rural Health 2000;8:41-46.

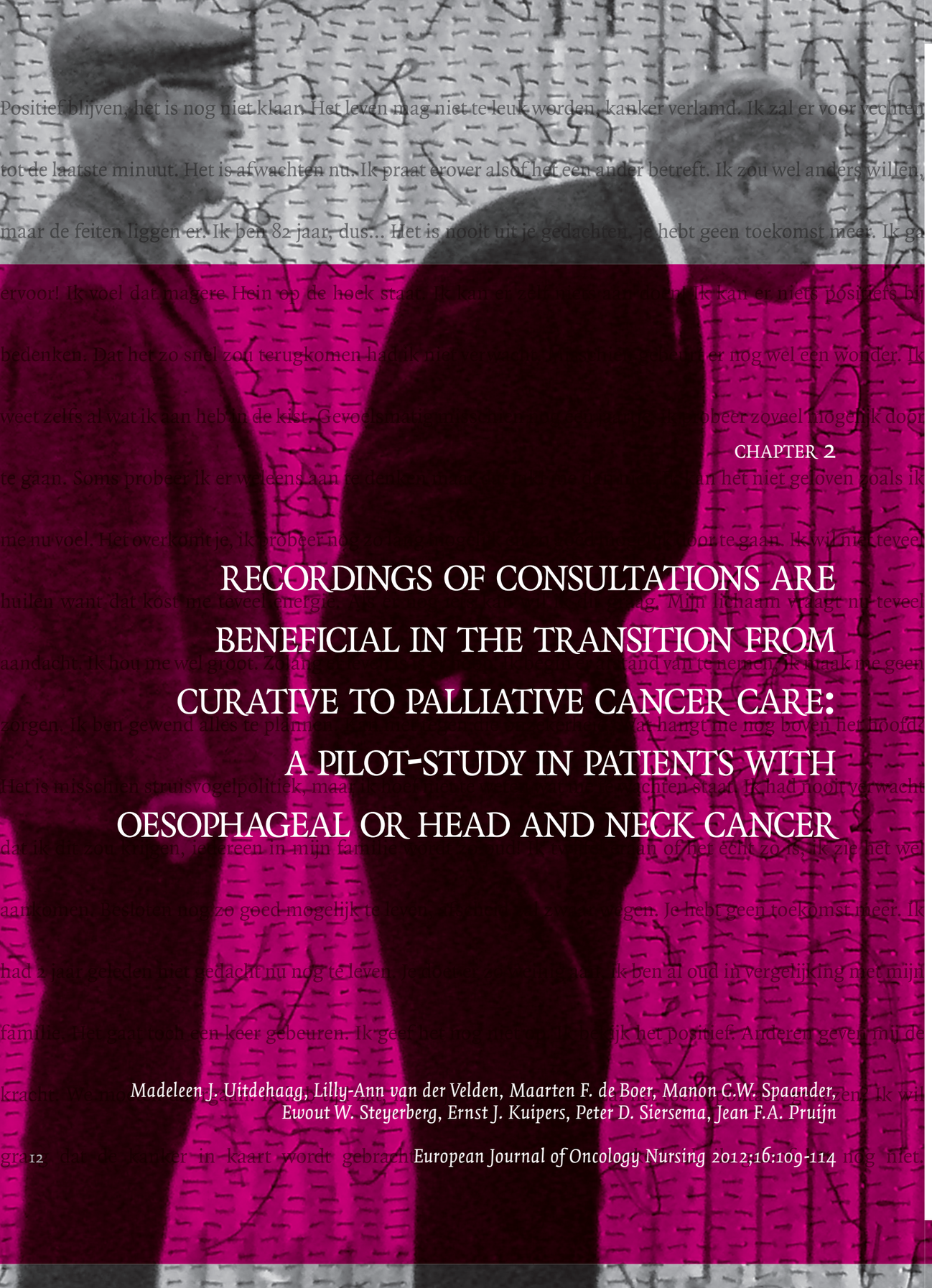
20. Davison BJ, Degner LF. Empowerment of men newly diagnosed with prostate cancer. Cancer Nurs 1997;20:187-196.

21. Gaston CM, Mitchell G. Information giving and decision-making in patients with advanced cancer: a systematic review. Soc Sci Med 2005;61:2252-2264.

22. Chekan EG, Clark L, Wu J, et al. Laparoscopic biliary and enteric bypass. Semin Surg Oncol 1999;16:313-320.

23. Verschuur EM, Kuipers EJ, Siersema PD. Nurses working in GI and endoscopic practice: a review. Gastrointest Endosc 2007;65:469-479.

24. Verschuur EM, Steyerberg EW, Tilanus HW, et al. Nurse-led follow-up of patients after oesophageal or gastric cardia cancer surgery: a randomised trial. Br J Cancer 2009;100:70-76.



CHAPTER 2

# RECORDINGS OF CONSULTATIONS ARE BENEFICIAL IN THE TRANSITION FROM CURATIVE TO PALLIATIVE CANCER CARE: A PILOT-STUDY IN PATIENTS WITH OESOPHAGEAL OR HEAD AND NECK CANCER

*Madeleen J. Uitdehaag, Lilly-Ann van der Velden, Maarten F. de Boer, Manon C.W. Spaander, Ewout W. Steyerberg, Ernst J. Kuipers, Peter D. Siersema, Jean F.A. Pruijn*

*European Journal of Oncology Nursing 2012;16:109-114*





**Purpose:** There is reluctance in providing incurable cancer patients with recordings of their consultation. In this pilot-study, we explored the feasibility and utility of providing consultation recordings when patients are told a new diagnosis of non-curable cancer, and the impact of the recordings on quality of life and the openness to discuss cancer-related issues in the family.

**Method:** Seventeen patients with a new diagnosis of incurable oesophageal or head and neck cancer were randomized to receive a CD (n = 10) or no CD (n = 7) of their consultation in which the diagnosis was told and the decision to provide only palliative care was discussed. Data were collected before consultation and 1 week and 1 month afterwards. After 1 month, patients allocated to the control group were offered to receiving the CD of their consultation as well.

**Results:** No major technical or procedural problems were encountered. Three-quarters of the patients appreciated receiving the CD, which was listened to by 8/10 patients and by 10/10 others in the CD group. After 1 month, two-thirds of the patients in the control group also asked to receive the CD. We found a trend towards a poorer quality of life but an improved openness to discuss cancer-related issues, in the CD group.

**Conclusion:** The provision of a CD recording on the consultation in which the transition from a curative to a palliative care stage was communicated is feasible and was well-received by most cancer patients and their family. These findings require however verification in a study with a larger sample size.

## INTRODUCTION

Cancer patients and their relatives have been shown to appreciate receiving a recording of oncological consultations.[1-8] This is particularly true when patients are overwhelmed by the complexity and emotional impact of the information. The recording can help to recall and understand the information provided.[3, 4, 6, 8-14] However, patients with a poor prognosis recalled less of the provided information.[15] In addition, the recording may also help patients to receive support from family members. The provided information could be a starting point to initiate discussions about the illness, its treatment and its implications.[3, 4, 6, 8, 10, 16] It has been shown that patients feel more empowered during subsequent consultations when they have listened to a recording of a previous consultation.[9, 17] Finally, recordings may improve patients' confidence and trust in cancer healthcare providers[3], as well as patients' satisfaction with the consultation .[6, 12, 18]

Despite these benefits of a recording, only one study has found evidence of a positive effect on psychological well-being of patients, i.e., a reduction of anxiety.[11] All other studies assessing psychological well-being in terms of anxiety, depression, mood state, psychological adjustment or quality of life (QoL), were not able to demonstrate a differential effect between the groups that did or did not receive recordings of their consultation.[1, 2, 6, 8, 10, 19-21] Moreover, it has even been suggested that providing recordings of cancer consultations might be detrimental for a subgroup of patients, i.e., patients with a poor prognosis.[5, 7] These patients showed less improvement in psychological well-being during follow-up than controls without a recording, probably because the detailed information had a negative impact on the process of adaptive denial.[10]

Patients diagnosed with oesophageal or head and neck cancer often present with debilitating

symptoms from advanced disease and a poor prognosis.[22, 23] Furthermore, these cancer types have been found to correlate with socio-economic deprivation.[24, 25] It is known that a lower socio-economic status is related to a lower family income, lower educational attainment and limited access to health information (human capital), a widowed/divorced status and unemployment (social capital), and a lower quality of life. The consultation in which the transition from curative to palliative care is discussed is distressing to most advanced cancer patients and their relatives[26-28], but even more distressing to patients with less material-, human- and social capital.[29-31]

To the best of our knowledge, no previous studies have investigated the effect of CD recordings of consultations on QoL in patients with a new diagnosis of incurable oesophageal or head and neck cancer. We therefore performed a pilot-study to explore: i) the feasibility of receiving a CD recording in terms of technical and procedural problems, ii) the utility (did patients appreciate to receive the CD and did they listen to the CD), and iii) the impact on quality of life of patients and their ability to discuss cancer-related issues with relatives.

## MATERIALS AND METHODS

### Patients

Sixty-eight consecutive patients with incurable or recurrent oesophageal or head or neck cancer from the departments of Gastroenterology and Hepatology and Otorhinolaryngology of a large university referral hospital were identified between January 2007 and April 2008. Patients were eligible if during a multidisciplinary, tumour-specific oncology group meeting it was decided that a curative modality was no (longer) possible. Twenty-five of the 68 patients were found to be eligible, whereas 43 (63%) patients were excluded because they met one of the exclusion criteria, i.e., already partially or fully informed on the diagnosis and/or the palliative treatment options by telephone or in another way (n = 40), no CD player at home (n = 2) or bring their own recorder to the consultation (n = 1) (Figure 1). The medical ethics committee of the hospital approved the study. All patients gave written informed consent.

### Procedure

Eight physicians (2 gastroenterologists, 3 otolaryngologists and 3 surgeons) recorded the 'transition to palliative care' consultations of included patients. At least one day before the consultation, all patients were informed about the study by the investigator (MU). Patients were told that they would receive the results of diagnostic investigations and/or therapeutic options during the following consultation and were asked to participate in the study. When interested in participating, patients received the informed consent form. Just before the consultation, they were asked to fill out a questionnaire in a separate room at the outpatient clinic (T0). After informed consent, the consultation was recorded using a small digital voice recorder with a built-in microphone (Olympus WS-320M®). All patients gave permission to the investigator to be present in the room during the consultation as well. The investigator documented all procedures performed and managed any technical problems during the consultation. During the consultation, the patient, physician and the investigator were blinded to whether the patient was randomized to the CD or no CD group. Randomization was done with stratification for type of cancer using numbered forms corresponding to the patients' order of entry into the study. Patients who were randomised to receive the CD of the consultation received this within 2 days by mail. Questionnaires were sent by mail to the patients 1 week (T1) and 1 month (T2) after the consultation.

Once the investigator received the second follow-up assessment, patients allocated to the control group were offered to receive the CD of the consultation as well.

### Questionnaires

At baseline (T0), patient (age, gender, educational level, marital status, need for information), disease (tumour site, previous treatment, months since initial diagnosis) and consultation characteristics (discussed indication for palliative stage and palliative treatment) were recorded.

Outcome measures at T1 and T2 included all procedural and technical problems, interest in receiving the CD and use of the CD. Patients completed these outcome data on a self-developed questionnaire, whereas technical and procedural problems during consultation were observed by the researcher. Quality of life and openness to discuss cancer in the family were evaluated with the EORTC QLQ-C15-PAL[32], the Patient Information Need Questionnaire (PINQ)[33], the Hospital Anxiety and Depression (HAD) scale, the Loss of Control scale[34] and the Openness to Discuss Cancer in the Family scale (ODCF scale).[34,35] The questionnaires (except the ODCF scale) comprise a total of 17 quality of life issues.

### Statistics

Procedural and technical problems were reported and main endpoints were extracted. Frequencies were calculated for descriptive analyses. Differences in patient characteristics between compliant and dropout patient were analysed by the Chi square test. The differences between the CD and no CD group in quality of life questionnaires and ability to discuss cancer-related topics with relatives at 1 week and 1 month were analysed by linear regression, corrected for baseline score. Internal reliability of the questionnaires was assessed using Cronbach's alpha, with values ≥ 0.7 considered to be acceptable.[36] Analyses were conducted using Statistical Package for Social Sciences (SPSS) version 14.0.

## RESULTS

Twenty-one (84%) of the eligible 25 patients agreed to participate, of which a total of 10/11 patients from the CD group and 7/10 patients from the control group could be analysed (68%) (Figure 1). Of these, 4 patients were lost to follow-up in the first week after consultation. One was too ill and one was admitted to the hospital for cancerrelated morbidity. Two other patients, both from the no CD group, gave no reason for their refusal for further participation. The dropout patients (n = 4) were more frequently living alone and had less frequently undergone a curative treatment in the past than the other included patients (75% vs. 24% (p = .05) and 0% vs. 47% (p = .05), respectively) (results not shown). Three other patients were lost to follow-up at 1 month (Figure 1). Patient, disease and consultation characteristics are shown in Table 1. All patients who were living alone were allocated to the CD group. Nine patients received a previous curative treatment and the time since the initial diagnosis of cancer was for most patients around two (no CD group) and six months (CD group) ago. Six patients saw their physician for the first time, of which two for the first time heard a diagnosis of cancer (besides the diagnosis of incurability) and four were referred for a second opinion.







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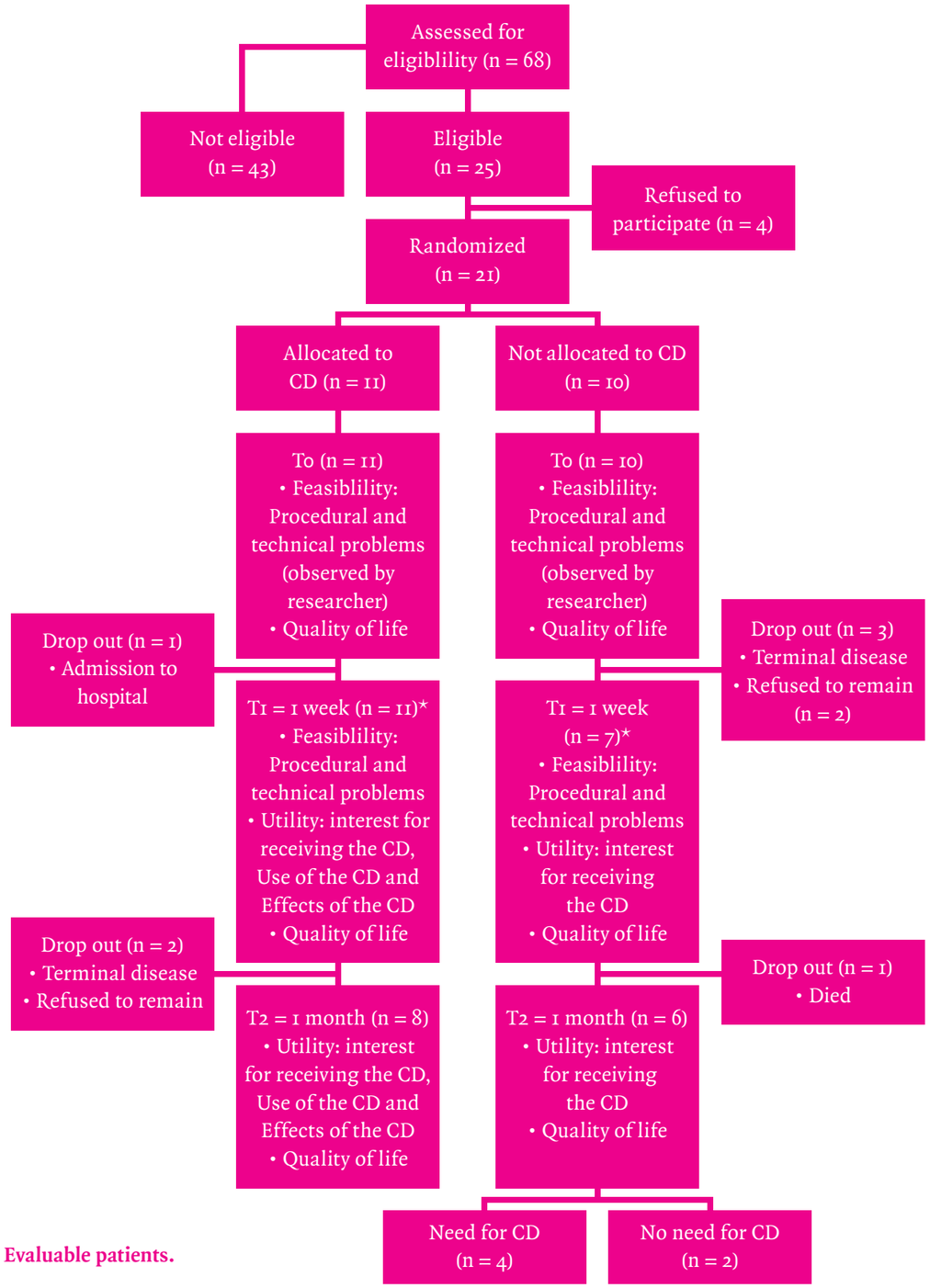


*** Evaluable patients.**

**Figure 1.** *Flow diagram of recruitment.*

### Feasibility of receiving a CD recording

**Technical problems** We observed no technical problems during the consultation; there were no recording failures (Table 2). After consultation, two patients experienced difficulties in playing the CD at home, probably due to a weak laser in their (old) CD player. However, both found a solution for this problem. Furthermore, two patients evaluated the sound quality of the CD as unsatisfactory. In one case, the physician and in the other, the patient spoke not loud enough according to the patient.

**Procedural problems** Six (29%) consultations started later than scheduled, which was mainly due to postponing the appointment to the end of the consultation period to avoid time pressure (Table 2). Three patients were not satisfied with their consultation; only one patient gave a reason for this, which was not related to the CD recording. Patients in the CD group were all satisfied with the period of 2 days before they received the CD.

### Utility of receiving a CD recording

**Patients' interest** Table 2 shows the qualifications for receiving the CD in both arms. Most patients rated this as highly important, 71% after one week and 57% after one month. Three patients rated receiving the CD as being of low importance on both time points. These patients were all allocated to the CD group and had a moderate need for information before consultation. Two of these patients stated that they had not expected the type of information that they received. One of them saw the physician for the first time and was very dissatisfied with the consultation because the physician had told him the information in an unbalanced way. All patients were satisfied with the choice of voice recording instead of video recording. After one month, 75% patients in the CD group would recommend the CD for other patients in the same situation. Two patients in the no CD group had no interest in receiving the CD after 1 month. All other patients in the no CD group, who were still alive at 1 month, were willing to receive the CD at this stage.

### Use of the CD

Within the first month after consultation, 8 patients (80%) listened to the CD, most commonly accompanied by their spouses (Table 2). All CDs were listened to by others, i.e., spouses, children, a friend and the general practitioner (GP). At a later stage, patients as well as the relatives more listened to the CD on their own. Six patients listened to the CD on their own, whereas one GP, one friend and 2 children did so as well. One month after the consultation, 4 patients stated that they expected that they would listen to the CD again in the future.

### Effect of receiving a CD recording

**Quality of life and on ability to discuss the disease with the family** No significant differences were observed in both outcome scores at baseline and during follow-up between the CD and no CD group. Nonetheless, the mean QoL scores were worse in the CD group than in the no CD group on 7/17 QoL scales/items at baseline, 9/17 QoL scales/items at 1 week, and on 12/17 QoL scales/items at 1 month. Patients in the CD group reported more openness to discuss cancer-related topics in the family than patients in the no CD group at all time points. The reliability for all scales used in this study was high to very high ($\alpha$ = 0.75-0.93), except for the physical functioning scale of the EORTC QLQ-C15-PAL questionnaire ($\alpha$ = 0.68) and the loss of control scale ($\alpha$ = 0.68).







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**Table 1a.**
*Patient and disease characteristics of patients with non-curable oesophageal or head and neck cancer (n = 17).*

| | | CD group (n = 10) | No CD group (n = 7) |
|---|---|---|---|
| **Patient and disease characteristics** | | | |
| Primary tumour site | N (%) | | |
| • Head or neck (ENT) | | 6 (60) | 3 (43) |
| • Esophagus | | 4 (40) | 4 (57) |
| Age | Mean (range) | 68 (50-89) | 62 (42-77) |
| Male | N (%) | 7 (70) | 5 (71) |
| Polytechnic college or higher education completed | N (%) | 3 (30) | 2 (29) |
| Living alone | N (%) | 4 (40) | 0 |
| Need for information | N (%) | | |
| • High (want to know everything) | | 2 (20) | 4 (57) |
| • Moderate (only what is important) | | 8 (80) | 2 (29) |
| • Low (as less as possible) | | 0 | 1 (14) |
| Received previous curative treatment | N (%) | 7 (70) | 2 (28) |
| Months since initial cancer diagnosis | Median [IQR] | 6 [0.5-14.7] | 2 [1.3-7.3] |
| Expected the information[a] | N (%) | | |
| • Yes | | 4 (44) | 3 (50) |
| • Somewhat | | 3 (33) | 3 (50) |
| • No | | 2 (22) | 0 |

[a] **Missing values in both groups.**

**Table 1b.**
*Consultation characteristics of patients with non-curable oesophageal or head and neck cancer (n = 17).*

| | | CD group (n = 10) | No CD group (n = 7) |
|---|---|---|---|
| **Consultation characteristics** | | | |
| Indication palliative stage discussed (more indications possible per patient) | N (%) | | |
| • Inoperable | | 1 (10) | 0 |
| • Irresectable | | 2 (20) | 1 (14) |
| • Metastasis/second primary tumour | | 5 (50) | 5 (71) |
| • Recurrent/progressive cancer | | 5 (50) | 2 (29) |
| Palliative treatment discussed (more treatments possible per patient) | N (%) | | |
| • Chemotherapy (optional) | | 5 (50) | 4 (57) |
| • Radiation (optional) | | 4 (40) | 1 (14) |
| • Stent placement | | 1 (10) | 3 (43) |
| • Pain-relieving medication | | 4 (40) | 2 (29) |
| First contact with physician | N (%) | 3 (30) | 3 (43) |

## DISCUSSION

Previous studies on recordings of bad news consultations have shown that this is an accepted intervention for most cancer patients, relatives and physicians. However, there is reluctance in providing such a recording in patients with a poor prognosis, as this intervention might have a negative effect on their quality of life.[5, 7, 10] The present pilot-study is to our knowledge the first published study with recordings of consultations of cancer patients receiving a new diagnosis of non-curable oesophageal or head and neck cancer. It shows that the application of this intervention is feasible and of interest to this group of patients. Our results must, however, be interpreted with caution as the sample size was small. This conclusion is based on the following outcomes:

First, there seems to be a need in these patients to receive a CD, even when its content confirms a poor prognosis. Eight of ten patients who received the CD after consultation also listened to the CD, within one month after consultation. Moreover, a recording of the consultation was important for the majority of patients (Table 2). This is important as it is adds to the patients' need for information on their clinical situation and the treatment options[37], even in the later stage of the disease and when the message of the consultation hardly or not gives any hope for the future.[38-41] Such information is, for example, needed for patients to understand the situation, to decide whether he/she should undergo a (palliative) treatment or not, to get a realistic idea of the prognosis, to aid in coping, and to help others to understand the situation.[42] Using this information, patients are able to reorganise and adapt their lives towards more realistic and achievable goals, hopes and aspirations for their remaining life.[43, 44] The importance can also be motivated by just receiving the CD, which patients can listen to but also file and refer to in the future .[45, 46] Remarkably, 50% of the patients in the CD group stated that they expected that they would listen to the CD again in the future.

Second, nine of 10 CDs were also listened to by the relatives of patients. It seems likely that they also have a need for this. Similar findings have been obtained in patients who had advanced cancer and heard the poor prognostic news.[8, 10, 21] It has been shown that relatives and friends also need information to cope with the situation and to prepare for a caring, protecting, representing or acting role on behalf of the patient.[26, 47]

**Table 2.**
*Feasibility and utility outcomes of the studies intervention, i.e., provision of a CD recording of the consultation.*

| Outcome | Measurements | | Time point[g] | Completed by | CD group N = 10 To or T1[a] | CD group N = 10 T2[d] | No CD group N = 7 To or T1[a] | No CD group N = 7 T2[e] |
|---|---|---|---|---|---|---|---|---|
| Feasibility | Technical problems | Problems observed during consultation | To | Researcher | 0 out of 10 | - | 0 out of 7 | - |
| | | Experienced difficulties in replaying the CD | T1 | Patient | 2 out of 8[f] | - | - | - |
| | | Not satisfied with sound quality of CD | T1 | Patient | 2 out of 8[f] | - | - | - |
| | Procedural problems | Problems observed during consultation | To | Researcher | 3 out of 10[b] | - | 3 out of 7[b] | - |
| | | Not or moderate satisfied with consultation | T1 | Patient | 2 out of 9[c] | - | 1 out of 7 | - |
| | | Not satisfied with period of time receiving the CD | T1 | Patient | 0 out of 10 | - | - | - |
| Utility | Interest for | High importance for receiving CD | T1 - T2 | Patient | 5 out of 9[c] | 4 out of 8 | 5 out of 5[c] | 4 out of 6 |
| | receiving the CD | Satisfied with type of recording | T1 - T2 | Patient | 9 out of 9[c] | 8 out of 8 | - | - |
| | | Recommendation the CD to others | T1 - T2 | Patient | 6 out of 8[c] | 5 out of 8 | - | - |
| | | Interest in receiving the CD after study | T2 | Patient | - | - | - | 4 out of 6 |
| | Listen to the CD | By the patient alone, at least once | T1 - T2 | Patient | 3 out of 9[c] | 4 out of 7[c] | - | - |
| | | By others without the patient, at least once | T1 - T2 | Patient | 1 out of 9[c] | 4 out of 8 | - | - |
| | | By the patients in company with others, at least once | T1 - T2 | Patient | 7 out of 9[c] | 5 out of 7[c] | - | - |
| | | Expected to listen again to the CD in future | T1 - T2 | Patient | 5 out of 8[c] | 4 out of 8 | - | - |

**[a] See column 'time point'.**
**[b] Consultation started later as scheduled.**
**[c] Missing values, patient was not lost to follow-up.**
**[d] Two patients were lost to follow-up within the CD group.**
**[e] One patient was lost to follow-up in the control group.**
**[f] Two patients did not listen to the CD.**
**[g] To: before/during consultation, T1: 1 week after consultation, T2: 1 month after consultation.**

Third, we only experienced a few technical and procedural problems. Two patients experienced difficulties in playing the CD. We therefore suggest that the care giving facility should consider to also provide the equipment that patients can borrow to listen to the recording, especially for those that have no access to this equipment.

Despite the feasibility of the intervention and patients and relatives' interest, our preliminary results suggest that a CD was not beneficial to patients in all aspects. This should, however, be interpreted with caution as the sample size was small and onethird of the patients in the no CD group was not available for follow-up. On the other hand, it is in line with the results of a previous study in which a subgroup of cancer patients with a poor prognosis did not appreciate this method.[10]

Furthermore, patients rated the provision of the CD differently. A possible reason could be that a CD is less useful in the very initial phase of the coping process, as patients were not prepared to hear the bad news and needed some time to adjust to the new situation. Another reason could be that for some coping strategies, such as escape-avoidance or distancing coping strategies, the CD does not help to maintain emotional well-being.[48] This is supported by findings of Ong et al.[12], who reported that a major reason for patients not listening to the CD was that they experienced this as too threatening. A third reason could be that patients were not satisfied with the consultation. It might well be that certain aspects of the consultation, such as communication style and the message given by the physician, affected the appreciation of the CD. It has been shown that physicians' qualities and the type of words they use are of paramount importance for patients' perceptions of the bad news consultation in the transition from curative to palliative care.[28, 49] A fourth reason is that the relationship between physicians and patients might play a role in the patients' appreciation of the CD. It has been emphasised that the development of a trusting relationship between physicians and patients is important when patients receive a bad news message.[28, 44]

### Limitations

Our results, both positive and negative, should be interpreted with caution as the sample size was small. The results on quality of life and abilities to discuss the disease in the family should be seen as an indication for further research because only 17 patients were included, one-third of the patients in the control group (3/10) was not available for follow-up and we found a main difference in social status between the two groups. Finally, we had some missing values that could be due to the questionnaire burden, especially in this violent period of the lives of these patients.

### Recommendations for future research

For now, it is important to know that cancer patients were willing to participate (84%) in a randomised trial on CD recordings. Moreover, most patients continued to provide consent during the first month of follow-up whenever their health status this permitted. All patients knew that they would hear the results of the recently performed medical investigations during the consultation, although they did not know what the type of news was. We had in fact expected that some patients would withdraw consent after hearing the bad news of incurability, as this information dramatically and negatively affected the patients' future; however, this was not the case. A large randomized study investigating the actual effects on quality of life issues of patients and their relatives is therefore needed to gain more generalised results on these issues. A qualitative component could add strength to a large study also addressing the reasons why patients rated the provision of the CD differently. It is important to identify subgroups of patients that may benefit from this intervention. In such a large randomized study it is important to learn from our difficulties in performing this study. One-third of the identified patients were excluded because they were already partially informed on the palliative stage of the disease. In clinical practice, it is difficult to clearly determine what 'the' initially palliative consultation is. The transition to palliative care is a process, with each step leading to more or less certainty of incurability. This may necessitate that more than one consultation is recorded.

## CONCLUSION

Our findings suggest that the provision of a CD with a recording of the consultation about the transition from curative to palliative care is feasible and most cancer patients and their relatives found it acceptable or even appreciated it. Nonetheless further empirical evaluation of the effectiveness of this intervention on quality of life is needed.

## REFERENCES

1. Hack TF, Pickles T, Bultz BD, et al. Impact of providing audiotapes of primary treatment consultations to men with prostate cancer: a multi-site, randomized, controlled trial. Psychooncology 2007;16:543-552.

2. Hack TF, Pickles T, Bultz BD, et al. Impact of providing audiotapes of primary adjuvant treatment consultations to women with breast cancer: a multisite, randomized, controlled trial. Journal of Clinical Oncology 2003;21:4138-4144.

3. Hogbin B, Fallowfield L. Getting it taped: the 'bad news' consultation with cancer patients. British Journal of Hospital Medicine 1989;41:330-333.

4. Knox R, Butow PN, Devine R, et al. Audiotapes of oncology consultations: only for the first consultation? Annals of Oncology 2002;13:622-627.

5. McClement SE, Hack TF. Audio-taping the oncology treatment consultation: a literature review. Patient Education and Counseling 1999;36:229-238.

6. Pitkethly M, Macgillivray S, Ryan R. Recordings or summaries of consultations for people with cancer. Cochrane Database of Systematic Reviews 2008:CD001539.

7. Scott JT, Harmsen M, Prictor MJ, et al. Recordings or summaries of consultations for people with cancer. Cochrane Database of Systematic Reviews 2003:CD001539.

8. Stephens MR, Gaskell AL, Gent C, et al. Prospective randomised clinical trial of providing patients with audiotape recordings of their oesophagogastric cancer consultations. Patient Education and Counseling 2008;72:218-222.

9. Ford S, Fallowfield L, Hall A, et al. The influence of audiotapes on patient participation in the cancer consultation. European Journal of Cancer 1995;31A:2264-2269.

10. McHugh P, Lewis S, Ford S, et al. The efficacy of audiotapes in promoting psychological well-being in cancer patients: a randomised, controlled trial. British Journal of Cancer 1995;71:388-392.

11. North N, Cornbleet MA, Knowles G, et al. Information giving in oncology: a preliminary study of tape-recorder use. The British Journal of Clinical Psychology 1992;31(Pt3):357-359.

12. Ong LM, Visser MR, Lammes FB, et al. Effect of providing cancer patients with the audiotaped initial consultation on satisfaction, recall, and quality of life: a randomized, double-blind study. Journal of Clinical Oncology 2000;18:3052-3060.

13. Tattersall MH, Butow PN. Consultation audio tapes: an underused cancer patient information aid and clinical research tool. The Lancet Oncology 2002;3:431-437.

14. van der Meulen N, Jansen J, van Dulmen S, et al. Interventions to improve recall of medical information in cancer patients: a systematic review of the literature. Psychooncology 2008; 17:857-868.

15. Jansen J, Butow PN, van Weert JC, et al. Does age really matter? Recall of information presented to newly referred patients with cancer. Journal of Clinical Oncology 2008;26:5450-5457.

16. Rutten LJ, Arora NK, Bakos AD, et al. Information needs and sources of information among cancer patients: a systematic review of research (1980-2003). Patient Education and Counseling 2005;57:250-261.

17. Belkora JK, Loth MK, Chen DF, et al. Monitoring the implementation of Consultation Planning, Recording, and Summarizing in a breast care center. Patient Education and Counseling 2008;73:536-543.

18. Bruera E, Pituskin E, Calder K, et al. The addition of an audiocassette recording of a consultation to written recommendations for patients with advanced cancer: A randomized, controlled trial. Cancer 1999;86:2420-2425.

19. Dunn SM, Butow PN, Tattersall MH, et al. General information tapes inhibit recall of the cancer consultation. Journal of Clinical Oncology 1993;11:2279-2285.







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20. Hogbin B, Jenkins VA, Parkin AJ. Remembering 'bad news' consultations: an evaluation of tape recorded consultations. Psycho-oncology 1992;1:147-154.

21. Tattersall MH, Butow PN, Griffin AM, et al. The take-home message: patients prefer consultation audiotapes to summary letters. Journal of Clinical Oncology 1994;12:1305-1311.

22. Siersema PD. New developments in palliative therapy. Best Practice & Research. Clinical Gastroenterology. 2006;20:959-978.

23. Ledeboer QC, van der Schroeff MP, Pruyn JF, et al. Survival of patients with palliative head and neck cancer. Head & Neck 2011;33:1021-1026.

24. Robertson G, Greenlaw N, Bray CA, et al. Explaining the effects of socio-economic deprivation on survival in a national prospective cohort study of 1909 patients with head and neck cancers. Cancer Epidemiology 2010;34:682-688.

25. Islami F, Kamangar F, Nasrollahzadeh D, et al. Socio-economic status and oesophageal cancer: results from a population-based case-control study in a high-risk area. International Journal of Epidemiology 2009;38:978-988.

26. Friedrichsen MJ, Strang PM, Carlsson ME. Receiving bad news: experiences of family members. Journal of Palliative Care 2001;17:241-247.

27. Bertero C, Vanhanen M, Appelin G. Receiving a diagnosis of inoperable lung cancer: patients' perspectives of how it affects their life situation and quality of life. Acta Oncologica 2008;47:862-869.

28. Friedrichsen MJ, Strang PM, Carlsson ME. Breaking bad news in the transition from curative to palliative cancer care: patient's view of the doctor giving the information. Support Care Cancer 2000;8:472-478.

29. de Moor JS, Partridge AH, Winer EP, et al. The role of socioeconomic status in adjustment after ductal carcinoma in situ. Cancer 2010;116:1218-1225.

30. Simon AE, Wardle J. Socioeconomic disparities in psychosocial wellbeing in cancer patients. Eur J Cancer 2008;44:572-578.

31. Myer L, Stein DJ, Grimsrud A, et al. Social determinants of psychological distress in a nationally-representative sample of South African adults. Soc Sci Med 2008;66:1828-1840.

32. Groenvold M, Petersen MA, Aaronson NK, et al. The development of the EORTC QLQ-C15-PAL: a shortened questionnaire for cancer patients in palliative care. European Journal of Cancer 2006;42:55-64.

33. Mesters I, van den Borne B, De Boer M, et al. Measuring information needs among cancer patients. Patient Education and Counseling 2001;43:253-262.

34. van den Borne HW, Pruyn J. Contacts between fellow cancer patients. Assen/Maastricht: Van Gorcum; 1985.

35. Mesters I, van den Borne H, McCormick L, et al. Openness to discuss cancer in the nuclear family: scale, development, and validation. Psychosomatic Medicine 1997;59:269-279.







36. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. Journal of Clinical Epidemiology 2007;60:34-42.

37. Jenkins V, Fallowfield L, Saul J. Information needs of patients with cancer: results from a large study in UK cancer centres. British Journal of Cancer 2001;84:48-51.

38. Hoff L, Tidefelt U, Thaning L, et al. In the shadow of bad news - views of patients with acute leukaemia, myeloma or lung cancer about information, from diagnosis to cure or death. BMC Palliative Care 2007;24:1.

39. Dunn SM, Patterson PU, Butow PN, et al. Cancer by another name: a randomized trial of the effects of euphemism and uncertainty in communicating with cancer patients. Journal of Clinical Oncology 1993;11:989-996.

40. Barnett MM. Does it hurt to know the worst? Psychological morbidity, information preferences and understanding of prognosis in patients with advanced cancer. Psychooncology 2006;15:44-55.

41. Sapir R, Catane R, Kaufman B, et al. Cancer patient expectations of and communication with oncologists and oncology nurses: the experience of an integrated oncology and palliative care service. Supportive Care in Cancer 2000;8:458-463.

42. Coulter A, Entwistle V, Gilbert D. Sharing decisions with patients: is the information good enough? British Medical Journal 1999;318:318-322.

43. Fallowfield LJ, Jenkins VA, Beveridge HA. Truth may hurt but deceit hurts more: communication in palliative care. Palliative Medicine 2002;16:297-303.

44. Gattellari M, Voigt KJ, Butow PN, et al. When the treatment goal is not cure: are cancer patients equipped to make informed decisions? Journal of Clinical Oncology 2002;20:503-513.

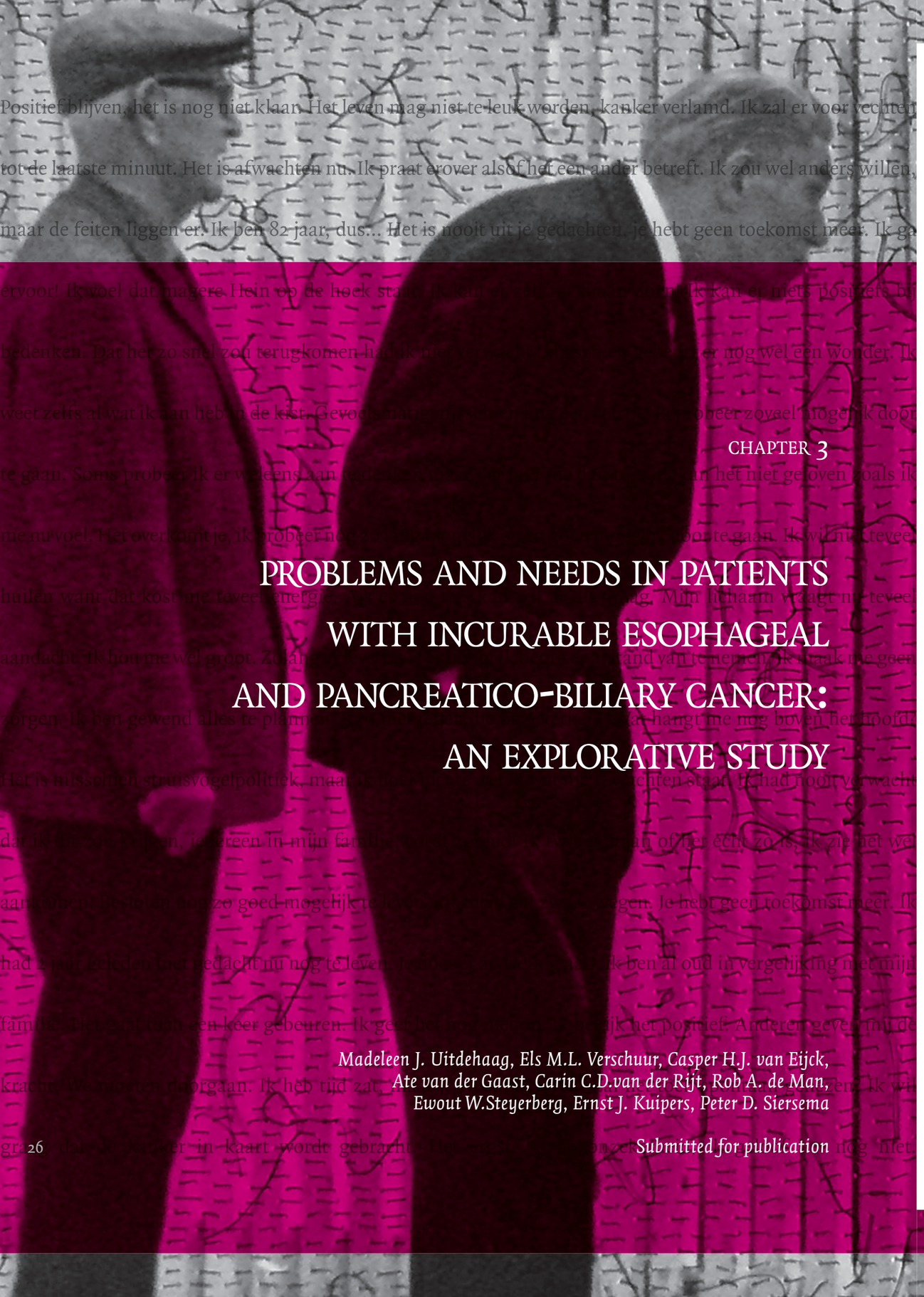
45. Ong LM, de Haes JC, Hoos AM, et al. Doctor-patient communication: a review of the literature. Social Science Medicine 1995;40:903-918.

46. McConnell D, Butow PN, Tattersall MH. Audiotapes and letters to patients: the practice and views of oncologists, surgeons and general practitioners. Br J Cancer 1999;79:1782-1788.

47. Clayton JM, Butow PN, Tattersall MH. The needs of terminally ill cancer patients versus those of caregivers for information regarding prognosis and end-of-life issues. Cancer 2005;103:1957-1964.

48. Watson M, Greer S, Blake S, et al. Reaction to a diagnosis of breast cancer. Relationship between denial, delay and rates of psychological morbidity. Cancer 1984;53:2008-2012.

49. Friedrichsen MJ, Strang PM, Carlsson ME. Cancer patients' interpretations of verbal expressions when given information about ending cancer treatment. Palliative Medicine 2002;16:323-330.



CHAPTER 3

# PROBLEMS AND NEEDS IN PATIENTS WITH INCURABLE ESOPHAGEAL AND PANCREATICO-BILIARY CANCER: AN EXPLORATIVE STUDY

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*Submitted for publication*





## INTRODUCTION

Knowledge of symptom prevalence in patients at the palliative stage of their disease is important in clinical practice as it enables professional caregivers to focus on these issues. Early identification and effective symptom management control and palliation is the key to achieve the best quality of life possible for patients in the last phase of their life.[1] However, only a few studies have considered physical, psychosocial and spiritual symptom prevalence in patients diagnosed with esophageal cancer (EC) or pancreatico-biliary cancer (PBC).[2-4] Furthermore, studies have shown a poor quality of life in patients with these cancers.[5-11] Optimal care in these patients, with a dismal prognosis and deaths usually occurring within the first year of diagnosis[12, 13], remain a serious clinical challenge for health care providers.

In order to achieve effective symptom control, not only experienced problems but also needs for professional care should be assessed. Previously, it has been shown that cancer patients do not expect professional care for all their problems, moreover, patients particularly expected care for potential problems in the near future.[14-16] In order to respond to the challenge for optimal professional care to patients with incurable EC and PBC, we investigated the specific problems and needs for care among a cohort of patients with an irresectable or recurrent stage of these malignancies not being amendable to curative treatment.

## METHODS

### Patients

From September 2005 to June 2006, consecutive patients with irresectable or recurrent EC and PBC were recruited from the outpatient clinics of the medical oncology, gastroenterology or surgery department of a large university referral hospital for these malignances in the southwest of the Netherlands. Patients were eligible when a multidisciplinary panel had concluded that a curatively aimed treatment modality was no longer possible.

Ninety eligible patients were identified of whom 57 agreed to participate (63%). The patients that were not wiling to participate did so because they expected that completing the questionnaire was too burdensome (n = 22) or they had the expectation that cure was still possible (n = 2). The other nine patients did not give a reason for refusal. All patients who agreed to participate in the study signed an informed consent form and filled out the questionnaires at home. If needed, the questionnaires were completed with the help of a research nurse (M.U).

### Questionnaires

At baseline, patient socio-demographics, clinical characteristics, fear of death (each day or week - not weekly - never), satisfaction with life as a whole (yes-no)[17] and patients' own belief about curability of the disease (not curable-(maybe) curable) were assessed.

Subsequently, patients filled out the Problem and Needs in Palliative Care (PNPC) questionnaire[18] and two disease-specific quality-of-life questionnaires developed by the European Organization for Research and Treatment in Cancer (EORTC), i.e., the EORTC QLQ-OES18 (esophageal carcinoma)[19, 20] and the EORTC QLQPAN26 (pancreatic carcinoma).[21]

The PNPC questionnaire has been developed in the Netherlands and is constructed from a patient-centered perspective with empirically collected data. The items address relevant issues for all domains of palliative care as well as the need for support from professional caregivers for these issues. The internal reliability of most domains has been shown to be satisfactory.[18] The questionnaire

comprises 90 items being distributed over 9 domains focusing on activities of daily living (ADL), role performance, physical problems, loss of autonomy (LOA), social issues, health care providers, and emotional, spiritual, and financial issues. The patients were asked to relate their replies to the situation at the time of completing the questionnaire. Replies related to experienced problems were rated as frequent, moderately frequent or never problematic. Expected care was rated as more, equal to the present situation, or no care expected.[18]

The EORTC QLQ-OES18 comprises 18 physical issues, whereas the EORTC QLQ-PAN26 comprises 17 physical, 6 psychosocial issues and 3 issues with regard to health care provision. Both questionnaires have widely been used and have demonstrated good psychometric and clinical validity.[20, 22]

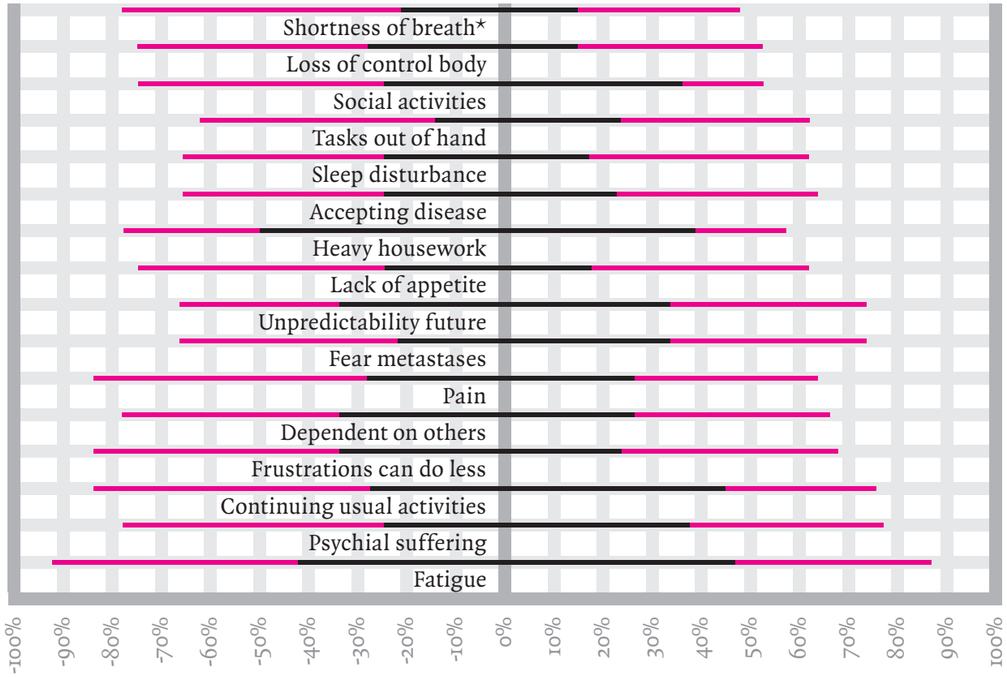
### Statistical analysis

Descriptive statistics were used to analyze the replies to all three questionnaires. Regarding the PNCP questionnaire, this included frequencies of experienced problems and expected care for each item separately. Problems were considered to be present if they were rated as frequent or moderately frequent problematic. Expected care was considered to be present if it was rated as more than or equal to the present situation. For the EORTC QLQ-OES18 and EORTC QLQ-PAN26 module, we calculated the mean values for the scales, after conversion to 0-100 scales according to the EORTC scoring manuals. For single items, 0 indicates 'not at all', 33.3 indicates 'a little', 66.7 indicates 'quite a bit' and 100 indicates 'very much'.[4] Next, we estimated the proportion of patients with a mean score ≥ 33.3 for symptom scales/single items (those who experienced the scale or item as problematic: a little to very much) or ≤ 66.7 for functional scales (those who functioned worse on the scale: not at all to quite a bit), for comparability with the PNPC replies. A two-sided p-value < .05 was considered statistically significant. Analyses were conducted using Statistical Package for Social Sciences version 14.0 (SPSS Inc., Chicago, IL, USA).

| Characteristics | Esophageal n = 24 | Pancreatico-biliary n = 33 |
|---|---|---|
| Mean age in years [SD] | 65 [11.8] | 64 [12.2] |
| Gender; male (%) | 92[1] | 70[1] |
| Indication for palliative policy (%) | | |
| • Irresectable or inoperable | 83 | 88 |
| • Recurrent | 17 | 12 |
| Months since diagnosis of 'cancer'; median [IQR] | 8 [4.1-17.4] | 7 [1.8-7.3] |
| Months since diagnosis incurable disease; median [IQR] | 2 [1.5-4.8] | 2 [0.8-7.4] |
| Months before death; median [IQR] | 4 [1.7-7.4] | 4 [1.5-8.8][2] |
| Living alone (%) | 33 | 15 |
| Believing that the disease is (maybe) curable (%) | 17 | 27 |
| Fearing death (%) | 71 | 73 |
| Feeling satisfied with life as a whole (%) | 58[1] | 91[1] |
| Structural follow-up by physician at outpatient clinic | 74 | 70 |
| Structural follow-up by general practitioner | 50 | 61 |

[1] P-value for difference between % patients with EC and PBC < .05.
[2] 6 patients missing because date of death is unknown.

**Table 1.** *Characteristics of 57 patients with incurable esophageal and pancreatico-biliary cancer.*




[1] Twelve items for the PBC group due to three items with the same % on tenth place (tasks out of hand, sleep disturbance and lack of appetite), four items do not overlap with the top 10 of the EC pts (heavy housework, social activities, loss of control body, shortness of breath).
[2] Percentages are ranked on highest percentage in both groups.
[3] On the right the % of the PBC patients (positive %), on the left the % of the EC patients (negative %).
* P-value for difference between % patients with PBC and EC patients < .05.

**Figure 1.** *Top 10[1] of items which are most problematic[2] for patients with incurable esophageal[3] or pancreato-biliary[3] cancer on the PNPC-questionnaire (total 90 items).*

## RESULTS

### Subjects

Twenty-four patients with EC and 33 patients with PBC participated in the study, a median of 2 months (IQR 1.5-4.8 vs. 0.8-7.4, respectively) after having been diagnosed with incurable malignant disease and a median of four months before death (IQR 1.7-7.4 vs. 1.5-8.8, respectively). Other patient characteristics are summarized in Table 1. We found a statistically significant difference between the two groups in gender (92% male in EC group vs. 70% male in PBC group, p = .05), and the number of patients who felt satisfied with life as a whole (58% EC group vs. 91% PBC group, p < .01). Fifty-six patients completely filled out the questionnaires, while one patient did this partially.

| Scales/Items | Total (n = 24)[1] Score[2] Mean (95% CI) | Total (n = 24)[1] Patients reporting item or scale as problematic[3] % |
|---|---|---|
| Fear of future health | 68 (54-83) | 96 |
| Ability to plan future | 58 (39-77) | 83 |
| Dry mouth | 54 (38-71) | 79 |
| Changed bowel habit scale | 46 (33-60) | 79 |
| Flatulence | 49 (30-68) | 75 |
| Loss of muscle strength | 47 (29-66) | 75 |
| Weight loss | 56 (38-74) | 72 |
| Pain scale | 55 (41-69) | 71 |
| Swollen abdomen | 44 (25-62) | 71 |
| Changes in tastes | 49 (31-67) | 67 |
| Restriction in consumption of certain food types | 39 (21-56) | 67 |
| Indigestion | 35 (17-53) | 63 |
| Sexuality scale | 49 (28-70) | 60 |
| Satisfaction with health care scale | 68 (54-81) | 57 |
| Body image scale | 27 (15-40) | 38 |
| Hepatic scale | 21 (5-37) | 33 |

**[1] 24 patients with pancreatic cancer in the PBC group.**
**[2] High scores represents inferior quality of life except for the functioning scales sexuality and satisfaction, for which high scores represent better functioning and higher satisfaction, respectively).**
**[3] For single items and symptom scales a mean score ≥ 33.3 (a little, quite a bit or very much) or a functional scale mean score of ≤ 66.7 (not at all, a little or quite a bit).**

**Table 2.** *Mean QoL scores and percentages of patients reporting scale or items as problematic on EORTC QLQ-PAN26.*







### Experienced problems

On average, 36/90 (40%) items in the PNPC questionnaire were rated as problematic in EC patients and 30/90 (33%) items in PBC patients (range 10-72, SD 16.5 vs. range 4-70, SD 15.1, respectively). These problems were distributed over all nine domains. Two of 57 (4%) patients experienced less than 10 items as problematic (both from the PBC group), whereas six of them (11%) experienced more than 60 items as problematic (three from each group). Figure 1 shows the ten most problematic items in both groups of patients. Fatigue was the main problem in both groups (92% EC patients vs. 88% PBC patients, p = NS). The next predominant problems for EC patients were pain (83%), the impossibility to continue usual activities (83%), and frustration about impossibility to do as much as before (83%). For PBC patients fear of physical suffering (79%) and metastases (73%), the impossibility to continue usual activities (76%), and the unpredictability of the future (73%) were the next predominant problems. The ten most problematic problems were found to be almost similar in both groups, a significant difference was found for shortness of breath (79% EC patients vs. 50% PBC patients, p = .03).

### Disease-specific problems

In terms of disease-specific problems on the EORTC QLQ-PAN26, emotional problems were most common among patients with PBC, with the highest scores for fear of future health (96%) and disability to plan the future (83%). Furthermore, the most frequently rated physical problems in this questionnaire were dry mouth (79%) and changed bowel habits (79%) (Table 2). On the other hand, disease-specific problems on the EORTC QLQ-OES18 were less frequently rated as high by patients with EC, with eating problems (64%), pain (63%), trouble with coughing (58%) and dysphagia (56%) being the most common problems (Table 3).

| Scales/Items | Total (n = 24) Score[1] Mean (95% CI) | Total (n = 24) Patients reporting item or scale as problematic[2] % |
|---|---|---|
| Eating scale | 36 (25-48) | 64 |
| Pain scale | 29 (20-37) | 63 |
| Trouble with coughing | 25 (15-35) | 58 |
| Dysphagia scale | 28 (17-39) | 56 |
| Reflux scale | 22 (13-30) | 50 |
| Problems with taste | 22 (9-35) | 42 |
| Dry mouth | 18 (7-29) | 38 |
| Difficulty in swallowing saliva | 15 (4-27) | 29 |
| Problems with choking | 6 (0-11) | 17 |
| Problems with speech | 4 (-1-9) | 13 |

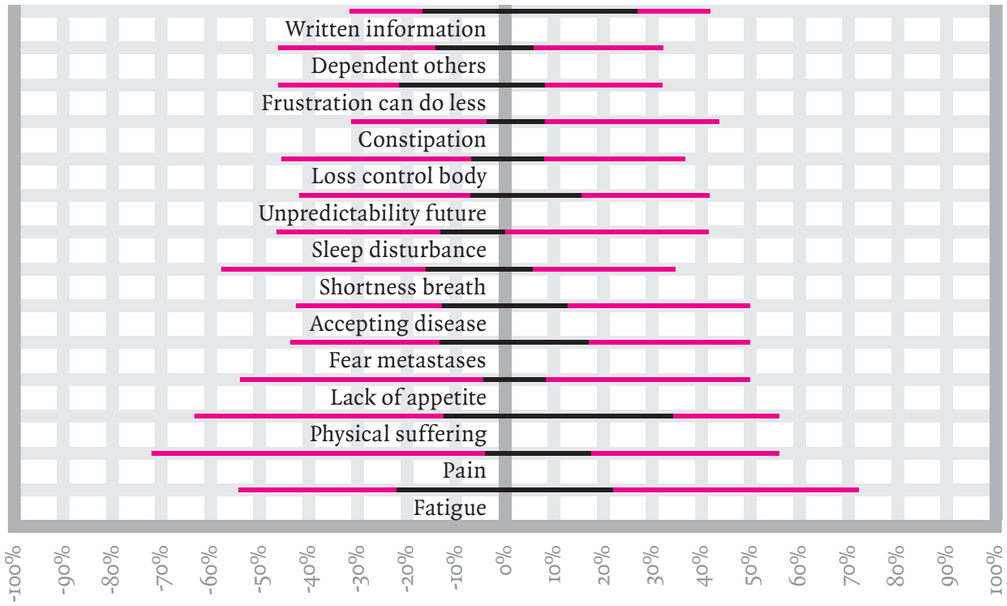
**[1] High scores represent inferior results.**
**[2] Mean score ≥ 33.3 (a little, quite a bit or very much).**

**Table 3.** *Mean QoL scores and percentages of patients reporting scale or items as problematic on EORTC QLQ-OES18.*

### Expected care

On average, EC patients expected professional care for 25/90 (28%) items and PBC patients for 22/90 (24%) (range 0-71, SD 22.5 vs. range 0-74, SD 21.5, respectively). In both groups, the number of items that patients experienced as problematic was higher than the number of items for which professional care was needed (EC p = .03 vs. PBC p = .05).

Figure 2 shows the items for which the patients most frequently expected professional care, rated as 'more' or 'equal to the present situation'. The highest need for professional care was found for fatigue (54% EC, 72% PBC), pain (71% EC, 56% PBC), fear of physical suffering (63% EC, 56% PBC) and lack of appetite (54% EC, 50% PBC) (Figure 2). All these items were also experienced as problematic as shown in Figure 1. The discrepancy in the percentages of patients who indicated an item as problematic versus the percentages of patients who expected professional care for the respective item was most remarkable for difficulties in continuing usual activities (problematic 83% EC, 76% PBC vs. need for care 33% EC, 34% PBC), and employment or study (problematic 46% EC, 45% PBC vs. need for care 4% EC, 10% PBC), overcaring of others (problematic 63% EC, 49% PBC vs. need for care 17% EC, 19% PBC), and frustration because of the inability to do as much as before (problematic 70% EC, 83% PBC vs. need for care 31% EC, 46% PBC). On the other hand, we found that patients expected professional care for items that were less problematic at the moment of inquiring. These items included someone confidential to talk with (problematic 8% EC, 9% PBC vs. need for care 25% EC, 16% PBC), the assurance that hospitalization would be possible when necessary (problematic 30% EC, 12% PBC vs. need for care 39% EC, 22% PBC), difficulties in saying to the physician that one does not understand (problematic 17% EC, 12% PBC vs. need for care 17% EC, 25% PBC), and the availability of emergency help when needed (problematic 30% EC, 22% PBC vs. need for care 35% EC, 29% PBC).




**[1] Six items belong to the top 10 of both groups, other eight items belong in the top 10 of the EC (shortness of breath, loss control body, frustration can do less, dependent others) or the PBC patients (accepting disease, unpredictability future, constipation, written information).**
**[2] Percentages are ranked on highest percentage of both groups added together.**
**[3] On the right the % of the PBC patients (positive %), on the left the % of the EC patients (negative %).**

**Figure 2.** *Top 10[1] needs for professional care[2] of patients with incurable esophageal[3] or pancreato-biliary[3] cancer on the PNPC-questionnaire.*

At the time of inquiring, PBC patients experienced inadequate professional care for their fear of physical suffering (34%), need for written information (28% ), and fatigue (22%), whereas EC patients also experienced inadequate professional care for fatigue (21%), assurance that hospitalization would be possible when necessary (22%), and frustration because of the inability to do as much as before (21%) (Figure 3).

## DISCUSSION

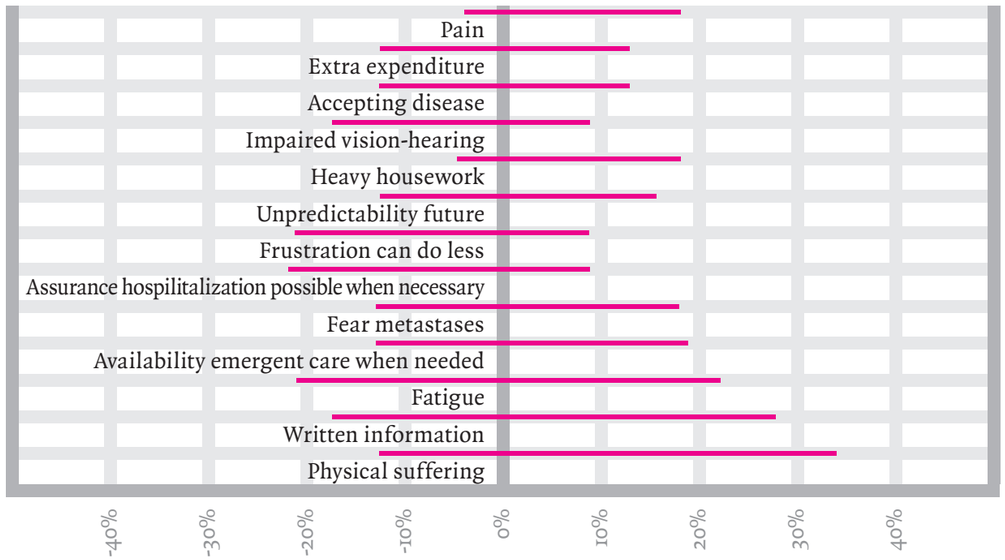
This study shows that patients with incurable EC and HBC experienced multiple problems on all nine domains of the PNPC questionnaire, of which physical, emotional and loss of autonomy (LOA) problems were predominant (Figure 1). The extent to which these problems occur was not significantly different in both groups, except for shortness of breath (Figure 1). Our results are in line with other prospective studies on physical symptoms in patients with advanced upper GI cancer[3, 4, 23], but also with results on symptoms in incurable cancer patients with other tumor types: a systematic review found that more than 50% of the 25074 included patients experienced fatigue, pain, lack of energy, weakness and appetite loss.[24] Moreover, Salona et al[25] found that the symptoms pain, fatigue and breathlessness were common in more than 50% of patients with advanced cancer, but also in four other incurable disorders, i.e., acquired immunodeficiency syndrome (AIDS), heart disease, chronic obstructive pulmonary disease, and renal disease. They speculated on a common pathway prior to dying in malignant as well as nonmalignant diseases.

Specific emotional problems and LOA problems have rarely been reported in upper GI cancer. In the literature, mainly specific upper GI cancer symptoms, i.e., dysphagia[3], symptoms of obstructive jaundice, gastric outlet obstruction, and pancreatic enzyme insufficiency[2, 26, 27], have been evaluated in detail. As a high prevalence of these symptoms was not found in our study (Table 2 and 3), it seems likely that these symptoms were reasonably controlled in our patients. Therefore, incurable upper GI cancer patients at the palliative stage of their disease share the same main problems with other patients at this stage, with an exception for some (temporary) disease-specific symptoms. Further longitudinal research on this will be relevant for the planning and rationalization of palliative care services.

Patients most frequently expected professional care for physical and emotional problems (Figure 2). These problems are also discussed most frequently by physicians, which mainly applies for the physical problems.[28-30] Despite the fact that the questionnaire measured the need for care, regardless of the

specific professional, it is interesting to determine whether the need for care is determined by the expected offer. Compared to the high frequency of experienced problems, the expected care for LOA problems and issues concerning employment or study and overcaring of others was found to be much lower. It seems that patients considered these problems as being untreatable or being an inevitable part of the disease at this stage of illness.[31] In case patients are not discussing these problems spontaneously, they may remain unrecognized and consequently not adequately addressed.[31] It is therefore advisable to specifically address these issues with patients during follow-up.

Patients in both groups expected care for anticipated problems with health care providers. It seems likely that these needs are related to the Dutch health care system, with an important role allocated to insurance companies and regulated competition.[32] Admission stops to hospitals and home care organizations have become a reality in the more recent years in the Netherlands. Moreover, palliative care was previously not a well-defined 'product' within this system[32], although the costs are likely to be considerable. Since 2012, there is an incentive for




**[1] Three items do not overlap with the top 10 of the EC pts (impaired vision hearing, frustration can do less, uncertain possibility admission hospital).**
**[2] Percentages are ranked on highest percentage in both groups.**
**[3] On the right the % of the PBC patients (positive %), on the left the % of the EC patients (negative %).**

**Figure 3.** *Top 10 items[1] which are high in needs[2] for more professional care of patients with incurable esophageal[3] or pancreato-biliary[3] cancer on the PNPC-questionnaire.* ■ More







hospitals to develop specific palliative care 'products', such as palliative care units or multidisciplinary follow-up teams for these patients, which can be financed by a official diagnosis treatment combination.[33] The high number of symptoms in incurable upper GI patients found in this study supports such initiatives in the future.

Inadequate care was experienced for fatigue (both groups), need for written information (EC), fear of physical suffering (EC), the assurance that hospitalization is possible when necessary (PBC), and frustration because of the inability to do as much as before (PBC) (Figure 3). As fatigue is strongly associated with an impaired overall HRQoL, effective symptom control appear to be of the utmost importance.[23] Although, similar to fear of physical suffering, uncertainty about hospitalization and frustration about the inability to do as much as before, fatigue is frequently overlooked by professionals.[34-36] There are limited interventions available for effective treatment of these problems[35, 37] and more studies are needed to improve this situation. For now, professionals should focus on these problems in patients with upper GI cancer, preferably by sensitive communication about the impact on daily live activities of these problems and its meaning to the patient.

This study has some limitations. First, we used a cross-sectional design, which means that the results are only available for one time point in a particular patient. We previously found that replies to some of these questions may change over a relatively short period of time (unpublished results). Further progression of the disease is likely to result in other problems and needs[38], especially in the terminal phase of the disease.[24] A longitudinal study of cancer patients followed from the start of the palliative phase of a malignancy until death would help to resolve possible inconsistencies in our results. Second, there is probably an underestimation of certain problems and needs in these types of cancer patients due to the exclusion of patients who were actually too ill to participate in this study. Third, it is known that symptoms are related to each other.[39, 40] This suggests that it might be better to assess problems as symptom clusters, in which different problems are related to each other, rather than in individual symptoms. Moreover, for implications for symptom management it seems important to report in symptom clusters. Finally, only a relatively low number of patients was included, which may have influenced our analyses and thus the final results.

In conclusion, patients with incurable upper GI cancer experience in particular physical and emotional problems and most patients express a need for professional care for these. This was, however, not the case for LOA problems which are also frequently experienced as problematic. Therefore, it is advisable to pay attention to these problems as they can be of major importance, even in patients without explicitly expressing a need for them. In addition, it is important for professionals to be alert of symptoms of fatigue, fear, frustration and uncertainty, for which inadequate care was received. These results can be used to further improve the multidisciplinary follow-up policy of patients with incurable upper GI cancer.

## REFERENCES


1. WHO. World Health Organisation. 2002; http://www.who.int/cancer/palliative/definition/en/; (assessed 19-9-2008).

2. Krech RL, Walsh D. Symptoms of pancreatic cancer. J Pain Symptom Manage 1991;6:360-367.

3. Andreassen S, Randers I, Naslund E, et al. Patients' experiences of living with oesophageal cancer. J Clin Nurs 2006;15:685-695.

4. Labori KJ, Hjermstad MJ, Wester T, et al. Symptom profiles and palliative care in advanced pancreatic cancer: a prospective study. Support Care Cancer 2006;14:1126-1133.

5. Chen L, Liu Y, Li GG, et al. Quality of life in patients with liver cancer after operation: a 2-year follow-up study. Hepatobiliary Pancreat Dis Int 2004;3:530-533.

6. Blazeby JM, Farndon JR, Donovan J, et al. A prospective longitudinal study examining the quality of life of patients with esophageal carcinoma. Cancer 2000;88:1781-1787.

7. Homs MY, Essink-Bot ML, Borsboom GJ, et al. Quality of life after palliative treatment for oesophageal carcinoma: a prospective comparison between stent placement and single dose brachytherapy. Eur J Cancer 2004;40:1862-1871.

8. Nieveen van Dijkum EJ, Kuhlmann KF, Terwee CB, et al. Quality of life after curative or palliative surgical treatment of pancreatic and periampullary carcinoma. Br J Surg 2005;92:471-477.

9. Steel JL, Chopra K, Olek MC, et al. Health-related quality of life: Hepatocellular carcinoma, chronic liver disease, and the general population. Qual Life Res 2007;16:203-215.

10. Crippa S, Dominguez I, Rodriguez JR, et al. Quality of life in pancreatic cancer: analysis by stage and treatment. J Gastrointest Surg 2008;12:783-793.

11. Sun V, Ferrell B, Juarez G, et al. Symptom concerns and quality of life in hepatobiliary cancers. Oncol Nurs Forum 2008;35:E45-52.

12. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin 2008;58:71-96.

13. IKNL. Integraal Kankercentrum Nederland (Comprehensive Cancer Center the Netherlands). http://cijfersoverkanker.nl/; (2012, assessed 18 February 2012).

14. Steinert Y, Rosenberg E. Psychosocial problems: what do patients want? What do physicians want to provide? Fam Med 1987;19:346-350.

15. Osse BH, Vernooij-Dassen MJ, Schade E, et al. The problems experienced by patients with cancer and their needs for palliative care. Support Care Cancer 2005;13:722-732.

16. Verschuur EM, Steyerberg EW, Kuipers EJ, et al. Experiences and expectations of patients after oesophageal cancer surgery: an explorative study. Eur J Cancer Care (Engl) 2006;15:324-332.

17. Stewart AL, Teno J, Patrick DL, et al. The concept of quality of life of dying persons in the context of health care. J Pain Symptom Manage 1999;17:93-108.

18. Osse BH, Vernooij MJ, Schade E, et al. Towards a new clinical tool for needs assessment in the palliative care of cancer patients: the PNPC instrument. J Pain Symptom Manage 2004;28:329-341.

19. Blazeby JM, Alderson D, Winstone K, et al. Development of an EORTC questionnaire module to be used in quality of life assessment for patients with oesophageal cancer. The EORTC Quality of Life Study Group. Eur J Cancer 1996;32A:1912-1917.

20. Blazeby JM, Conroy T, Hammerlid E, et al. Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with oesophageal cancer. Eur J Cancer 2003;39:1384-1394.

21. Fitzsimmons D, Johnson CD, George S, et al. Development of a disease specific quality of life (QoL) questionnaire module to supplement the EORTC core cancer QoL questionnaire, the QLQ-C30 in patients with pancreatic cancer. EORTC Study Group on Quality of Life. Eur J Cancer 1999;35:939-941.

22. Fitzsimmons D, George S. Quality of life in surgical research. In: Johnson CD, Taylor I, editors. Recent advances in surgical research. Edinburgh: Churchill Livingstone; 1998:137-146.

23. Muller-Nordhorn J, Roll S, Bohmig M, et al. Health-related quality of life in patients with pancreatic cancer. Digestion 2006;74:118-125.

24. Teunissen SC, Wesker W, Kruitwagen C, et al. Symptom Prevalence in Patients with Incurable Cancer: A Systematic Review. J Pain Symptom Manage 2007;34:94-104.

25. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 2006;31:58-69.

26. Nakakura EK, Warren RS. Palliative care for patients with advanced pancreatic and biliary cancers. Surg Oncol 2007;16:293-297.

27. Fazal S, Saif MW. Supportive and palliative care of pancreatic cancer. Jop 2007;8:240-253.

28. Meeussen K, Van den Block L, Echteld MA, et al. End-of-life care and circumstances of death in patients dying as a result of cancer in Belgium and the Netherlands: a retrospective comparative study. J Clin Oncol 2011;29:4327-4334.

29. Abarshi E, Echteld M, Donker G, et al. Discussing end-of-life issues in the last months of life: a nationwide study among general practitioners. J Palliat Med 2011;14:323-330.

30. Johnson C, Paul C, Girgis A, et al. Australian general practitioners' and oncology specialists' perceptions of barriers and facilitators of access to specialist palliative care services. J Palliat Med 2011;14:429-435.

31. Vernooij-Dassen MJ, Osse BH, Schade E, et al. Patient autonomy problems in palliative care: systematic development and evaluation of a questionnaire. J Pain Symptom Manage 2005;30:264-270.

32. Jansen WJ, Vissers KC, Zuurmond WW, et al. Palliative care is not yet a welldefined product within the Dutch healthcare insurance system. Health Policy 2009;91:156-161.

33. Governement-The-Netherlands. Palliative care; letter from the secretary of state for health, welfare and sport.; https://zoek.officielebekendmakingen.nl/kst- 29509-30.html; (2011, assessed 13 March 2012).





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34. Hawthorn M. Fatigue in patients with advanced cancer. Int J Palliat Nurs 2010;16:536-541.

35. Roth AJ, Massie MJ. Anxiety and its management in advanced cancer. Curr Opin Support Palliat Care 2007;1:50-56.

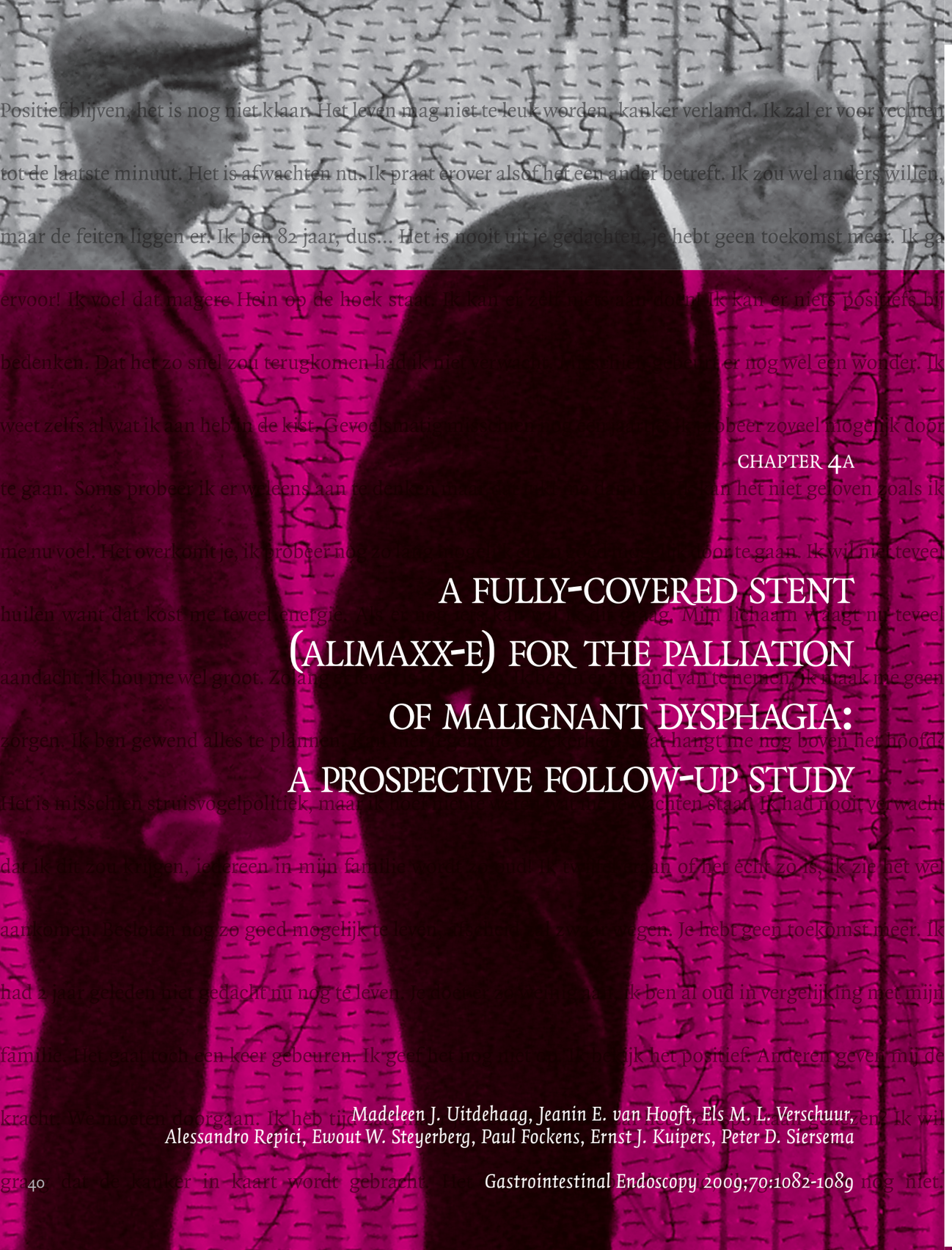
36. Detmar SB, Muller MJ, Schornagel JH, et al. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. Jama 2002;288:3027-3034.

37. Olson K, Turner AR, Courneya KS, et al. Possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion in advanced cancer. Support Care Cancer 2008;16:241-249.

38. Mercadante S, Casuccio A, Fulfaro F. The course of symptom frequency and intensity in advanced cancer patients followed at home. J Pain Symptom Manage 2000;20:104-112.

39. Fan G, Filipczak L, Chow E. Symptom clusters in cancer patients: a review of the literature. Curr Oncol 2007;14:173-179.

40. Fan G, Hadi S, Chow E. Symptom clusters in patients with advanced-stage cancer referred for palliative radiation therapy in an outpatient setting. Support Cancer Ther 2007;4:157-162.



CHAPTER 4A

# A FULLY-COVERED STENT (ALIMAXX-E) FOR THE PALLIATION OF MALIGNANT DYSPHAGIA: A PROSPECTIVE FOLLOW-UP STUDY

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*Gastrointestinal Endoscopy 2009;70:1082-1089*





**Background:** The majority of the currently available metal stents are partially covered to reduce migration risk. However, one of the remaining issues is tissue ingrowth through the uncovered stent parts.

**Objective:** To determine efficacy, recurrent dysphagia, and complications of a fully covered stent, i.e., the Alimaxx-E stent, and to compare two stent delivery systems, i.e., one introducing the stent over a guidewire and one introducing the stent over a small-caliber endoscope.

**Design:** A prospective, follow-up study evaluating a new stent design, with randomization for type of introduction system.

**Setting:** Three tertiary referral centers.

**Patients:** Forty-five patients with inoperable or metastatic esophageal or gastric cardia cancer.

**Interventions:** Stent placement.

**Main Outcome Measurements:** (1) Functional outcome, recurrent dysphagia, complications, and mortality of the Alimaxx-E stent; (2) functional aspects of the delivery system.

**Results:** At 4 weeks after stent placement, the dysphagia score improved in all patients (P < .001). Twenty-two of 45 patients (49%) developed among them 28 episodes of recurrent dysphagia, predominantly stent migration (n = 16). Major complications occurred in 9 of 45 patients (20%), with all 5 early (< 1 week) complications (severe pain [n = 3], hemorrhage [n = 1], and fever [n = 1]) occurring in patients in whom the stent was introduced over the endoscope (P = .02). During follow-up, 44 patients died, 3 (7%) from hemorrhage.

**Limitation:** The Alimaxx-E stent was not randomly compared with other stent designs.

**Conclusions:** Placement of Alimaxx-E stents is safe and produces long-term relief of dysphagia, particularly when introduced over a guidewire. The migration rate of the Alimaxx-E stent is, however, unacceptably high, and an adapted stent design is needed.

Self-expanding metal or plastic stents are frequently used for the relief of dysphagia from inoperable esophageal or gastric cardia cancer.[1,2] During the last few years, procedure-related complications and long-term complications of stent placement have remained unchanged, with rates less than 10%[3-5] and less than 15%,[4,5] respectively. In contrast, recurrent dysphagia after stent placement is a frequently encountered problem, occurring in 30% to 50% of patients, mainly due to nontumoral or tumoral tissue ingrowth and overgrowth, stent migration, and, to a lesser extent, food-bolus obstruction.[4,5]

The relatively high frequency of recurrent dysphagia has resulted in efforts to improve stent design. Currently, several stent designs are available.[4,6] The most commonly used stents worldwide are the metal, partially covered Ultraflex stent (Boston Scientific, Natick, Mass) and the nonmetal (plastic) fully covered Polyflex stent (Boston Scientific). Nontumoral and tumoral tissue ingrowth is a frequently observed cause of recurrent dysphagia with Ultraflex stents,[4,5,7,8] whereas stent migration commonly occurs with Polyflex stents.[4,5,9-11] A relatively new stent is the fully covered Niti-S stent (Taewoong Medical, Seoul, Korea), which has an outer nitinol wire that reduces the risk of stent migration.[4,12]

The newly designed Alimaxx-E stent (Alveolus, Charlotte, NC) is fully covered to resist tissue ingrowth and has 20 struts on the outside to prevent migration (Figure 1). The stent can be introduced by using 2 different procedures: (1) over a guidewire (Alimaxx-E GW; Alveolus) or (2) by direct vision using a special delivery system with the delivery catheter fitting over a small-caliber endoscope (Alimaxx-E DV; Alveolus).

The aim of the current study was to determine functional outcome, recurrent dysphagia, and complications of the Alimaxx-E stent in patients with inoperable esophageal or gastric cardia cancer. Furthermore, stent placement by introducing it over a guidewire or by direct vision was compared for functional aspects.

## PATIENTS AND METHODS

Between March 2006 and January 2007, all consecutive patients with dysphagia due to esophageal or gastric cardia cancer who met the inclusion and did not meet the exclusion criteria of the study and gave informed consent were treated with an Alimaxx-E stent. Inclusion criteria included an inoperable malignant obstruction of the esophagus or gastric cardia, or recurrent dysphagia after prior radiation with curative or palliative intent for esophageal or gastric cardia cancer. A tumor was considered inoperable if the patient had distant metastases or local tumor infiltration in neighboring organs and/or a poor condition because of concomitant disease. Exclusion criteria included a tumor length of more than 12 cm, tumor growth within 2 cm of the upper esophageal sphincter, a fistula between the esophagus and respiratory tree, and previous stent placement. Patients who were unfit to undergo conscious sedation were also excluded. Finally, 45 patients gave written informed consent, and 2 patients refused to participate in the study. Stent placement was performed at 3 centers: (1) the Erasmus MC – University Medical Center Rotterdam, The Netherlands; (2) the Academic Medical Center Amsterdam, The Netherlands; and (3) the Istituto Clinico Humanitas, Milan, Italy. The institutional review boards at all 3 hospitals approved the study.

All patients were evaluated before stent placement and at 4-week intervals after stent placement, until death. Evaluations were performed by scheduled telephone interviews of the patient and included the following items: (1) ability to eat and/or swallow, as assessed by the dysphagia score, graded as, 0 = ability to eat a normal diet; 1 = ability to eat some solid food; 2 = ability to eat some semi-solids only; 3 = ability to swallow liquids only; and 4 = complete dysphagia; (2) general health, as assessed by the World Health Organization performance score, graded as, 0 = normal activity; 1 = symptoms but ambulatory; 2 = in bed less than 50% of time; 3 = in bed more than 50% of time; and 4 = 100% bedridden; and (3) specific symptoms, such as pain, heartburn, and weight loss. When indicated, eg, in case of recurrent dysphagia or complications, patients were clinically evaluated and treated.

### Stent design

The Alimaxx-E stent is made of nitinol, and it is fully covered with polyurethane to resist tissue ingrowth (Figure 1). The Alimaxx-E stent used in this study had a luminal diameter of 18 or 22 mm. If prestenotic dilation was observed during endoscopy, then a larger-diameter stent was used. The outward force of the stent is most pronounced at the body. The stent has 20 antimigration struts to prevent migration.







**Capsule summary**

**What is already known on this topic**

- Partially covered esophageal stents are susceptible to tissue in-growth but have a low risk of stent migration.

**What this study adds to our knowledge**

- In a prospective follow-up evaluation of a new, fully covered stent in 45 patients with inoperable or metastatic esophageal or gastric cardia cancer, dysphagia scores universally improved at 4 weeks.
- Twenty-two patients developed 28 episodes of recurrent dysphagia, mostly because of stent migration.

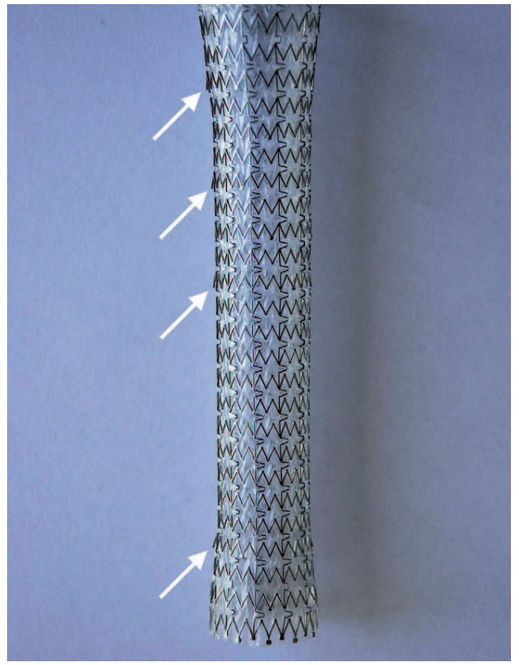

**Figure 1.** *Fully covered Alimaxx-E stent with 20 anti-migration struts on the outside (arrows).*

### Procedure

If a tight stricture was present, then the tumor was dilated to a maximum diameter of 12 mm by using Savary dilation or (preferably) a small-caliber (5.9 mm) endoscope (Olympus BV, Zoeterwoude, The Netherlands) was used to allow the tumor to be inspected, the tumor margins to be marked, and a guidewire to be placed. A stent measuring 2 to 4 cm longer than the stricture was chosen to allow for a 1 to 2 cm extension above and below the proximal and distal tumor shoulder.

The stent was introduced over a guidewire (Alimaxx-E GW) or by direct vision by using a new delivery system in which the delivery catheter fitted over a small-caliber endoscope (Alimaxx-E DV). The choice for either delivery system was at random, after stratification for previous chemotherapy and/or radiotherapy, and for tumor location. The Alimaxx-E DV features a window at the end of the introduction system to view stent deployment. The size of the introduction catheter of the Alimaxx-EDV is 30F, whereas that of the Alimaxx-E GW is smaller, with a size of 22F. We only used fluoroscopy with the DV introduction system when stent placement was technically difficult and additional information during placement was considered to be indicated.

### Statistical analysis

The results were expressed as mean (SD), and medians with interquartile range (IQR) and range; survival was expressed as median survival (Kaplan-Meier). Differences in dysphagia score and World Health Organization performance score and weight before treatment and at 1, 3, and 6 months after treatment were analyzed by the Wilcoxon rank sum test.

Complications between the 2 introduction systems were compared with the Kaplan-Meier and log-rank test to adjust for time of occurrence of the event and

survival differences. Factors influencing the frequency of migration were analyzed with Cox regression analysis with tumor location, introduction system, stent diameter, prior and post radiation, and/or chemotherapy, histology, and tumor length as covariates. A 2-sided P < .05 was considered statistically significant. All analyses were conducted with SPSS, version 14.0 (SPSS Inc, Chicago, Ill).

| Characteristics | Patients (n = 45) |
|---|---|
| Age (y) (mean SD) | 63 (11) |
| Males, no. of patients (%) | 33 (73) |
| Dysphagia score before treatment, median (IQR, range) | 3 (1, 2-4) |
| WHO performance score before treatment, median (IQR, range) | 1 (1, 0-4) |
| Tumor length, cm, mean (SD) | 7.1 (2.1) |
| Tumor location, no. of patients (%) | |
| • Mid-esophagus | 10 (22) |
| • Distal esophagus/gastric cardia | 35 (78) |
| Histology, no. of patients (%) | |
| • Squamous cell carcinoma | 15 (33) |
| • Adenocarcinoma | 29 (64) |
| • Unknown | 1 (2) |
| Prior radiation and/or chemotherapy, no. of patients (%) | 14 (31) |
| • Chemotherapy | 8 (18) |
| • Radiation | 1 (2) |
| • Both | 5 (11) |

IQR, interquartile range; WHO, World Health Organization.

**Table 1.** *Clinical characteristics of 45 patients treated with an Alimaxx-E stent for palliation of dysphagia due to carcinoma of the esophagus or gastric cardia.*

## RESULTS

### Clinical characteristics

Clinical characteristics of 45 patients treated with an Alimaxx-E stent are shown in Table 1. The length of the tumor was longer for patients treated with the Alimaxx-E GW system (mean 7.7 cm; SD 1.8) than for those treated with the Alimaxx-E DV system (mean 6.4 cm; SD 2.2 (P = .04)). All other characteristics were not different between the 2 introduction systems.

### Procedural characteristics

In total, 22 patients were treated with the Alimaxx-E GW system and 23 with the Alimaxx-E DV system (Table 2). In 11 of 23 (48%) patients treated with the DV system, and in none of the patients treated with the GW system, difficulties were experienced passing the introduction system through the stricture (P < .001). Endoscopic vision through the window at the end of the introduction system of the DV system was poor in 2 patients (9%), which resulted in fluoroscopy-guided stent placement in these patients. The procedural time with the DV system was longer compared with the GW system (16 vs 10 minutes, respectively; P = .04).

### Functional outcome

Functional outcome is shown in Figures 2 to 4. The dysphagia score improved in surviving patients from a median score of 3 before stent placement to a median of 1 at 1 month, and zero in patients still alive at 6 months after treatment (both intervals: P < .001). The median World Health Organization performance status remained stable in the first month (score: 1) after stent placement (P = .05), but slightly deteriorated 6 months after treatment (score: 2) (P < .01). The median weight remained stable shortly after placement (66 kg) (P = .05) and had slightly increased 6 months later (70 kg) (P = .49).





| Characteristics | ALIMAXX-E GW (n = 22) | ALIMAXX-E DV (n = 23) | P value* |
|---|---|---|---|
| Diameter stent, no. of patients (%) | | | .46 |
| • Small (18 mm) | 12 (55) | 10 (44) | |
| • Large (22 mm) | 10 (46) | 13 (57) | |
| Dilation before treatment, no. of patients (%) | 3 (14) | 2 (9) | .60 |
| Technical problems, no. of patients (%) | | | |
| • Difficulties passing the system through stricture | 0 (0) | 11 (48) | <.001 |
| • Poor endoscopic vision | – | 2 (9) | – |
| • Difficulties with deployment stent | 0 (0) | 3 (13) | .09 |
| • Repositioning stent required | 5 (23) | 5 (22) | .86 |
| • Difficulties removing delivery system | 3 (14) | 1 (4) | .25 |
| Use of fluorosocopy during stent placement, no. of patients (%) | 22 (100) | 2 (9) | <.001 |
| Procedure time, min, median (IQR, range) | 10 (5, 6-30) | 16 (8, 6-25) | .04 |

*** Comparing the Alimaxx-E GW with the Alimaxx-E DV introduction system.**

**Table 2.** *Procedural characteristics of the Alimaxx-E GW and Alimaxx-E DV delivery system.*

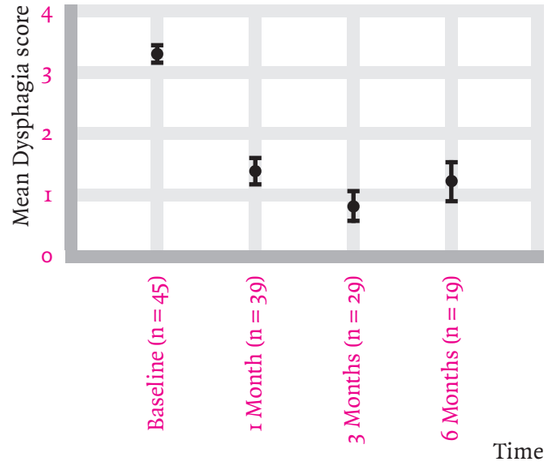


**Figure 2.** *Mean dysphagia score for a period of time in 45 patients treated with an Alimaxx-E stent for palliation of dysphagia due to carcinoma of the esophagus or gastric cardia.*

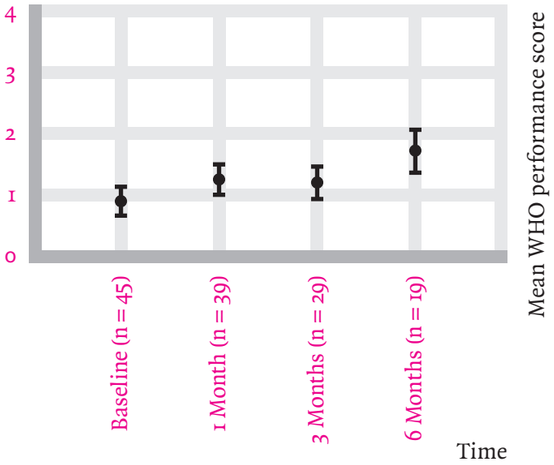


**Figure 3.** *Mean World Health Organization performance score for a period of time in 45 patients treated with an Alimaxx-E stent for palliation of dysphagia due to carcinoma of the esophagus or gastric cardia.*





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| Complications and recurrent dysphagia | Patients (n = 45) |
|---|---|
| Total complications (major-minor), no. of patients (%) | 20 in 17 (38) |
| Major complications, no. of patients (%) | 10 in 9 (20) |
| ≤ 7 days | 5 in 5 (11)* |
| • Severe pain | 3 |
| • Hemorrhage | 1 |
| • Fever | 1 |
| • Perforation | 0 |
| ≥ 7 days | 5 in 5 (11) |
| • Severe pain | 0 |
| • Hemorrhage | 2 |
| • Fistula | 3 |
| Minor complications, no. of patients (%) | 10 in 10 (22) |
| • Mild pain | 7 |
| • Gastroesophageal reflux | 3 |
| Recurrent dysphagia, no. of patients (%) | 28 in 22 (49) |
| • Stent migration | 16 |
| • Tissue overgrowth | 7 |
| • Food bolus obstruction | 4 |
| • Other | 1† |

***P = .02, comparing Alimaxx-E DV with Alimaxx-E GW introduction system.**
**† = Stent not fully deployed.**

**Table 3.** *Complications and recurrent dysphagia after placement of an Alimaxx-E esophageal stent in 45 patients with dysphagia due to inoperable carcinoma of the esophagus or gastric cardia.*

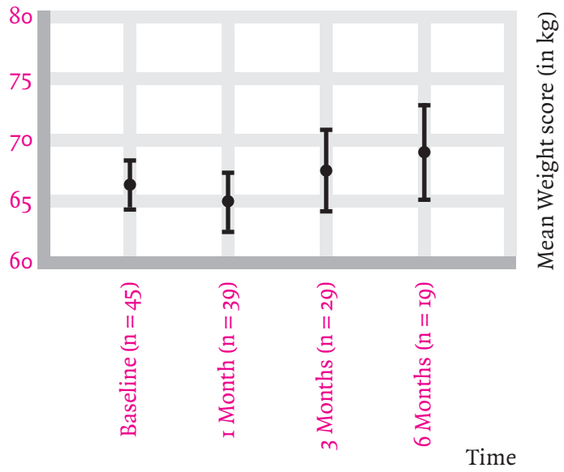


**Figure 4.** *Mean weight score (in kg) for a period of time in 45 patients treated with an Alimaxx-E stent for palliation of dysphagia due to inoperable carcinoma of the esophagus or gastric cardia.*

### Recurrent dysphagia

Twenty-two of 45 patients (49%) with an Alimaxx-E stent developed 28 episodes of recurrent dysphagia, which was caused by tissue overgrowth (n = 7), stent migration (n = 16), food bolus obstruction (n = 4), or a stent that was not fully deployed (n = 1) (Table 3). All but 1 stent migrated into the stomach, and these were endoscopically removed, either with a snare or a grasping forceps, without encountering complications. In 1 patient, the stent migrated into the small bowel. This patient refused an endoscopic intervention to remove the stent, and the stent was surgically removed. Three patients had tissue overgrowth at both ends of the stent, and another 4 patients had tissue overgrowth at only the proximal end of the stent. Tissue overgrowth in 6 patients was treated with a second overlapping stent and in 1 patient by radiation therapy to treat concomitant bleeding. Tumor histology, particularly adenocarcinoma, was the only variable in univariable analysis that was associated with an increased risk of stent migration (hazard ratio [HR] = 5.5; P = .03); however, in multivariable analysis, no significant effect of any of these variables remained statistically significant (Table 4).

### Complications

In total, major and minor complications were seen in 17 of 45 patients (38%) treated with an Alimaxx-E stent (Table 3). Of these, 5 major complications occurred shortly ( < 1 week) after the procedure, all in patients treated with the Alimaxx-E DV system (P = .02 for a difference between both systems). Three patients had severe pain within 24 hours after stent placement; these patients were hospitalized for a short period and treated with analgesics. In the fourth patient, hemorrhage occurred 5 days after stent placement, and this patient died from the complication. The fifth patient had a fever develop 1 day after placement, without a focus being detected, and this patient was treated with a short course of antibiotics that helped resolve the fever without complications. Long-term major complications occurred in 5 of 45 patients (11%); 3 in the DV group and 2 in the GW group (P = .76). Three patients developed an esophagorespiratory fistula; 2 of the patients at the distal end of the stent and 1 patient at the proximal end, yet all occurred in the setting of a small-diameter stent. In 2 patients, a hemorrhage was detected after 3 and 9 months, respectively, and both patients died from this complication.

Minor complications, particularly retrosternal pain and symptoms of gastroesophageal reflux, were seen in 10 of 45 patients (22%) (Table 3). The pain was stent related in all 7 patients. These patients required temporary analgesics but were not admitted to the hospital.

### Survival

Follow-up was updated to August 2008. One patient was still alive at that time. The median survival after stent placement was 146 days (95% CI, 97-195 mm). The majority of patients died as a result of tumor progression (n = 40 (89%)). Three patients (7%) died from hemorrhage, which could have been related to the stent but was more likely related to tumor characteristics and/or progression, and 1 patient died from an unrelated cause.

## DISCUSSION

In this prospective follow-up series of 45 patients treated with an Alimaxx-E stent for dysphagia due to inoperable carcinoma of the esophagus or gastric cardia, we showed that this new stent design provided good symptomatic relief of malignant dysphagia. Placement of an Alimaxx-E stent was also safe and was not associated with a higher incidence of complications compared with those found in previous studies with other stent designs, i.e., Niti-S stents, Polyflex stents, and Ultraflex stents.[4,5,9,12,13]

However, the most remarkable finding was the rather high incidence of recurrent dysphagia due to stent migration (Table 3). This finding was somewhat unexpected in this group of patients with a stenotic esophageal or gastric cardia carcinoma. Stent migration was only associated with tumor histology, particularly adenocarcinoma, but not with other tumor- or stent-related factors in univariate analysis (Table 4). Nevertheless, because all adenocarcinomas were located in the distal esophagus, tumor location probably played a role in the high migration rate.[13,14] This may also explain why the migration rate was higher, although not significantly, with large-diameter stents compared with small-diameter stents. This is in contrast to findings in the literature.[7,8,15] Large-diameter stents were, however, more often placed across the gastroesophageal junction (21 of 23) than were





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| Characteristics | Patients | Events (migration) | Univariable analysis* 95% HR | CI | P value |
|---|---|---|---|---|---|
| Tumor location | | | | | |
| • Mid-esophagus | 10 | 2 | 1 | | |
| • Distal esophagus/gastric cardia | 35 | 13 | 3.1 | 0.7-14 | .14 |
| Prior chemotherapy and/or radiation | | | | | |
| • No | 31 | 12 | 1 | | |
| • Yes | 14 | 3 | 0.4 | 0.1-1.5 | .18 |
| Post chemotherapy | | | | | |
| • No | 35 | 9 | 1 | | |
| • Yes | 10 | 6 | 1.6 | 0.6-4.7 | .36 |
| Tumor histology | | | | | |
| • Squamous cell carcinoma | 15 | 2 | 1 | | |
| • Adenocarcinoma | 29 | 13 | 5.5 | 1.2-25 | .03 |
| Tumor length (per cm) | | | 0.9 | 0.7-1.2 | .60 |
| Stent introduction system | | | | | |
| • Guidewire (GW) | 22 | 9 | 1 | | |
| • Over the scope (DV) | 23 | 6 | 0.50 | 0.2-1.4 | .19 |
| Stent diameter | | | | | |
| • Small | 22 | 5 | 1 | | |
| • Large | 23 | 10 | 2.7 | 0.9-8.0 | .07 |

**HR, hazard ratio; CI, confidence interval.**

*** None of these issues remained significantly different in multivariable analysis.**

**Table 4.** *Univariable analysis on factors associated with occurrence of migration in 45 patients treated with an Alimaxx-E stent for palliation of dysphagia due to inoperable carcinoma of the esophagus or gastric cardia.*

small-diameter stents (9 of 22), which may well account for this finding. In addition, it seems likely that the high migration rate of the Alimaxx- E stent was also caused by characteristics of the stent itself, particularly the fact that the stent is fully covered to allow removal if indicated. Although the Alimaxx-E stent is flared, has an outward force that is most pronounced at the stent body, and has 20 struts on the outside of the stent, these features were probably not sufficient to prevent migration. An adapted stent design with 45 struts instead of 20 has recently been introduced. Our own (preliminary) experience suggests that the results of the migration rate with the adapted Alimaxx-E stent are reduced.







Recurrent dysphagia due to nontumoral or tumoral tissue overgrowth was found in 7 patients (16%). This is in line with tissue ingrowth or overgrowth rates reported with the Polyflex stent (10% - 20%), but this rate is lower than those reported with another fully covered metal stent, i.e., the Niti-S stent (24%), and a partially covered metal stent, i.e., the Ultraflex stent (up to 31%).[4,5,9,16,17] Mayoral et al[18] found that in almost half of the patients with tissue ingrowth or overgrowth, the cause was nontumoral tissue, mainly granulation tissue formation. Stent characteristics, such as radial force, stent diameter, and contact of the esophageal mucosa with the exposed metal stent part, have all been suggested to play a causative role in nontumoral tissue growth.[18]

As previously mentioned, the major complication rate in this study was similar to that observed with other recently introduced stents. Remarkably, all early ( < 1 week) major complications occurred with stents placed with the DV delivery system. We noted that passing this delivery system through a stenotic tumor was more difficult compared with the GW delivery system. The DV system has a diameter of 30F, whereas that of the GW delivery system is 22F. The fact that the DV delivery system is also rather rigid explains why placing stents with this system is associated with an increased risk of procedure-related complications. The characteristics of the DV system are not very much different from those of the formerly used delivery systems for placement of plastic endoprostheses, which have also been shown to be associated with a high procedure-related complication rate.[19,20] Therefore, we suggest an improvement of the design of the DV delivery system; however, as the system is made to fit over a small-caliber endoscope, the feasibility of this seems unlikely.

Although the outward force of the stent was less pronounced at both ends than at the body, remarkably, 3 patients (7%) had fistula formation develop at the stent end. Nonetheless, this occurrence rate and the time interval between stent placement and fistula formation, after 4, 5, and 13 months, respectively, were not different from those reported in other series in which fistula formation was observed in as many as 9% of patients after a similar follow-up period.[4,5,14] Therefore, the most likely cause of fistula formation was tumor progression, possibly in combination with pressure on the esophageal mucosa exerted by the flared stent ends.

In conclusion, the Alimaxx-E stent provides relief of dysphagia from esophageal and gastric cardia cancer; however, the initial design was associated with a high incidence of stent migration. It is unclear whether this stent offers any true clinical advantages in comparison with existing partially covered stents. Comparative studies with other stent designs are needed. Because the risk of procedure-related complications was lower and the placement was easier with the GW system compared with the DV system, we strongly recommend the former system for stent placement.

## REFERENCES

1. Homs MY, Kuipers EJ, Siersema PD. Palliative therapy. J Surg Oncol 2005;92:246-256.

2. Siersema PD. Treatment options for esophageal strictures. Nat Clin Pract Gastroenterol Hepatol 2008;5:142-152.

3. Sabharwal T, Hamady MS, Chui S, et al. A randomised prospective comparison of the Flamingo Wallstent and Ultraflex stent for palliation of dysphagia associated with lower third oesophageal carcinoma. Gut 2003;52:922-926.

4. Verschuur EM, Repici A, Kuipers EJ, et al. New design esophageal stents for the palliation of dysphagia from esophageal or gastric cardia cancer: a randomized trial. Am J Gastroenterol 2008;103:304-312.

5. Conio M, Repici A, Battaglia G, et al. A randomized prospective comparison of self-expandable plastic stents and partially covered selfexpandable metal stents in the palliation of malignant esophageal dysphagia. Am J Gastroenterol 2007;102:2667-2677.

6. Siersema PD, Marcon N, Vakil N. Metal stents for tumors of the distal esophagus and gastric cardia. Endoscopy 2003;35:79-85.

7. Homs MY, Steyerberg EW, Eijkenboom WM, et al. Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from oesophageal cancer: multicentre randomised trial. Lancet 2004;364:1497-1504.

8. Siersema PD, Hop WC, van Blankenstein M, et al. A comparison of 3 types of covered metal stents for the palliation of patients with dysphagia caused by esophagogastric carcinoma: a prospective, randomized study. Gastrointest Endosc 2001;54:145-153.

9. Conigliaro R, Battaglia G, Repici A, et al. Polyflex stents for malignant oesophageal and oesophagogastric stricture: a prospective, multicentric study. Eur J Gastroenterol Hepatol 2007;19:195-203.

10. Holm AN, de la Mora Levy JG, Gostout CJ, et al. Self-expanding plastic stents in treatment of benign esophageal conditions. Gastrointest Endosc 2008;67:20-25.

11. Dua KS, Vleggaar FP, Santharam R, et al. Removable self-expanding plastic esophageal stent as a continuous, non-permanent dilator in treating refractory benign esophageal strictures: a prospective two-center study. Am J Gastroenterol 2008;103:2988-2994.

12. Verschuur EM, Homs MY, Steyerberg EW, et al. A new esophageal stent design (Niti-S stent) for the prevention of migration: a prospective study in 42 patients. Gastrointest Endosc 2006;63:134-140.

13. Siersema PD. New developments in palliative therapy. Best Pract Res Clin Gastroenterol 2006;20:959-978.

14. Homann N, Noftz MR, Klingenberg-Noftz RD, et al. Delayed complications after placement of self-expanding stents in malignant esophageal obstruction: treatment strategies and survival rate. Dig Dis Sci 2008;53:334-340.

15. Verschuur EM, Steyerberg EW, Kuipers EJ, et al. Effect of stent size on complications and recurrent dysphagia in patients with esophageal or gastric cardia cancer. Gastrointest Endosc 2007;65: 592-601.

16. Dormann AJ, Eisendrath P, Wigginghaus B, et al. Palliation of esophageal carcinoma with a new self-expanding plastic stent. Endoscopy 2003;35:207-211.

17. Szegedi L, Gal I, Kosa I, et al. Palliative treatment of esophageal carcinoma with self-expanding plastic stents: a report on 69 cases. Eur J Gastroenterol Hepatol 2006;18:1197-1201.



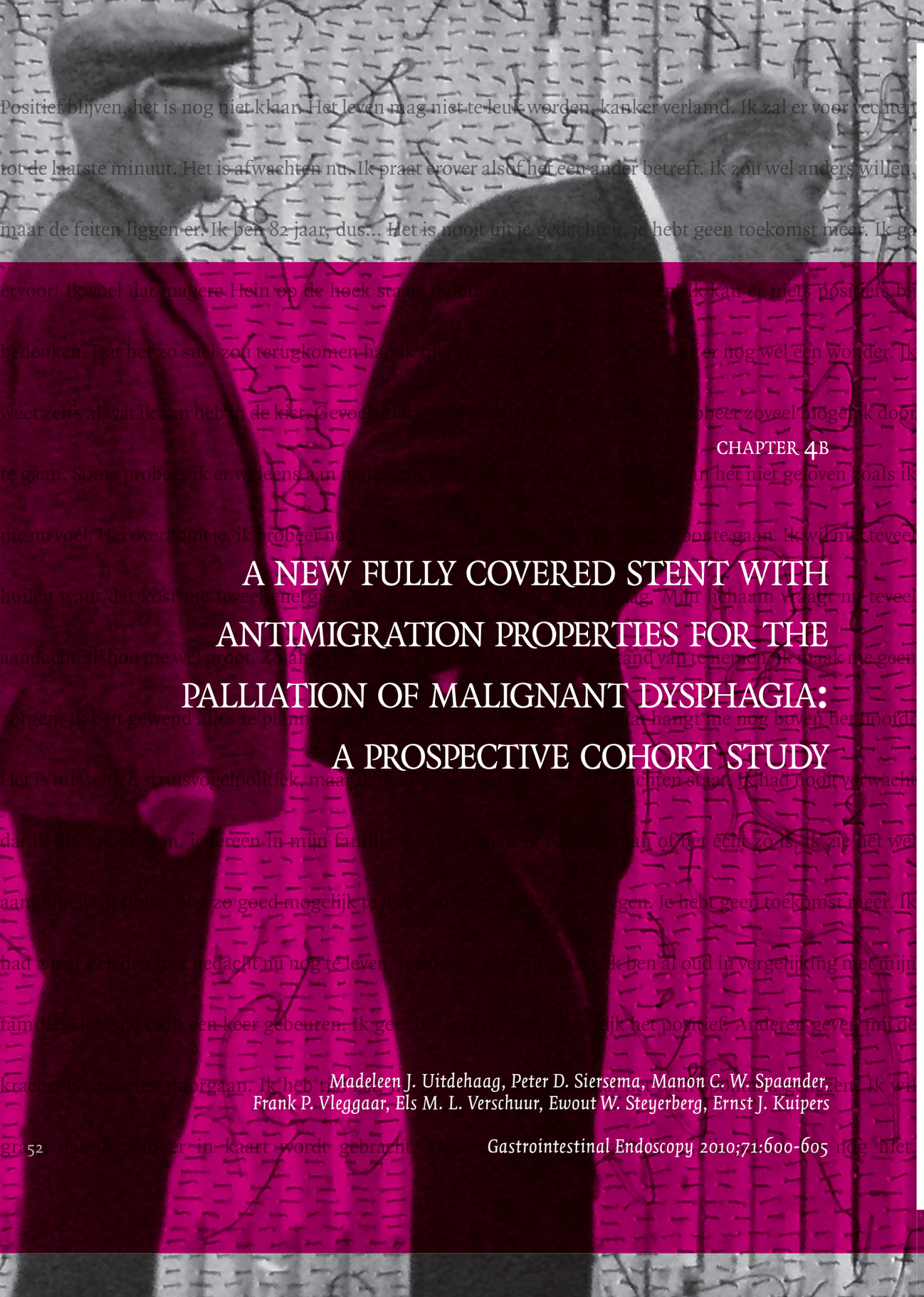




18. Mayoral W, Fleischer D, Salcedo J, et al. Nonmalignant obstruction is a common problem with metal stents in the treatment of esophageal cancer. Gastrointest Endosc 2000;51:556-559.

19. Knyrim K, Wagner HJ, Bethge N, et al. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med 1993;329:1302-1307.

20. Siersema PD, Hop WC, Dees J, et al. Coated self-expanding metal stents versus latex prostheses for esophagogastric cancer with special reference to prior radiation and chemotherapy: a controlled, prospective study. Gastrointest Endosc 1998;47:113-120.



CHAPTER 4B

# A NEW FULLY COVERED STENT WITH ANTIMIGRATION PROPERTIES FOR THE PALLIATION OF MALIGNANT DYSPHAGIA: A PROSPECTIVE COHORT STUDY

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*Gastrointestinal Endoscopy 2010;71:600-605*





**Background:** Fully covered stents are designed to resist tissue ingrowth that is often seen with partially covered stents. An issue with fully covered stents is the risk of migration.

**Objective:** We aimed to determine efficacy, recurrent dysphagia, and complications of the SX-ELLA stent Esophageal HV, which is fully covered to resist tissue ingrowth and has an antimigration ring to withstand migration.

**Design:** Prospective cohort study.

**Setting:** Two tertiary referral centers.

**Patients:** Forty-four patients with malignant esophageal strictures from inoperable or metastatic esophageal or gastric cardia cancer (n = 42) or lung cancer (n = 2).

**Interventions:** Placement of an SX-ELLA stent.

**Main outcome measures:** Functional outcome, recurrent dysphagia, complications, and survival.

**Results:** Dysphagia improved from a median score of 3 (liquids only) before stent placement to 1 (ability to eat some solid food) 4 weeks later ($P < .001$). Twelve of 44 (Kaplan Meier analysis = 40%) patients developed 18 episodes of recurrent dysphagia of which 6 were caused by stent migration and 2 by tissue overgrowth. In total, 14 episodes of major complications developed in 10 of 44 (Kaplan Meier analysis = 29%) patients, 8 of which were caused by hemorrhage. After a median follow-up of 15 months, 39 patients had died (median survival 110 days), 5 (11%) from hemorrhage.

**Limitations:** Nonrandomized study design.

**Conclusions:** Dysphagia caused by esophageal cancer can be successfully palliated by placement of a new, fully covered esophageal stent (SX-ELLA). Although this single-wire braided stent with an antimigration ring is supposed to be less traumatic and to reduce migration, this was not substantiated in this study. Further improvements of stent features are needed to achieve the goals set for this study.

Metal stents have become popular for the palliation of patients with malignant esophageal obstruction, especially patients with a poor prognosis.[1,2] Initially, most stents were partially covered. These stents have as a major disadvantage that recurrent dysphagia caused by tumoral and nontumoral tissue growth through the uncovered stent mesh frequently occurs.[3-8] In the past few years, fully covered stents have been introduced. Although the full covering of these stents prevents tissue ingrowth, the issues of both tissue overgrowth and stent migration remain.[4-9]

Recently, a new stent, the SX-ELLA stent Esophageal HV (Ella-CS, Hradec Kralove, Czech Republic), was developed for the palliation of malignant dysphagia. This stent (Figure 1) is made of a nickel-titanium alloy (nitinol) and is braided from 1 piece of wire that should make the stent ends less traumatic and improve the flexibility of the stent with expected reduced hyperplastic (nontumoral) tissue overgrowth.[10] To decrease the risk of migration, the SX-ELLA stent has a flip-flop type of antimigration ring that is circumferentially attached to the proximal stent portion (Figure 2). This ring functions as a circular hook preventing migration, but is also flexible and is everting when the traction force is too strong. This mechanism should reduce the risk of esophageal wall injury. The stent flares to 25 mm at its proximal and distal ends with a body diameter of 20 mm.

The aim of this study was to determine the efficacy

of the SX-ELLA stent for the palliation of malignant dysphagia in patients with inoperable or metastatic esophageal, gastric cardia, or lung cancer, with special emphasis on recurrent dysphagia particularly caused by tissue overgrowth and migration.

## METHODS

### Patients

Between February 2007 and May 2008, 45 patients with dysphagia caused by esophageal, gastric cardia, or lung cancer were consecutively enrolled in the study. Inclusion criteria were inoperable malignant obstruction of the esophagus or gastric cardia caused by esophageal, cardia, or lung carcinoma. All patients gave written informed consent. Exclusion criteria were an obstruction length of more than 12 cm, tumor growth within 2 cm of the upper esophageal sphincter, and a fistula between the esophagus and respiratory tree. Patients who were unfit to undergo conscious sedation were also excluded. Stent placement was performed at 2 tertiary referral hospitals, the Erasmus MC-University Medical Center Rotterdam and the University Medical Center Utrecht, both in The Netherlands. The medical ethics committees of both hospitals approved the study.

### Methods

All patients were evaluated before stent placement and at 4-week intervals after stent placement until death. Evaluations were performed by scheduled telephone calls to each patient and/or the patient's general practitioner and included the ability to eat and/or swallow (graded as follows: 0 = ability to eat a normal diet, 1 = ability to eat some solid food, 2 = ability to eat some semisolids only, 3 = ability to swallow liquids only, and 4 = complete dysphagia)[11] and specific symptoms such as pain, heartburn, and weight loss. In cases of recurrent dysphagia or complications, patients were seen for evaluation

**Capsule Summary**

**What is already known on this topic**

- Fully covered esophageal stents prevent tissue ingrowth, but tissue overgrowth and stent migration may still occur.

**What this study adds to our knowledge**

- In a prospective study of 44 patients with malignant esophageal strictures who underwent placement of fully covered, single-wire braided stents, dysphagia scores improved, but major complications developed in 10 patients, including stent migration and hemorrhage.

**Figure 1.** *The fully covered SX-ELLA stent with an antimigration ring at the upper stent end.*

**Figure 2.** *The antimigration ring of the SX-ELLA stent showing its flip-flop mechanism to prevent migration.*

and/or treatment. When a patient was referred to another hospital, relevant clinical information was obtained.

### Stent placement

All patients were consciously sedated with midazolam (Dormicum; Roche Nederland BV, Mijdrecht, The Netherlands) during stent insertion. If indicated, the stricture was first dilated to 9 to 10 mm by using Savary dilation or (preferably) a small-caliber (5.9 mm) endoscope (Olympus BV, Zoeterwoude, The Netherlands) to allow the tumor

| | Total (N = 44) |
|---|---|
| Age, y, mean ± SD | 64 ± 11 |
| Male sex, no. patients (%) | 35 (80) |
| Dysphagia score before treatment, median (IQR) | 3 (1) |
| WHO performance score before treatment (IQR) | 1 (1) |
| Tumor length, cm, mean ± SD | 6.8 ± 3.8 |
| Tumor location, no. patients (%) | |
| • Proximal or mid esophagus | 17 (39) |
| • Distal esophagus or gastric cardia | 25 (57) |
| • Lung | 2 (5) |
| Histology, no. patients (%) | |
| • Squamous cell carcinoma | 19 (43) |
| • Adenocarcinoma | 24 (55) |
| • Unknown | 1 (2) |
| Previous radiation and/or chemotherapy, no. patients (%) | |
| • Chemotherapy | 9 (21) |
| • Radiation | 3 (7) |
| • Radiation and chemotherapy | 6 (14) |
| Dilation before treatment, no. patients (%) | 4 (9) |

**Table 1.** *Characteristics of 44 patients treated with an SX-ELLA stent for palliation of dysphagia caused by esophageal, gastric cardia, or lung cancer.*

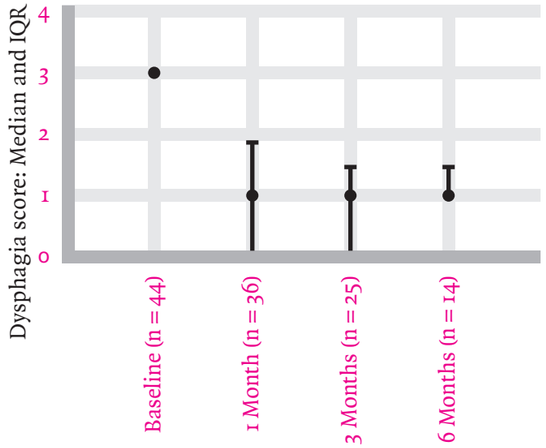


**Figure 3.** *Median dysphagia score over time after placement of an SX-ELLA stent for palliation of dysphagia caused by esophageal, gastric cardia, or lung cancer.*

**Table 2.** *Recurrent dysphagia and complications after placement of an SX-ELLA stent for palliation of dysphagia caused by esophageal, gastric cardia, or lung cancer.*

| | Total (n = 44) |
|---|---|
| Recurrent dysphagia (%)* | 18 episodes in 12 pts (27-40)* |
| • Stent migration | 6 episodes in 6 pts (14-20) |
| • Overgrowth | 2 episodes in 2 pts (5-8) |
| • Food impaction | 8 episodes in 5 pts (11-17) |
| • Other | 2 episodes in 2 pts † (5-9) |
| Total no. complications (%) | 26 complications in 18 pts (41-47) |
| No. major complications | 14 complications in 10 pts (23-29) |
| ≤7 days | |
| • Severe pain | 3 in 3 pts (7-7) |
| • Hemorrhage | 1 (2-2) |
| • Fever | 1 (2-2) |
| ≥7 days | |
| • Hemorrhage | 7 in 6 pts (14-25) |
| • Fistula | 2 in 2 pts (5-6) |
| Minor complications | 12 in 12 pts (27-30) |
| • Mild pain | 7 in 7 pts (16-16) |
| • Gastroesophageal reflux | 5 in 5 pts (11-13) |

*** % = valid percentage versus percentage measured by the Kaplan-Meier method (6 months), respectively.**

**† Stent not fully deployed (1 patient) and stent fracture (1 patient).**





to be inspected, the tumor margins to be marked, and a guidewire to be placed. A stent measuring 2 to 4 cm longer than the stricture was chosen to allowfor a 1 to 2 cm extension above and below the proximal and distal tumor shoulder.

### Statistical analysis

The results were expressed as mean ± standard deviation and medians and interquartile range (IQR); survival was expressed as median survival. Differences in dysphagia score before and 1, 3, and 6 months after treatment were analyzed by the Wilcoxon rank-sum test. The percentages of patients with complications and recurrent dysphagia were calculated by using the Kaplan-Meier (KM) method to adjust for time of occurrence of the event and survival differences.

## RESULTS

### Functional outcome

Successful placement of 46 SX-ELLA stents was achieved in all 45 patients. Because 1 patient was lost to follow-up, clinical characteristics of 44 patients are shown in Table 1. In all 25 (57%) patients with a tumor located in the distal esophagus or gastric cardia, the stent crossed the gastroesophageal junction. Eight patients died before the 4-week follow-up, with 1 of them having symptoms of hemorrhage and upper abdominal pain that were considered to be related to stent insertion. After 4 weeks, the dysphagia had improved from a median score of 3 to 1 ($P < .001$). This persisted in patients who were still alive after 3 and 6 months (Figure 3).

### Recurrent dysphagia

In total, 18 episodes of recurrent dysphagia developed in 12 of 44 (KM = 40%) patients with an SX-ELLA stent, which were caused by food impaction (8 episodes), stent migration (6 episodes), tumor overgrowth (2 episodes), stent fracture (1 episode), and an incomplete deployed distal part of the stent (1 episode) (Table 2). Three patients had more than 1 episode of recurrent dysphagia.

### Complications

In total, major and minor complications were seen in 18 of 44 (KM = 47%) patients (Table 2). Of these, 14 major complications occurred in 10 patients (KM = 29%), including hemorrhage (n = 8), severe pain (n = 3), fistula formation (n = 2), and fever (n = 1). Of the 7 patients with hemorrhage, it developed in 1 patient within 7 days of stent placement, whereas another patient had 2 episodes of hematemesis 43 and 84 days after stent placement. Five patients eventually died of this complication, and 2 patients were successfully treated with radiation therapy.

Minor complications were seen in 12 patients (KM = 30%; Table 2). Of these patients, 5 experienced gastroesophageal reflux symptoms after a median of 5 days (IQR 2-55 days) and 7 patients experienced mild retrosternal pain after a median of 6 days (IQR 3-14 days).

### Survival

After a median follow-up of 15 months (IQR 11-19 months), 39 (89%) of 44 patients had died, resulting in a median survival of 110 days (95% CI, 95-180 days). Five patients died of hemorrhage 5, 43, 107, 128, and 248 days after stent placement, respectively.

## DISCUSSION

In this prospective follow-up study of 44 patients, we demonstrated that the SX-ELLA stent provided good symptomatic relief of malignant dysphagia. In addition, we found a low rate of tissue overgrowth (KM = 8%), but a similar frequency of stent migration (KM = 20%), as previously reported with

| Author/year | Intervention | Covering | No. | No. patients (valid %) Recurrent dysphagia | | No. patients (valid %) Major complications (hemorrhage, fistula, fever, severe pain, perforation, aspiration pneumonia) | |
|---|---|---|---|---|---|---|---|
| | | | | Tumoral/nontumoral overgrowth | Migration | Total reported | Hemorrhage |
| Randomized trials | | | | | | | |
| • Verschuur et al, 2008[16] | Ultraflex stent | Partial | 42 | 13 (31) | 7 (17) | 9 (21) | 5 (12) |
| | Niti-S stent | Complete* | 42 | 10 (24) | 5 (12) | 5 (12) | 2 (5) |
| | Polyflex stent | Complete | 41 | 4 (10) | 12 (29) | 8 (20) | 5 (12) |
| • Conio et al, 2007[9] | Ultraflex stent | Partial | 54 | 14 (26) | 2 (4) | 3 (6) | 0 |
| | Polyflex stent | Complete | 46 | 14 (30) | 6 (13) | 4 (9) | 2 (4) |
| • Homs et al, 2004[1] | Ultraflex stent | Partial | 108 | 16 (15) | 18 (17) | 27 (25) | 14 (13) |
| | Brachytherapy | – | 101 | – | – | – | – |
| • Sabharwal et al, 2003[14] | Ultraflex stent | Partial | 31 | 1 (3) | 2 (6) | 3 (10) | 1 (3) |
| | Flamingo wallstent | Partial | 22 | 1 (5) | 1 (5) | 3 (14) | 1 (5) |
| Comparative studies | | | | | | | |
| • Verschuur et al, 2007[15,†] | Ultraflex stent | Partial | 153 | 20 (13) | 27 (18) | 38 (25) | 23 (15) |
| | Flamingo Wallstent | Partial | 96 | 16 (17) | 8 (8) | 18 (19) | 8 (8) |
| | Gianturco Z stent | Complete | 89 | 16 (18) | 5 (6) | 20 (22) | 13 (15) |
| • Homs et al, 2004[17] | Ultraflex stent | Partial | 75 | 7 (9)‡ | 17 (23)‡ | NR | NR |
| | Flamingo wallstent | Partial | 71 | 12 (17)‡ | 5 (7)‡ | NR | NR |
| | Gianturco Z stent | Complete | 70 | 11 (16)‡ | 4 (6)‡ | NR | NR |
| Prospective studies | | | | | | | |
| • Uitdehaag et al, 2008[18] | Alimaxx-E stent | Complete | 45 | 7 (16) | 16 (36) | 9 (20) | 2 (4) |
| • Conigliaro et al, 2007[12] | Polyflex stent | Complete | 60 | 8 (14) | 12 (20) | NR (10) | 4 (7) |
| • Szegedi et al, 2006[19] | Polyflex stent | Complete | 69 | 9 (13) | 3 (5) | 0 | 0 |
| • Verschuur et al, 2006[20] | Niti-S stent | Complete* | 42 | 2 (5) | 3 (7) | 5 (12) | 2 (5) |
| • Dormann et al, 2003[21] | Polyflex stent | Complete | 33 | 4 (12) | 2 (6) | 0 | NR |
| Retrospective studies | | | | | | | |
| • Ross et al, 2007[13] | Wallstent II | Partial | 97 | 5 (5) | 5 (5) | 17 (18) | 14 (14) |

**NR, Not reported.**

*** Inner fully covered with outer uncovered wire tube.**

**† Small- and large-diameter stents are counted as 1 group.**

**‡ Number of events rather than number of patients.**

**Table 3.** *Recurrent dysphagia and major complications after stent placement of partially or fully covered stents for the palliation of malignant dysphagia in other recently published series.*

other expandable stents.[1,9,12-21] In addition, despite the single-wire, braided, low-trauma design, the frequency of hemorrhage and fistula formation was considerable with this stent. This was particularly true for hemorrhage (KM = 25% after 7 days), which was fatal in 5 patients (Table 2).

The frequency of tumoral or nontumoral tissue overgrowth was reduced with the SX-ELLA stent (2 episodes in 2 patients, KM = 8%) compared with rates of tissue ingrowth and overgrowth with other stent designs (Table 3).[1,9,12-21] It is not clear what the predominant reason for the low rate of tissue ingrowth and overgrowth was with the SX-ELLA stent. Fully covered stents have been designed to prevent tissue ingrowth, but this advantage may be outweighed by the still high rate of tissue overgrowth over the edge of these stents. Mayoral et al[10] were the first to report nonmalignant tissue ingrowth and overgrowth as a cause of recurrent dysphagia in 47% of patients after stent placement for an esophageal malignancy. The larger size of the mid portion of the SX-ELLA stent (20 mm) compared with the Polyflex, Niti-S, and Gianturco Z stent (all 18 mm) could be a factor in the relatively low overgrowth rate. Verschuur et al[15] found that large-diameter stents reduced the risk of recurrent dysphagia from tissue overgrowth. They suggested that this was because of the fact that a longer time is required to obstruct the esophagus when larger-diameter stents are placed. Furthermore, the braiding of the stent from 1 piece of wire could also prevent nonmalignant tissue overgrowth to occur by making both stent ends cause less trauma.

The use of SX-ELLA stents did not reduce the migration rate (6 episodes in 6 patients, KM = 20%) compared with migration rates found in other fully covered stent designs (Table 3).[9,12,15-18] This suggests that the circumferential antimigration ring plus the flared ends are not sufficiently effective in

preventing migration. The fact that 40% of the patients still experienced an episode of recurrent dysphagia was also caused by a relative high food obstruction rate, i.e. 8 episodes in 5 patients (KM = 17%). Food obstruction occurred in 4 of 5 patients, 9 to 33 days after placement, with 1 patient even experiencing 3 episodes. The cause of food obstruction was not clear because all patients received specific dietary advice. It may well be, however, that the metal retrieval iron loop played a role because it was the obvious cause in at least 1 of the patients.

The SX-ELLA stent was associated with a considerable rate of major complications, with 14 occurring in 10 patients in this study. Of these, 7 patients experienced 8 episodes of hemorrhage. Until now, this is the highest hemorrhage rate observed with large-diameter stents as reported in the literature (Table 3).[1,9,12-16,18,22] We speculate that the antimigration ring of the SX-ELLA stent was involved because not only hemorrhage, but also severe pain (n = 3) and fistula formation at the upper end of the stent (n = 2) were observed. In normal circumstances, stents exert some pressure on the tumor and the normal mucosa of the esophagus to affix the stent to the esophageal wall to reduce migration risk. With the SX-ELLA stent, this effect may be more pronounced because of the pressure effect of the antimigration ring, particularly when it is flipping in and out for its antimigration effect. In addition, specific stent characteristics, particularly stent diameter and radial force, should be taken into consideration. As mentioned previously, the relatively large mid section of the SX-ELLA stent could also increase the risk of hemorrhage, as has been reported previously.[15] In conclusion, the SX-ELLA stent provided good symptomatic relief of malignant dysphagia with a low rate of tissue overgrowth. Migration rates occurred, however, at a similar (high) frequency as that observed with other currently available fully covered stents. In addition, a relatively high complication rate, particularly hemorrhage, was observed. It remains to be established whether friction from the antimigration ring or the large size of the mid section of the stent increased the risk of injury to the esophageal wall.

## REFERENCES


1. Homs MY, Steyerberg EW, Eijkenboom WM, et al. Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from oesophageal cancer: multicentre randomised trial. Lancet 2004;364:1497-1504.

2. Steyerberg EW, Homs MY, Stokvis A, et al. Stent placement or brachytherapy for palliation of dysphagia from esophageal cancer: a prognostic model to guide treatment selection. Gastrointest Endosc 2005;62:333-340.

3. Homs MY, Kuipers EJ, Siersema PD. Palliative therapy. J Surg Oncol 2005;92:246-256.

4. Siersema PD. Treatment options for esophageal strictures. Nat Clin Pract Gastroenterol Hepatol 2008;5:142-152.

5. Costamagna G, Marchese M, Iacopini F. Self-expanding stents in oesophageal cancer. Eur J Gastroenterol Hepatol 2006;18:1177-1180.

6. Mougey A, Adler DG. Esophageal stenting for the palliation of malignant dysphagia. J Support Oncol 2008;6:267-273.

7. Siersema PD, Marcon N, Vakil N. Metal stents for tumors of the distal esophagus and gastric cardia. Endoscopy 2003;35:79-85.

8. Saranovic D, Djuric-Stefanovic A, Ivanovic A, et al. Fluoroscopically guided insertion of self-expandable metal esophageal stents for palliative treatment of patients with malignant stenosis of esophagus and cardia: comparison of uncovered and covered stent types. Dis Esophagus 2005;18:230-238.

9. Conio M, Repici A, Battaglia G, et al. A randomized prospective comparison of self-expandable plastic stents and partially covered self-expandable metal stents in the palliation of malignant esophageal dysphagia. Am J Gastroenterol 2007;102:2667-2677.

10. Mayoral W, Fleischer D, Salcedo J, et al. Nonmalignant obstruction is a common problem with metal stents in the treatment of esophageal cancer. Gastrointest Endosc 2000;51:556-559.

11. Mellow MH, Pinkas H. Endoscopic laser therapy for malignancies affecting the esophagus and gastroesophageal junction. Analysis of technical and functional efficacy. Arch Intern Med 1985;145:1443-1446.

12. Conigliaro R, Battaglia G, Repici A, et al. Polyflex stents for malignant oesophageal and oesophagogastric stricture: a prospective, multicentric study. Eur J Gastroenterol Hepatol 2007;19:195-203.

13. Ross WA, Alkassab F, Lynch PM, et al. Evolving role of self-expanding metal stents in the treatment of malignant dysphagia and fistulas. Gastrointest Endosc 2007;65:70-76.

14. Sabharwal T, Hamady MS, Chui S, et al. A randomised prospective comparison of the Flamingo Wallstent and Ultraflex stent for palliation of dysphagia associated with lower third oesophageal carcinoma. Gut 2003;52:922-926.

15. Verschuur EM, Steyerberg EW, Kuipers EJ, et al. Effect of stent size on complications and recurrent dysphagia in patients with esophageal or gastric cardia cancer. Gastrointest Endosc 2007;65:592-601.

16. Verschuur EM, Repici A, Kuipers EJ, et al. New design esophageal stents for the palliation of dysphagia from esophageal or gastric cardia cancer: a randomized trial. Am J Gastroenterol 2008;103:304-312.

17. Homs MY, Steyerberg EW, Kuipers EJ, et al. Causes and treatment of recurrent dysphagia after self-expanding metal stent placement for palliation of esophageal carcinoma. Endoscopy 2004;36:880-886.

18. Uitdehaag MJ, Van Hooft JE, Verschuur EML, et al. A fully-covered stent (Alimaxx-E) for the palliation of malignant dysphagia: a prospective follow-up study. Gastrointest Endosc 2009;70:1082-1089.

19. Szegedi L, Gal I, Kosa I, et al. Palliative treatment of esophageal carcinoma with self-expanding plastic stents: a report on 69 cases. Eur J Gastroenterol Hepatol 2006;18:1197-1201.

20. Verschuur EM, Homs MY, Steyerberg EW, et al. A new esophageal stent design (Niti-S stent) for the prevention of migration: a prospective study in 42 patients. Gastrointest Endosc 2006;63:134-140.

21. Dormann AJ, Eisendrath P, Wigginghaus B, et al. Palliation of esophageal carcinoma with a new self-expanding plastic stent. Endoscopy 2003;35:207-211.

22. Siersema PD, Hop WC, van Blankenstein M, et al. A comparison of 3 types of covered metal stents for the palliation of patients with dysphagia caused by esophagogastric carcinoma: a prospective, randomized study. Gastrointest Endosc 2001;54:145-153.








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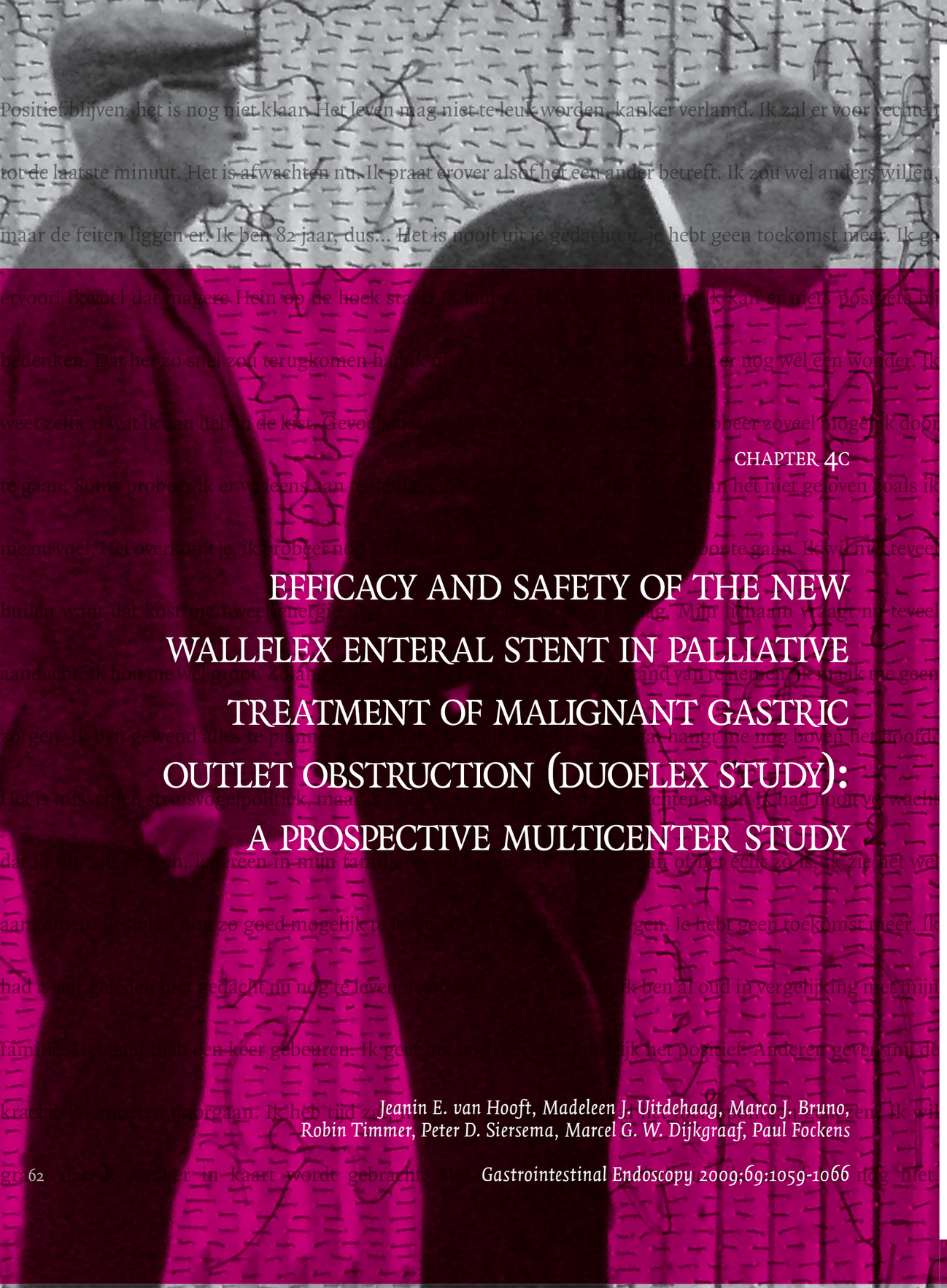

CHAPTER 4C

# EFFICACY AND SAFETY OF THE NEW WALLFLEX ENTERAL STENT IN PALLIATIVE TREATMENT OF MALIGNANT GASTRIC OUTLET OBSTRUCTION (DUOFLEX STUDY): A PROSPECTIVE MULTICENTER STUDY

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*Gastrointestinal Endoscopy 2009;69:1059-1066*





**Background:** Gastric outlet obstruction (GOO) is most commonly a complication of advanced distal gastric, periampullary, or duodenal malignancy. Palliation of obstruction is the primary aim of treatment in most of these patients. Self-expandable metal stents have emerged as an effective treatment option.

**Objective:** Our purpose was to investigate the efficacy and safety of a newly developed enteral metal stent (WallFlex).

**Design:** Prospective multicenter cohort study.

**Setting:** Three tertiary referral centers (2 academic).

**Patients:** Fifty-one consecutive patients with symptomatic malignant GOO from January 2005 to February 2006.

**Intervention:** Placement of a self-expandable metallic stent (WallFlex).

**Main Outcome Measurements:** The primary end point was defined as improvement of the GOO scoring system for the remainder of the patients' lives. Secondary end points focused on efficacy and safety and global quality of life.

**Results:** The Gastric Outlet Obstruction Scoring System score improved ($P < .001$), the body mass index decreased ($P < .001$), and theWorld Health Organization performance score improved ($P = .002$) when the score before stenting was compared with the mean score until death. Global quality of life did not improve. Technical and clinical success was achieved in 98% and 84% of the patients. Median survival was 62 days (75% alive at 35 days, 25% alive at 156 days). Median stent patency was 307 days (75% functional at 135 days, 25% functional at 470 days). Stent dysfunction was proved in 7 patients (14%), migration in 1 (2%), and tumor overgrowth or ingrowth in 6 (12%).

**Limitations:** Lack of a control group.

**Conclusion:** Placement of a WallFlex enteral stent in patients with nonresectable malignant GOO is safe and provides a statistically significant and clinically relevant relief of obstructive symptoms with a low need for reintervention.

Patients with cancer of the periampullary area (head of the pancreas, distal bile duct, papilla of Vater) and with distal stomach or duodenal cancer are often seen with advanced-stage disease, with only 15% to 20% of patients having a resectable tumor at diagnosis.[1,2] The majority of cases have locally advanced or metastatic cancer with a poor prognosis and a median survival of 3 to 6 months.[3-7] These patients have significant morbidity, including pain, jaundice, and gastric outlet obstruction (GOO), which contributes to a progressive deterioration of a patient's quality of life.[8] Palliation of symptoms is the primary aim in these patients. Traditionally, for patients with intestinal obstruction who are fit for surgery, the therapy of choice has been a gastrojejunostomy combined with a biliary-digestive bypass in cases of concomitant biliary obstruction.[9,10] Unfortunately, because of advanced disease and a poor general condition, surgical intervention in patients with malignant upper intestinal obstruction is associated with significant morbidity and mortality rates.[11-14] It has been reported that delayed gastric emptying after gastrojejunostomy occurs in up to 57% of patients and leads to prolonged hospital stay.[9,15-17]

Endoscopic placement of a self-expandable metal stent has emerged as an alternative minimally invasive treatment option in case of upper intestinal

| | |
|---|---|
| No. of patients | 51 |
| Age (y) (mean [SD]) | 67.6 (12.3) |
| Sex (male/female) | 25:26 |
| Tumor characteristics, no. (%) | |
| • Pancreatic cancer | 35 (69) |
| • Metastatic disease | 5 (10) |
| • Cholangiocarcinoma | 3 (6) |
| • Duodenal cancer | 3 (6) |
| • Gastric cancer | 2 (4) |
| • Gallbladder cancer | 2 (4) |
| • Cancer of the ampulla of Vater | 1 (2) |
| Biliary tract, no. (%) | |
| Drained | |
| • Metal stent | 31 (61) |
| • Plastic stent | 3 (6) |
| Signs of obstruction | 4 (8) |
| No signs of obstruction | 13 (25) |
| Severity of obstruction | |
| GOOSS score, median (IQR) | 1 (0-2) |
| • 0 No oral intake, no. (%) | 18 (35) |
| • 1 Liquids only, no. (%) | 19 (37) |
| • 2 Soft solids, no. (%) | 4 (8) |
| • 3 Low residue or normal diet, no. (%) | 10 (20) |
| General condition | |
| • BMI, mean (SD) | 22.7 (3.2) |
| • WHO performance score, mean (SD) | 2.06 (1.05) |
| • WHO 0-fully active, no. (%) | 2 (4) |
| • WHO 1-cannot carry out heavy physical work, no. (%) | 15 (29) |
| • WHO 2-up and about > 50% of the day, no. (%) | 17 (33) |
| • WHO 3-up and about < 50% of the day, no. (%) | 12 (24) |
| • WHO 4-bed or chair bound all day, no. (%) | 5 (10) |
| Quality of life | |
| • QLQ-C30 Global Health status (QL2), mean (SD) | 44.5 (20.9) |
| • EQ-VAS score, mean (SD) | 42.5 (18.4) |

**Table 1.** *Patient demographics and clinical characteristics at baseline.*

**Capsule Summary**

**What is already known on this topic**

- Patients with gastric obstruction from unresectable cancer often are not surgical candidates but require some form of palliative care.

**What this study adds to our knowledge**

- In 51 consecutive patients with symptomatic malignant gastric outlet obstruction who received self-expandable metallic stents, technical and clinical success was accomplished in 98% and 84%, respectively, resulting in a median survival time of 62 days and median stent patency of 302 days.

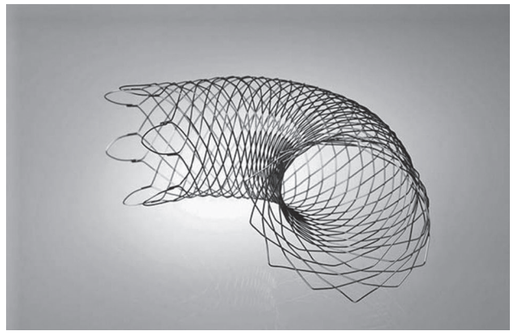

**Figure 1.** *WallFlex duodenal stent.*

obstruction.[18-23] Two recent review articles point to a technical success rate of 94% to 97%, a clinical success rate of 87% to 94%, no intervention-related deaths, a short procedure-related hospital stay, and resuming oral intake usually within 4 days after stent placement.[24,25] Nonetheless, there are complications associated with endoscopic duodenal stent placement, such as pain, perforation, bleeding, reobstruction, or stent migration. Severe complications occur on average in 1% (0%-10%) of patients, whereas minor





complications occur in 26% (0%-30%).[24,25] Most published data relate to patients treated with an enteral Wallstent (Boston Scientific, Natick, Mass), a self-expanding stainless-steel woven stent.[24,25] This stent is preloaded on a delivery system that can be introduced through the working channel of a therapeutic endoscope with subsequent deployment controlled by both fluoroscopic and endoscopic views. The limited flexibility of the metal wire mesh of the Wallstent might contribute to stent migration. Also, the sharp ends of the metal meshes of the Wallstent may injure the GI wall, leading to ulceration with the associated risk of bleeding and perforation.[26] Recently, a new enteral stent (WallFlex, Boston Scientific) was introduced that is made of nitinol instead of stainless steel (Figure 1). This new stent has been constructed to provide an improved flexibility while maintaining lumen integrity, has looped ends to reduce risk of mucosal injury, and has a proximal flared end to minimize risk of stent migration. A previously published retrospective series revealed an excellent short-term clinical success rate.[27] The purpose of this prospective single-arm observational study was to further investigate the efficacy and safety features of this new enteral stent.

## METHODS

The DUOFLEX study was designed as a multicenter, single-arm, prospective, observational clinical trial to evaluate the efficacy and safety of the WallFlex enteral stent in 3 large Dutch hospitals. The protocol was approved by the Medical Ethical Committee of the Academic Medical Center in Amsterdam. The study was conducted at the Department of Gastroenterology and Hepatology of the Academic Medical Center in Amsterdam, Erasmus Medical Center in Rotterdam, and St Antonius Hospital in Nieuwegein. Written informed consent was obtained from each patient.

### Patients

From January 2005 to February 2006, all consecutive patients more than 18 years of age with a histologically proven malignancy of the periduodenal area with symptoms compatible with GOO at 1 of the 3 participating Dutch hospitals were considered for inclusion in this trial.

After exclusion of potentially curable disease, proximal stomach obstruction, preprocedural evidence of additional strictures in the small bowel or colon, previous treatment with a self-expanding enteral metal stent for the same condition, inability to undergo upper GI endoscopy, or inability to complete quality-of-life questionnaires, patients were asked to participate in the study.

### Data collection

Medical history, medication use, disease-specific information (primary tumor site, level of obstruction, biliary obstruction/drainage), severity of obstruction (symptoms compatible with GOO and GOO Scoring System [GOOSS] score), general condition (body mass index [BMI], World Health Organization [WHO] performance score), additional therapy (biliary drainage, chemotherapy, radiotherapy), and pretreatment scores of quality-of-life questionnaires (European Organisation for Research and Treatment of Cancer [EORTC] QLQ-C30 version 3, EQ-5D including the EuroQol visual analog scale [EQ-VAS]) were collected by the research nurse immediately after inclusion. Procedure-related data were collected by the treating physician. Follow-up data were obtained by mail and completed through telephone interviews by the research nurse.

Follow-up included inquiries about adverse events, severity of obstruction, general condition, additional therapy, and quality of life. Patients were followed up at 7 and 14 days (GOOSS score, WHO





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performance score), 4 weeks (GOOSS score, BMI, WHO performance score, EORTC QLQ-C30 version 3 and EQ-5D including the EQ-VAS), monthly (GOOSS score), and bimonthly (BMI, WHO performance score, EORTC QLQ-C30 version 3 and EQ-5D including the EQ-VAS) after stent placement. Patients were followed up until death.

## Definitions and end points

The primary end point of the study was defined as improvement of the GOOSS score (a 4-point scoring system; Table 1) for the remainder of the patients' lives.[18] Secondary end points were technical success (successful stent placement and deployment at the site of the stricture), clinical success (defined as relief of symptoms compatible with GOO or improvement of the GOOSS score 1 week after inclusion), median survival, time until regain of oral intake, procedure-related hospitalization time, stent patency, intervention-related complications including 30-day mortality rate, impact on general condition, and global quality of life reflected by the global health status (QL2) scale from the validated EORTC QLQ-C30 version 3 measure and the EQ-VAS.

Symptoms compatible with GOO were defined as early satiety, nausea, and vomiting. In case of clinical suspicion of stent dysfunction (decrease in GOOSS score of 2 points), a small-bowel series or endoscopy were performed to investigate the underlying cause (tumor overgrowth or ingrowth, migration, compression, or food impaction) unless patients refused further investigations or interventions. If the enteral stent was shown to be patent and no secondary stricture was identified by endoscopy or small-bowel follow-through, disturbance of food passage was considered to be due to motility dysfunction, for example, peritonitis carcinomatosis or gastroparesis caused by neural involvement. Stent patency was defined as the period between initial stent placement and first stent dysfunction (migration, reobstruction).

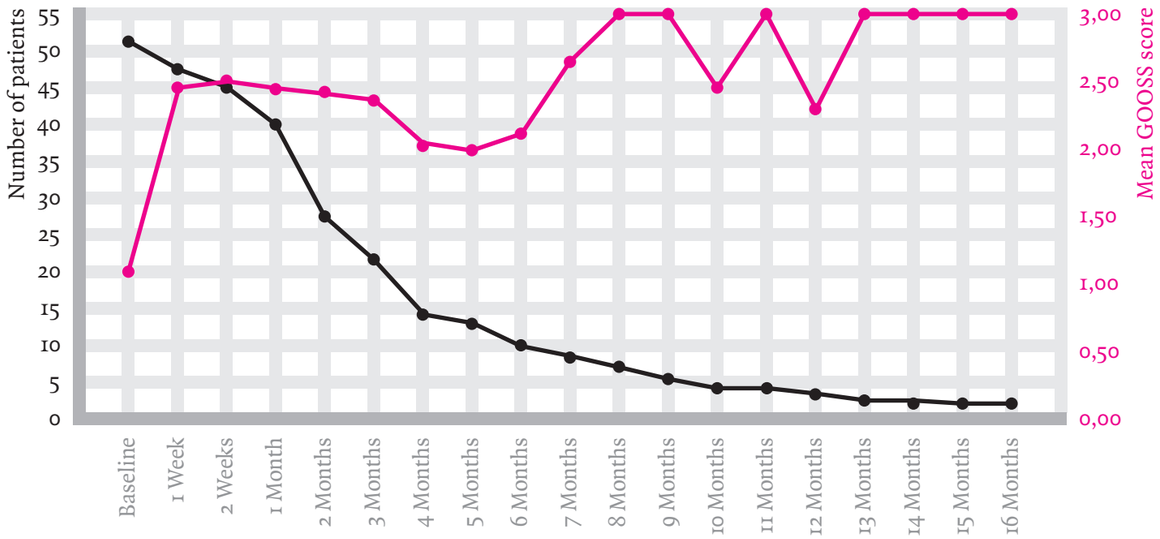


**Figure 2a.** *Mean GOOSS score over time.*







## Intervention

After inclusion, biliary patency was evaluated. If patients did not already have a biliary stent placed or cholestatic liver functions, enteral stenting was pursued without prior biliary drainage. Patients with a suspicion of biliary obstruction (cholestatic liver functions) underwent biliary drainage by insertion of an expandable metal stent, either endoscopically or radiologically. If patients had already a plastic biliary stent in situ, this was replaced by an expandable metal biliary stent regardless of liver function test results.

To prevent enteral stent migration, placement was not attempted within 48 hours after enteral stricture dilation had been performed for biliary stent placement. All patients in this study were treated with a WallFlex enteral stent (Boston Scientific, Natick, Mass). The enteral Wall-Flex stent was available with a diameter of 27 mm at the flared end and 22 mm at the body; lengths available for this study were 6 cm, 9 cm, and 12 cm. The stent is already preloaded on a 10F delivery system and was Conformité Européenne approved at the time of the study.

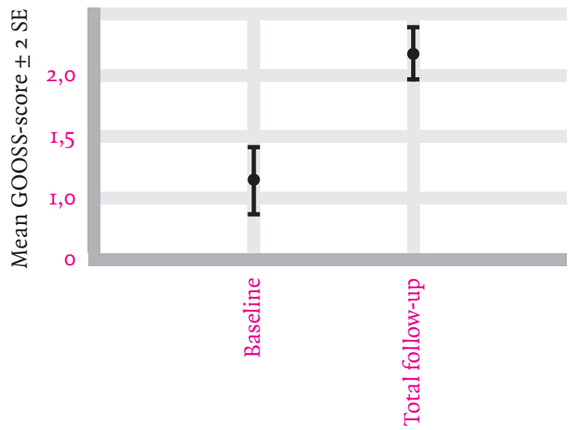


**Figure 2b.** *Mean GOOSS score at baseline versus total follow-up. Bars represent 2 times SE.*

Stent placement was done with the patient under conscious sedation (midazolam or fentanyl). A therapeutic endoscope (working channel ≥ 3.7 mm), either forward or side viewing, was used for placement of the through-the-scope WallFlex enteral stent. The length of the stricture was assessed either endoscopically or fluoroscopically.[28] To avoid dilation of the stricture by advancing the endoscope through it, which might facilitate stent migration, the endoscope was only passed in case of no resistance; otherwise a catheter and a guidewire were used to pass the stricture. Subsequently, the guidewire was advanced into the horizontal part of the duodenum. The length of the stent had to exceed the stricture length for at least 2 cm, and, preferably, the flared proximal end of the stent was placed proximal to the pylorus. This was not based on any literature but on our belief that the antimigration purpose of the flared end could be further prospered by doing so. After the required stent length was determined, it was advanced through the endoscope over the guidewire until it passed the distal end of the stricture; after this the stent was deployed under continuous fluoroscopic control. The stent was not repositioned once fully deployed. The position of the stent was confirmed endoscopically and fluoroscopically.

## Statistical analysis

The expected number of eligible patients to be included at the participating hospital sites during a year was 50. Descriptive statistics were used for data of all included patients (intention-to-treat). Depending on distributional properties, Wilcoxon matched-pairs signedrank test (GOOSS score) or

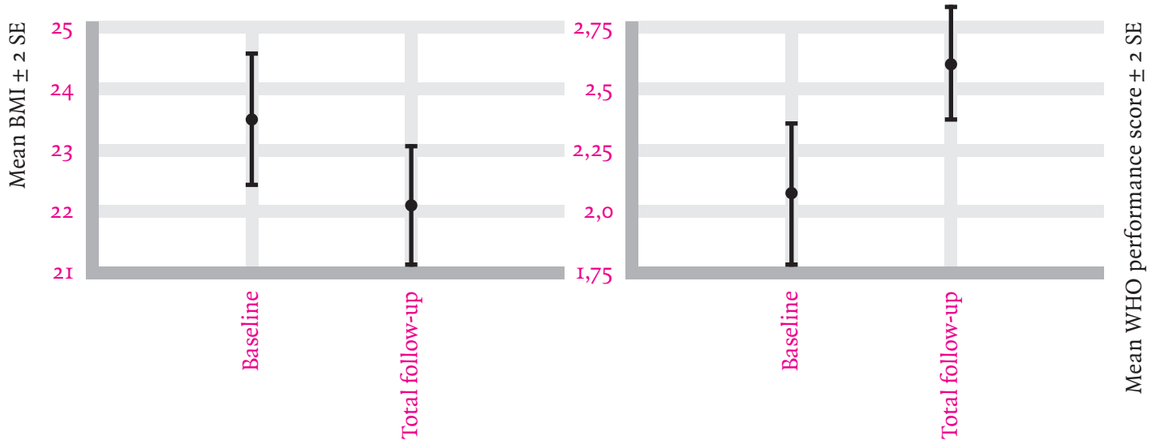


**Figure 3a.** *Mean BMI at baseline versus total follow-up. Bars represent 2 times SE.*




**Figure 3b.** *Mean WHO performance score at baseline versus total follow-up. Bars represent 2 times SE.*

paired-sample *t* tests (QL2, EQ-VAS, BMI, and WHO performance score) were used to assess improvements from baseline, after calculation of the average score per patient from available follow-up assessments until death, weighed for the length of the preceding time interval in between planned assessments. Stent patency was assessed by Kaplan-Meier analysis with stent dysfunction taken as event and death before stent dysfunction as censored observation. Kaplan-Meier analyses were also performed for times until oral intake, hospital discharge, and death. Statistics were performed with the SPSS (version 12.0.2) software package (SPSS, Chicago, Ill). Statistical significance in all analyses was set at $P < .05$.

## RESULTS

Between January 2005 and February 2006, 51 patients (25 men, 26 women; mean age ± SD 67.6 ± 12.3 years) were included. Fourteen of the 51 patients had already been included in a previous multicenter European study reporting only short-term (30-day) results.[27] Patient demographics and clinical characteristics are summarized in Table 1.

### Primary end point

The GOOSS score improved significantly ($P < .001$) when the score before stenting was compared with the mean score during follow-up until death (Figure 2).

### Secondary end points

Stent placement was technically successful in 50 patients (98%). In 1 patient the proximal end of the stent was balloon dilated directly after stent placement because of insufficient deployment; during the completion of the follow-up there were no additional complications. Two patients died within the first week, 1 from severe cholangitis and 1 from progressive malignant disease without procedure- or stent-related complications. Of the remaining 49 patients, clinical success was achieved in all but 6 patients (88%), resulting in overall clinical success after 1 week in 43 of 51 patients (84%). At the time of







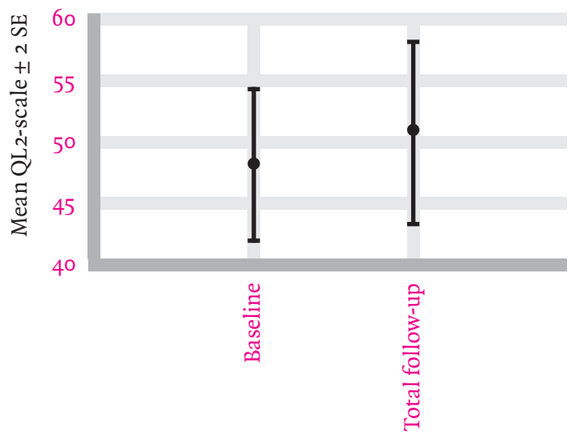


**Figure 4a.** *Mean QL2 at baseline versus total follow-up. Bars represent 2 times SE.*

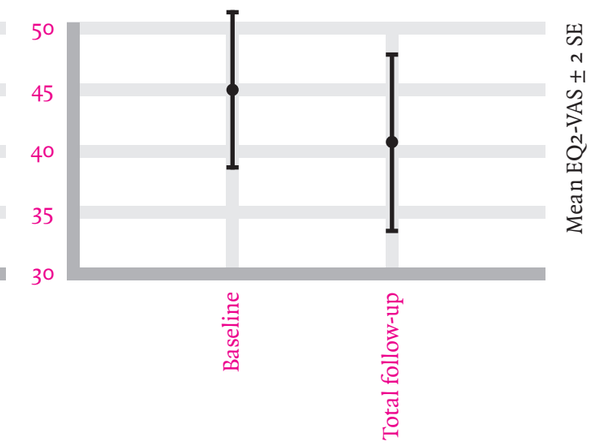


**Figure 4b.** *Mean EQ-VAS at baseline versus total follow-up. Bars represent 2 times SE.*

initial stent placement, 54 stents were placed. In total, in 48 patients 1 stent proved sufficient to cover the stricture, whereas 3 patients required 2 stents, either because of too distal placement of the first stent (n = 2) or because of the presence of 2 strictures located too far from each other to be covered with one stent (n = 1). In these patients, both enteral stents were placed during the same procedure.

Of the 54 enteral stents, 40 (74%) were 9 cm, 8 (15%) 6 cm, and 6 (11%) 12 cm. The mean length of the stricture was 4.0 cm (SD ± 1.6 cm, range 2-8 cm).

Median survival was 62 days (75% alive at 35 days, 25% alive at 156 days). Oral intake was resumed by 46 patients (90%) either at the day of or at the day after stent placement. The median procedure-related hospital stay was 3 days; 75% of the patients were discharged within 5 days after stent placement.

Clinical suspicion of stent dysfunction occurred in 12 of 51 (24%) patients. Three patients (6%) were terminally ill at the time of stent dysfunction and refrained from further treatment. Six patients (12%) had endoscopic evidence of tumor overgrowth or ingrowth (n = 1 and n = 5, respectively) at a median time interval of 121 days after stent placement; in another patient the enteral stent had migrated distally (2%) after 13 days. These 7 patients were successfully managed by the insertion of an additional enteral stent (1 patient received inadvertently a D-Weave Niti-S stent [Taewoong Medical, Seoul, Korea] instead of a WallFlex enteral stent). The 2 remaining patients (4%) with a patent enteral stent and no evidence of a downstream anatomic obstruction were classified as having motility dysfunction and were respectively treated with a duodenal feeding tube and gastroenterostomy. No incomplete stent expansions were seen. Median stent patency was 307 days (75% functional at 135 days, 25% functional at 470 days).

Other complications included intermittent pain (n = 2) directly after stent placement treated with

analgesics, cholangitis (n = 3) treated with antibiotics in 2 patients and percutaneous drainage in 1 patient, and bleeding (n = 2) for which 1 patient was treated with radiotherapy and 1 patient endoscopically. Two of the 3 patients who had cholangitis had a metal biliary stent in situ. Eleven patients (22%) died within 30 days after stent placement: 1 had clinical symptoms of cholangitis and was unsuccessfully treated with antibiotics; all others died from progressive malignant disease, but without clinical signs of biliary or enteral obstruction.

Over time, the BMI decreased (P < .001), whereas the WHO performance score improved (P = .002) when the score before stenting was compared with the mean score until death (Figure 3). The QL2 scale and the EQ-VAS did not improve (P = .52 and P = .31, respectively) (Figure 4).

## DISCUSSION

Several studies have assessed clinical and technical success of endoscopic duodenal stenting in the palliative treatment of advanced periampullary, distal stomach, or duodenal cancer. Our prospective series is the first to focus on the duodenal WallFlex stent. The clinical and technical success rate (intention-to-treat) with this new enteral stent in the management of malignant duodenal strictures was 84% and 98%, respectively, which is in accordance with the recent literature.[24,25] A more important observation was that after enteral stent placement the mean GOOSS score significantly improved for the remainder of the patients' lives compared with pretreatment scores. In light of this observation, it is worth mentioning that 10 of our patients (20%) had already a maximum GOOSS score before stent placement. Despite a maximum GOOSS score, these patients had symptoms compatible with GOO, particularly nausea and (intermittent) vomiting. Clinical success was

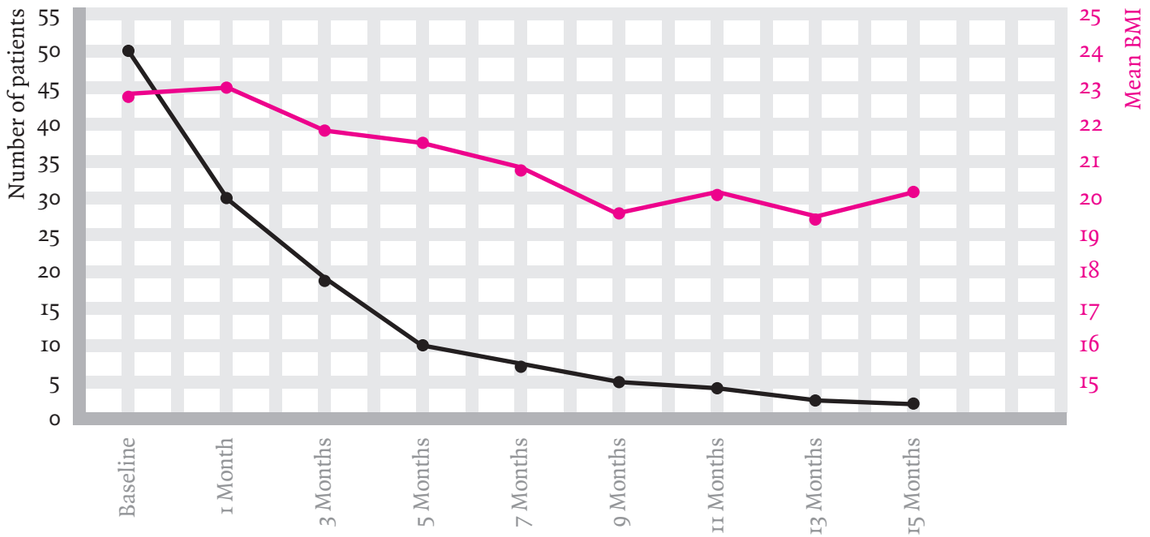


**Figure 5.** *Mean BMI over time.*



achieved in 7 of these 10 patients. Importantly, this indicates that, when deciding on the necessity of duodenal stent placement in patients with incurable malignancy of the periduodenal region, not just the GOOSS score should be taken into account.

There was a large difference between median stent patency (307 days) and median survival (62 days), suggesting that adequate resolution of the GOO is achieved with the WallFlex enteral stent in the majority of patients until death. Chemotherapy was of no significant influence because only 3 patients received chemotherapy in our series after enteral stent placement. Recent data of 2 larger series revealed that chemotherapy after stent placement was associated with an increase in maintenance of stent patency.[29,30]

Stent dysfunction was proved in 7 patients: migration in 1 (2%) and tumor overgrowth or ingrowth in 6 (12%). The low rate of stent migration may be partly explained by the stent design with a proximal large-diameter flare that was preferably positioned proximal to the pylorus. In addition, duodenal stricture dilatation to enable drainage of the bile duct, which might negatively affect the migration rate of enteral stents when placed during the same session, was not done within 48 hours of stent placement. Stent reobstruction caused by tumor overgrowth or ingrowth occurred after a median of 121 days, which implies that enteral stent obstruction is a late complication. The longer the patients survive, the higher the risk of reobstruction from tumor overgrowth or ingrowth. With continuing efforts for a more effective palliative chemoradiotherapy regimen aiming for a longer survival, the prevention and management of reobstruction becomes an even more important topic. The use of covered duodenal stents would be one way of trying to avoid stent obstruction by preventing tumor ingrowth through the metal meshes. However, the observed migration rate of covered stents between 21% and 26% has withheld their routine use.[31,32] A recently published large prospective series evaluating the use of fluoroscopically placed dual expandable nitinol stents, consisting of an inner uncovered and outer partially covered stent, revealed promising results. Migration occurred in 4%, recurrent symptoms in 16% (as opposed to 24% in the current series), and minor bleeding in 1%.[29]

In the current study, 13 of 51 patients (25%) did not have a biliary stent placed or cholestatic liver function at the time of enteral stenting. Only 1 patient had biliary obstruction, presenting with cholangitis 21 days after enteral stent placement. Four patients (8%) with GOO had concomitant biliary obstruction (cholestatic liver function) for which a metal biliary stent was inserted. The majority of patients (67%) had already had biliary obstruction before GOO and had a good functioning biliary stent at the time of duodenal stent placement. These data are in accordance with the result of a large systematic review in which 41% of the patients had biliary obstruction before, 18% at the same time, and only 2% after enteral stenting for GOO.[18,24] An argument of a proactive approach with regard to drainage of the biliary duct before enteral stent placement has always been the expected difficulty in the placement of biliary (metal) stents through the meshes of a duodenal stent placed across the papilla. Recently Mutignani et al[33] published a study in which they were successful in placing a biliary stent through the meshes of duodenal stents. After achieving biliary cannulation they either widened the meshes of the enteral stent with a pneumatic balloon or removed those covering the papilla with a rat-tooth foreign body forceps or argon plasma coagulation. They even treated patients with concurrent biliary and duodenal obstruction by initially placing a duodenal stent followed by a





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biliary stent, which was successful in 13 of 14 patients, 95%. These results provide evidence that enteral balloon dilation of the duodenal stricture to reach the papilla for placement of a biliary stent before enteral stent placement is not a prerequisite, which potentially should avoid the risk of perforation.[19] However, these results come from a single expert center, and it remains to be established whether the same results can be achieved by others.

Our series reveal that patients with gastric outlet obstruction resulting from incurable periampullary, distal stomach, or duodenal cancer have a poor quality of life (mean EQ-VAS ± SD: 42.5 ± 18.4, mean QL2 scale ± SD: 44.5 ± 20.9) compared with the general population (mean EQ-VAS ± SD: 79.7 ± 15.9, mean QL2 scale: 64.1).[34,35] Unfortunately, we did not achieve a significant improvement of the global quality of life during the remainder of patients' lives. It remains uncertain how the global quality of life would have developed without enteral stent placement because of the absence of a control group. It appears feasible that palliative treatment for these patients should absolutely not only be focused on food passage but also on other factors that might potentially decrease the quality of life, such as pain, deterioration of patient's physical condition, and mental support.

With regard to the general condition (BMI and WHO performance score) of patients, an apparent contradiction was observed: the BMI score significantly decreased it ($P < .001$), whereas the WHO performance score significantly improved it ($P = .002$). Apparently the improved ability to pass food is appreciated by patients and makes them more energetic although their intake is still too low to keep a stable weight during follow-up. As shown by Figure 5, the mean BMI decreased gradually after 1 month of follow-up. These figures are even more striking when taking into account that, according to common practice in The Netherlands, the majority of patients expectedly have been seen by a nutritionist and given pancreatic enzyme supplementation when indicated. The weight loss would otherwise have been detrimental.

## CONCLUSION

This single-arm prospective cohort study showed that placement of a WallFlex enteral stent in patients with nonresectable malignant GOO is safe and provides a statistically and clinically significant relief of obstructive symptoms until death.

## REFERENCES

1. Lillemoe KD, Cameron JL, Hardacre JM, et al. Is prophylactic gastrojejunostomy indicated for unresectable periampullary cancer? A prospective randomized trial. Ann Surg 1999;230:322-328.

2. Van Heek NT, van Geenen RC, Busch OR, et al. Palliative treatment in "peri"-pancreatic carcinoma: stenting or surgical therapy? Acta Gastroenterol Belg 2002;65:171-175.

3. Bakkevold KE, Arnesjo B, Dahl O, et al. Adjuvant combination chemotherapy (AMF) following radical resection of carcinoma of the pancreas and papilla of Vater-results of a controlled, prospective, randomised multicentre study. Eur J Cancer 1993;29A:698-703.

4. Geer RJ, Brennan MF. Prognostic indicators for survival after resection of pancreatic adenocarcinoma. Am J Surg 1993;165:68-72.

5. Trede M, Schwall G, Saeger HD. Survival after pancreatoduodenectomy: 118 consecutive resections without an operative mortality. Ann Surg 1990;211:447-458.

6. Tsao JI, Rossi RL, Lowell JA. Pylorus-preserving pancreatoduodenectomy: is it an adequate cancer operation? Arch Surg 1994;129:405-412.

7. Warshaw AL, Fernandez-del Castillo C. Pancreatic carcinoma. N Engl J Med 1992;326:455-465.

8. Chekan EG, Clark L, Wu J, et al. Laparoscopic biliary and enteric bypass. Semin Surg Oncol 1999;16:313-320.

9. Lillemoe KD, Pitt HA. Palliation: surgical and otherwise. Cancer 1996;78:605-614.

10. Sohn TA, Lillemoe KD, Cameron JL, et al. Surgical palliation of unresectable periampullary adenocarcinoma in the 1990s. J Am Coll Surg 1999;188:658-666.

11. Del Piano M, Ballare M, Montino F, et al. Endoscopy or surgery for malignant GI outlet obstruction? Gastrointest Endosc 2005;61:421-426.

12. Johnsson E, Thune A, Liedman B. Palliation of malignant gastroduodenal obstruction with open surgical bypass or endoscopic stenting: clinical outcome and health economic evaluation. World J Surg 2004;28:812-817.

13. Mehta S, Hindmarsh A, Cheong E, et al. Prospective randomized trial of laparoscopic gastrojejunostomy versus duodenal stenting for malignant gastric outflow obstruction. Surg Endosc 2006;20:239-242.

14. Watanapa P, Williamson RC. Surgical palliation for pancreatic cancer: developments during the past two decades. Br J Surg 1992;79:8-20.

15. Doberneck RC, Berndt GA. Delayed gastric emptying after palliative gastrojejunostomy for carcinoma of the pancreas. Arch Surg 1987;122:827-829.

16. van der Schelling GP, van den Bosch RP, Klinkenbij JH, et al. Is there a place for gastroenterostomy in patients with advanced cancer of the head of the pancreas? World J Surg 1993;17:128-132.

17. Wong YT, Brams DM, Munson L, et al. Gastric outlet obstruction secondary to pancreatic cancer: surgical vs endoscopic palliation. Surg Endosc 2002;16:310-312.

18. Adler DG, Baron TH. Endoscopic palliation of malignant gastric outlet obstruction using self-expanding metal stents: experience in 36 patients. Am J Gastroenterol 2002;97:72-78.

19. Nassif T, Prat F, Meduri B, et al. Endoscopic palliation of malignant gastric outlet obstruction using self-expandable metallic stents: results of a multicenter study. Endoscopy 2003;35:483-489.

20. Nevitt AW, Vida F, Kozarek RA, et al. Expandable metallic prostheses for malignant obstructions of gastric outlet and proximal small bowel. Gastrointest Endosc 1998;47:271-276.

21. Soetikno RM, Lichtenstein DR, Vandervoort J, et al. Palliation of malignant gastric outlet obstruction using an endoscopically placed Wallstent. Gastrointest Endosc 1998;47:267-270.

22. Venu RP, Pastika BJ, Kini M, et al. Self-expandable metal stents for malignant gastric outlet obstruction: a modified technique. Endoscopy 1998;30:553-558.







M.J. Uitdehaag | Living in the face of death

23. Yim HB, Jacobson BC, Saltzman JR, et al. Clinical outcome of the use of enteral stents for palliation of patients with malignant upper GI obstruction. Gastrointest Endosc 2001;53:329-332.

24. Dormann A, Meisner S, Verin N, et al. Self-expanding metal stents for gastroduodenal malignancies: systematic review of their clinical effectiveness. Endoscopy 2004;36:543-550.

25. Holt AP, Patel M, Ahmed MM. Palliation of patients with malignant gastroduodenal obstruction with self-expanding metallic stents: the treatment of choice? Gastrointest Endosc 2004;60:1010-1017.

26. Zollikofer CL, Jost R, Schoch E, et al. Gastrointestinal stenting. Eur Radiol 2000;10:329-341.

27. van Hooft J, Mutignani M, Repici A, et al. First data on the palliative treatment of patients with malignant gastric outlet obstruction using the WallFlex enteral stent: a retrospective multicenter study. Endoscopy 2007;39:434-439.

28. Baron TH. Expandable metal stents for the treatment of cancerous obstruction of the gastrointestinal tract. N Engl J Med 2001;344:1681-1687.

29. Kim JH, Song HY, Shin JH, et al. Metallic stent placement in the palliative treatment of malignant gastroduodenal obstructions: prospective evaluation of results and factors influencing outcome in 213 patients. Gastrointest Endosc 2007;66:256-264.

30. Telford JJ, Carr-Locke DL, Baron TH, et al. Palliation of patients with malignant gastric outlet obstruction with the enteral Wallstent: outcomes from a multicenter study. Gastrointest Endosc 2004;60:916-920.

31. Jung GS, Song HY, Kang SG, et al. Malignant gastroduodenal obstructions: treatment by means of a covered expandable metallic stent-initial experience. Radiology 2000;216:758-763.

32. Park KB, Do YS, Kang WK, et al. Malignant obstruction of gastric outlet and duodenum: palliation with flexible covered metallic stents. Radiology 2001;219:679-683.

33. Mutignani M, Tringali A, Shah SG, et al. Combined endoscopic stent insertion in malignant biliary and duodenal obstruction. Endoscopy 2007;39:440-447.

34. Essink-Bot ML, Stouthard ME, Bonsel GJ. Generalizability of valuations on health states collected with the EuroQol-questionnaire. Health Econ 1993;2:237-246.

35. Schwarz R, Hinz A. Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. Eur J Cancer 2001;37:1345-1351.







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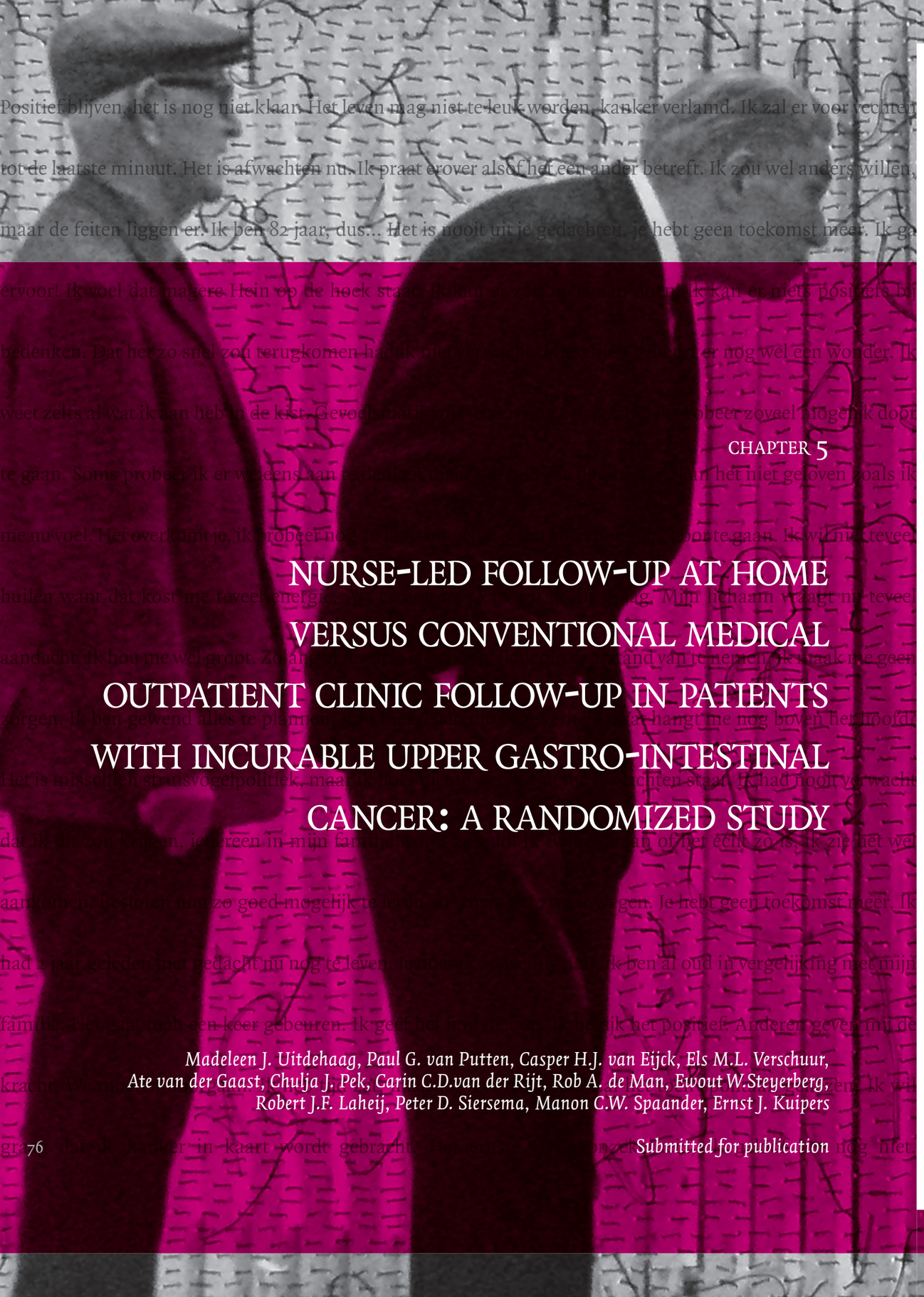

CHAPTER 5

# NURSE-LED FOLLOW-UP AT HOME VERSUS CONVENTIONAL MEDICAL OUTPATIENT CLINIC FOLLOW-UP IN PATIENTS WITH INCURABLE UPPER GASTRO-INTESTINAL CANCER: A RANDOMIZED STUDY

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**Background:** Upper gastro-intestinal (GI) cancer is associated with a poor prognosis. The multidimensional problems of incurable patients require close monitoring and frequent support, which can not sufficiently been given during conventional 1-2 monthly follow-up at the outpatient clinic.

**Objective:** To compare nurse-led follow-up at home with conventional medical follow-up at the outpatient clinic for patient satisfaction, quality of life and health care consumption in patients with incurable primary or recurrent oesophageal-, pancreatic-, or hepatobiliary cancer.

**Methods:** Patients were randomized to nurse-led follow-up at home or conventional medical follow-up at the outpatient clinic. Outcome parameters were patient satisfaction, quality of life, and health care consumption, measured by different questionnaires at 1½ and 4 months after randomization. Furthermore, cost-analyses were made for both follow-up strategies in the first four months.

**Results:** 138 patients were randomized of which 66 (48%) completed at least one questionnaire regarding quality of life and satisfaction within 4 months after inclusion (36 nurse-led follow-up, 30 conventional medical follow-up). At baseline, both groups were similar with respect to clinical, sociodemographic characteristics, and health related quality of life (HRQoL). Patients in the nurse-led follow-up group were significant more satisfied with the visits, while quality of life and healthcare consumption within the first four months were comparable in the two groups of patients. Nurse-led follow-up was cheaper than conventional medical follow-up. However, the total costs for the first four months follow-up in this study were higher in the nurse-led follow-up group due to a higher frequency of visits.

**Conclusion**
Nurse-led follow-up at home resulted in a marked increase in satisfaction with palliative upper GI cancer patients and their relatives compared with conventional medical follow-up at outpatient clinic. The intervention had no significant effect on quality of life and health care consumption and was less costly. The results suggest that conventional medical follow-up is interchangeable for nurse-led follow-up. A cost-utility study is necessary to determine the preferred frequency and duration of the home visits.

## INTRODUCTION

Symptoms of upper gastro-intestinal (GI) cancer tend to appear at a relatively late stage of the disease.[1-3] This explains why these cancers are generally associated with a poor prognosis. Moreover, many patients develop recurrent disease after surgical resection. When curative options are no longer available, 1-year survival rates are less than 15%.[4, 5]

For patients with irresectable or recurrent oesophageal-, pancreatic- or hepatobiliary cancer, no curative options are available. Median survival of these patients is less than ten months. Palliative treatment aims to improve quality of life of patients and their family by the prevention, early identification and treatment of pain and other physical, psychosocial and spiritual problems.[6] The high prevalence of these multiple problems in patients at a palliative stage underline the need for close monitoring and support.[7-11] The interval between follow-up visits, therefore, depends on the adequacy of controlling these multidimensional symptoms. Currently, patients are usually followed by means of regular visits to the outpatient clinic. The frequency of these visits is low in our hospital, with an average of once in 1-3 months or even no

follow-up. Outpatient clinic visits is a burden for many palliatively treated patients, among others in terms of travelling distance while physically unfit. In addition, the short contact during these visits often leave little time to deal with all issues and concerns.[12, 13] We performed a study in which 109 patients after intentionally curative surgery for oesophageal or gastric cardia cancer were randomized to standard follow-up by surgeons at the outpatient clinic or by regular home visits of a specialist nurse.[14] We found that nurses were able to perform follow-up of patients at their home and we found positive effects on quality of life and satisfaction of patients and spouses. In addition, this follow-up strategy seemed to be cost-effective compared with standard follow-up at the outpatient clinic.[15] Based on these results, we hypothesised that nurse-led home visits could have the same positive effects in patients in the palliative stage of the disease. This study, therefore, evaluated whether nurse-led follow-up by home visits could be an acceptable alternative to our standard medical follow-up at the outpatient clinic by a physician in palliative upper GI cancer patients and their relatives.

## MATERIALS AND METHOD

### Participants and allocation

Consecutive patients with irresectable or recurrent upper gastro-intestinal cancer were recruited from the departments oncology, gastroenterology, and surgery of the Erasmus MC - University Medical Center Rotterdam between June 2006 and August 2009. The Erasmus MC is a large university tertiary referral center in the Netherlands for patients with oesophageal, pancreatic and hepatobiliary cancer. Patients were eligible when a multidisciplinary panel had decided that a curative modality or disease modifying anti-tumour therapy (i.e. palliative chemotherapy, radiotherapy or surgery) was not or no longer possible. Excluded were patients who were admitted to a nursing home or hospice, patients who could not be followed by a physician at the outpatient clinic of the Erasmus MC, and patients who were unable to understand the Dutch language or to complete questionnaires. Patients were followed for a maximum period of 13 months from inclusion or to either death, or loss to follow-up. The institutional review board of the hospital approved this study and written informed consent was obtained from all patients. After informed consent, patients were randomized to conventional medical follow-up at the outpatient clinic or nurse-led follow-up at home. Randomization was performed using permutated blocks of size 4 and 6, in random order, and stratified by group of oesophageal or gastric cancer, duodenal or pancreatic cancer, and hepatobiliary cancer. Patients were assigned to their randomized allocation by the study coordinator using a central telephone or fax number. Patients were asked to nominate a relative who was most involved in their care. If available, this relative was also contacted by the study coordinator and asked for additional informed consent.

### Interventions

*Nurse-led follow-up* - Nurse-led follow-up was performed by home visits of a specialist nurse, with more than 10 years experience in oncology nursing care. Follow-up was performed at 14 days and then monthly after randomization, up to 13 months or death. If necessary, telephone contact was possible between visits. The protocol for the nurse-led follow-up is shown in appendix 1.

The nurse-led care focused primarily on relief of patients' suffering and complaints. For repeated assessment of the actual situation, the nurse used a modified version of the Edmonton Symptom Assesment System (ESAS) questionnaire.[16] The nurse worked under the responsibility of the attending medical specialist(s) in the Erasmus MC, and had regular contact with both the attending physician and the general practitioner of the patient.

*Conventional medical follow-up* - Conventional medical follow-up consisted of scheduled appointments to the outpatient clinic of the Erasmus MC. Follow-up was performed 1 month and then 2-monthly after randomization, up to 13 months or death. If patients were unable to come to the hospital, appointments could be performed by telephone.

In both patient groups, in case of symptoms and a subsequent palliative treatment, visits were frequently performed to evaluate the effect of this treatment on symptom burden.

### Questionnaires

At baseline, patient socio-demographics, clinical characteristics, and preference for follow-up were assessed. Outcome measures were based on structured questionnaires assessing patient (and relative) satisfaction, health-related quality of life (HRQol), and health care consumption (use of general practitioner and hospital admission).

*Patient satisfaction* - As no specific validated, Dutch questionnaire was available to assess patient satisfaction in this setting, a satisfaction questionnaire was developed for patients as well as their relatives. The questionnaire of Verschuur et al.[14] was used as basis. The questionnaire in the present study contained three general propositions related to the follow-up procedure (rated as agree, neutral, not agree), nine questions with regard to satisfaction with the content of the visit (rated as being very satisfied, satisfied, neutral, dissatisfied, very dissatisfied), and a report mark from 1 tot 10 for overall satisfaction and the burden of the visit.

*HRQoL* - HRQoL was assessed using two measures. The first was the generic EORTC QLQ-C30 measure[17], which incorporates nine multi-item scales: five functional scales (physical, role, emotional, cognitive, social), three symptom scales (nausea/vomiting, fatigue, pain), 6 single items (dyspnoea, insomnia, appetite loss, constipation, diarrhea and financial difficulties) and a global health/quality of life scale. The second was the generic EuroQol-5D (EQ-5D)[18], which contains a five-item classifier plus a visual analogue scale (EQ-VAS) of the overall health status. In addition to these quality of life measurements, the degrees of anxiety and depression were assessed with the hospital anxiety and depression scale (HAD)[19, 20], and pain intensity was measured on a numerical rating scale from 0 (no pain) to 10 (maximum pain imaginable).

*Health care consumption* - Patients or their relatives provided a monthly overview by means of a questionnaire of all contacts with the general practitioner and (re) admissions to the hospital.

### Data collection

The initial assessment at randomization was performed at the outpatient clinic or at the hospital ward. HRQol and satisfaction questionnaires for patients and the latter as well as for relatives were completed at 1½, 4, 7, 10 en 13 months after randomization (postal mailing). General practitioner visits and hospital admissions were monthly assessed, also by postal mailing. Patients or relatives were contacted by telephone if the questionnaires were not returned on time. If desired, the questionnaires were completed with help of the study coordinator at home or at the outpatient clinic.







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### Statistical analysis

Analyses were performed on an intention-to-treat basis. We ignored missing items on the QoL and satisfaction questionnaires when making the calculations, whenever at least half the items for multi-item scales were completed. The assumption was that these likely occurred at random. Otherwise we registered the scores as missing. The results were expressed as mean ± standard deviation and medians and interquartile range (IQR). Survival time from inclusion to death was calculated by using the Kaplan-Meier (KM) method. Comparisons of nominal variables were made using the chi-square test, whereas comparisons of ordinal or numerical variables were made using with the Mann Whitney- test or Student's t-test, respectively. Patients were evaluable if they completed at least one questionnaire regarding quality of life and satisfaction. For calculating costs of both follow-up strategies we estimated time and travel prices for one visit and for the actual costs incurred in this study for four months follow-up. Standard costs as determined for cost research in health care[21] were used as basis for these calculations, with all costs being reported in euros. For all analyses, in order to minimize the impact of multiple comparisons, a two-sided p-value of less than .01 was considered statistically significant. Calculations were performed with SPSS version 14.0 (SPSS Inc., Chicago, IL, USA). According to a power calculation in advance, a total sample size of 150 evaluable patients was needed.

## RESULTS

### Patient demographics

*Patients who refused and consented* - In total, 204 patients were eligible and informed on the study and 68% (n = 138) agreed to participate (Figure 1). Reasons for refusal to participate were that the study was considered too burdensome (53%), there was no need for hospital based follow-up (33%), and the patient preferred a doctor-led follow-up (14%).

*Patients with and without follow-up data* - Of 138 patients allocated to either nurse-led follow-up or out-patient clinic follow-up. 66 (48%) completed at least one questionnaire regarding quality of life and satisfaction within 4 months after inclusion (36 nurse-led follow-up, 30 out-patient clinic follow-up). The remainder of included patients (n = 72) were closer to death at inclusion (median survival 1.6 month [IQR 0.92-3.02] vs. patients with follow-up data median survival 6.8 months [IQR 3.90-10.50], p = .00) and they had less often a relative to provide input for the satisfaction questionnaire (dropout patients with relative n = 38, 53% vs. patients with follow-up data with relative n = 47, 71%, p = .03). On baseline, the patients without follow-up data scored on all quality of life items/scales, except for financial problems, worse than the patients with follow-up data.

*Patients with nurse-led follow-up vs. conventional medical follow-up* - Our findings reflect patient satisfaction, quality of life, and health care consumption in the first four months after inclusion because with later follow-up too few patients remained alive to allow for meaningful analyses. Regarding the 66 patients with follow-up data, there was no statistically significant difference between the two follow-up strategies groups according to the demographic or clinical characteristics (Table 1). The largest difference was found for travel distance to the hospital. Patients with at least one follow-up allocated to conventional medical follow-up at the outpatient clinic had less travel distance (median 19 km, IQR 13.8-29.3) than patients allocated to the nurse-led follow-up at home (median 38 km, IQR 10.3-64.3). The median follow-up time was 6 months in both groups and there was no significant difference in survival between both groups.







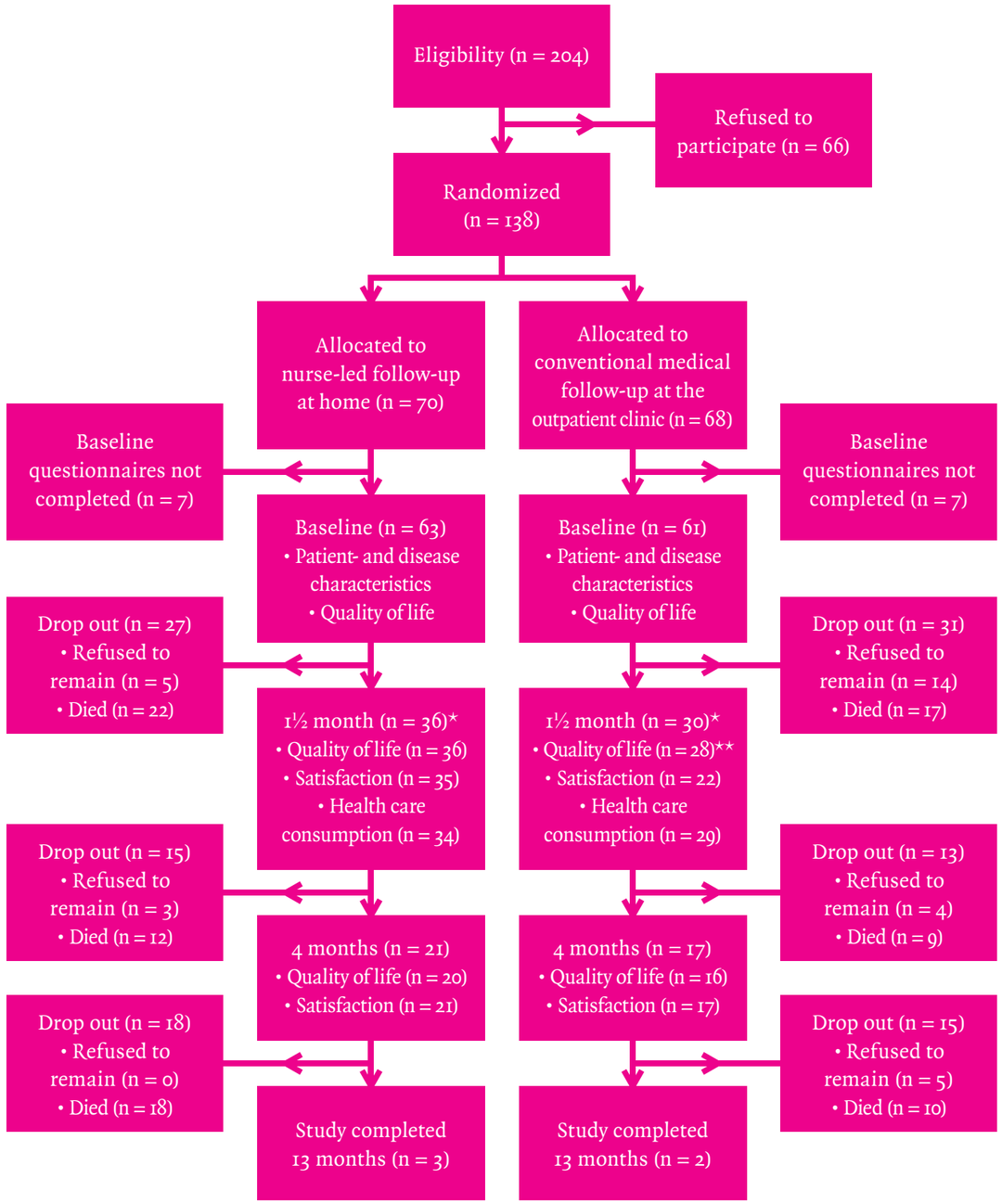


**Figure 1.** *Flow diagram of recruitment.*

*** Evaluable patients.**
**** 2 pts only had follow-up data at 4 months.**



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| Characteristics | Nurse-led follow-up n = 36 | Conventional medical follow-up n = 30 |
|---|---|---|
| Age; yrs, mean (SD) | 67 (10.4) | 64 (12.0) |
| Gender male; no. of patients (%) | 22 (61) | 18 (60) |
| Primary tumor site; no. of patients (%) | | |
| • Oesophagus/gastric | 18 (50) | 16 (53) |
| • Pancreatic/duodenum | 10 (28) | 5 (17) |
| • Hepatic/ common bile duct | 8 (22) | 9 (30) |
| Main indication for palliative policy; no. of patients (%) | | |
| • Irresectable tumor | 5 (14) | 6 (20) |
| • Inoperable disease | 2 (6) | 2 (7) |
| • Distant metastases | 4 (11) | 3 (10) |
| • Recurrence | 3 (8) | 4 (13) |
| • Unknown | 22 (61) | 15 (50) |
| Preference for follow-up strategy at baseline; no. of patients (%) | | |
| • Nurse-led follow-up at home | 27 (75) | 17 (57) |
| • Conventional medical follow-up at the outpatient clinic | 1 (3) | 1 (3) |
| • No preference | 8 (22) | 12 (40) |
| Marital status: Single/separated/divorced/widowed; no. of patients (%) | 11 (31) | 7 (23) |
| No religion; no. of patients (%) | 14 (39) | 12 (40) |
| Highest education*; no. of patients (%) | | |
| • Elementary school | 20 (56) | 11 (37) |
| • Intermediate school (VMBO/MBO) | 7 (19) | 10 (33) |
| • Higher school (HAVO/HBO/VWO/University) | 9 (25) | 7 (23) |
| • Unknown | - | 1 (3) |
| Travel distance to the hospital†; km, median [IQR] | 38 [10.3-64.3] | 19 [13.8-29.3] |

***See http://southholland.angloinfo.com/countries/holland/schooling.asp for levels of Education in the Netherlands.**
**†P = .02, comparing nurse-led follow-up with conventional medical follow-up.**

**Table 1.** *Characteristics of 66 patients with irresectabel of recurrent oesophagus-, pancreas- or hepatobiliair cancer with at least baseline and one follow-up data for all outcomes.*





| | Mean score (SD) at 1,5 month follow-up | | | | | |
|---|---|---|---|---|---|---|
| | Patients | | | Relatives | | |
| | Nurse-led follow-up | Conventional medical follow-up | P-value | Nurse-led follow-up | Conventional medical follow-up | P-value |
| | n = 35 | n = 22 | | n = 30 | n = 19 | |
| **Agreement with theorem (1-3, 1 = most agreed)** | | | | | | |
| • Visit is proceeded as expected | 1.0 (0.00) | 1.2 (0.59) | .07 | 1.1 (0.37) | 1.3 (0.65) | .18 |
| • I had chosen the same follow-up for myself | 1.0 (0.00) | 2.3 (0.90) | < .001 | 1.0 (0.00) | 2.2 (0.98) | < .001 |
| • They take enough time for me | 1.0 (0.00) | 1.1 (0.43) | .21 | 1.1 (0.31) | 1.2 (0.63) | .42 |
| **Report mark of item (1-10, 10 = best)** | | | | | | |
| • Overall satisfaction | 8.4 (0.95) | 7.5 (2.02) | .02 | 8.0 (1.13) | 6.8 (2.32) | .02 |
| • Extent of burden follow-up visit | 8.4 (1.90) | 6.0 (2.65) | < .001 | 8.4 (1.56) | 4.9 (2.44) | < .001 |
| **Satisfaction on item (1-5, 1 = most satisfied)** | | | | | | |
| • All items listed below together | 1.6 (0.42) | 1.8 (0.54) | .14 | 1.8 (0.39) | 2.1 (0.77) | .08 |
| • Care is readily available | 1.5 (0.70) | 2.1 (1.04) | .01 | 1.7 (0.76) | 2.4 (1.26) | .01 |
| • Knowledge of the physician/nurse | 1.6 (0.50) | 1.7 (0.72) | .35 | 1.8 (0.50) | 1.8 (0.75) | .91 |
| • Confidence given by physician/nurse | 1.5 (0.51) | 1.6 (0.73) | .36 | 1.7 (0.54) | 2.0 (1.03) | .18 |
| • Management of physical complaints | 1.8 (0.54) | 1.7 (0.70) | .69 | 1.8 (0.50) | 1.9 (0.91) | .44 |
| • Information given by physician/nurse | 1.7 (0.48) | 1.7 (0.47) | .75 | 1.8 (0.64) | 1.9 (0.87) | .40 |
| • Advices given by physician/ nurse | 1.6 (0.49) | 1.8 (0.70) | .37 | 1.8 (0.38) | 2.1 (0.97) | .27 |
| • Answers you get from physician/nurse | 1.6 (0.50) | 1.8 (0.69) | .21 | 1.8 (0.41) | 2.0 (0.82) | .25 |
| • How the physican/nurse involve you in careplanning | 1.7 (0.54) | 1.8 (0.66) | .32 | 1.9 (0.45) | 2.2 (1.03) | .12 |
| • Support you receive from physician/nurse | 1.5 (0.51) | 1.8 (0.66) | .08 | 1.8 (0.50) | 2.3 (1.15) | .06 |

**Table 2a.** *Satisfaction of patients and relatives on follow-up strategy after 1,5 month follow-up.*




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| | Mean score (SD) at 4 months follow-up | | | | | |
|---|---|---|---|---|---|---|
| | Patients | | | Relatives | | |
| | Nurse-led follow-up | Conventional medical follow-up | P-value | Nurse-led follow-up | Conventional medical follow-up | P-value |
| | n = 21 | n = 17 | | n = 21 | n = 12 | |
| **Agreement with theorem (1-3, 1 = highly agree)** | | | | | | |
| • Visit is proceeded as expected | 1.0 (0.00) | 1.4 (0.70) | .01 | 1.0 (0.00) | 1.5 (0.82) | < .001 |
| • I had chosen the same follow-up for myself | 1.0 (0.20) | 2.1 (1.00) | < .001 | 1.1 (0.22) | 2.1 (0.99) | < .001 |
| • They take enough time for me | 1.0 (0.00) | 1.3 (0.58) | .03 | 1.1 (0.31) | 1.3 (0.65) | .32 |
| **Report mark of item (1-10, 10=best)** | | | | | | |
| •Overall satisfaction | 8.5 (1.03) | 7.1 (1.18) | < .001 | 8.5 (0.98) | 6.9 (2.38) | .01 |
| •Extent of burden follow-up visit | 8.5 (1.42) | 5.2 (2.69) | < .001 | 8.8 (0.98) | 4.8 (2.64) | < .001 |
| **Satisfaction on item (1-5, 1=most satisfied)** | | | | | | |
| • All items listed below together | 1.6 (0.45) | 2.2 (0.62) | < .001 | 1.7 (0.49) | 2.1 (0.65) | .07 |
| • Care is readily available | 1.7 (0.64) | 2.2 (1.03) | .04 | 1.7 (0.64) | 2.1 (0.79) | .16 |
| • Knowledge of the physician/nurse | 1.5 (0.51) | 1.8 (0.53) | .03 | 1.6 (0.51) | 1.8 (0.45) | .35 |
| • Confidence given by physician/nurse | 1.5 (0.51) | 1.8 (0.81) | .08 | 1.6 (0.60) | 2.1 (0.79) | .06 |
| • Management of physical complaints | 1.8 (0.59) | 2.2 (0.78) | .14 | 1.7 (0.56) | 2.0 (0.95) | .35 |
| • Information given by physician/nurse | 1.7 (0.48) | 2.2 (1.03) | .03 | 1.8 (0.62) | 2.1 (0.83) | .28 |
| • Advices given by physician/ nurse | 1.6 (0.51) | 2.3 (0.87) | < .001 | 1.9 (0.58) | 2.2 (0.83) | .29 |
| • Answers you get from physician/nurse | 1.6 (0.50) | 2.2 (0.83) | < .001 | 1.8 (0.62) | 2.3 (0.97) | .12 |
| • How the physician/nurse involve you in careplanning | 1.6 (0.57) | 2.3 (0.85) | .01 | 1.9 (0.58) | 2.3 (0.97) | .21 |
| • Support you receive from physician/nurse | 1.6 (0.58) | 2.3 (0.92) | .01 | 1.8 (0.52) | 2.3 (0.89) | .04 |

**Table 2b.** *Satisfaction of patients and relatives on follow-up strategy after 4 months follow-up.*







| Status | Nurse-led follow-up n = 36 | | Conventional medical follow-up n = 30 | |
|---|---|---|---|---|
| Number of visits total (%) | Regular | Extra | Regular | Extra |
| • Total (row %) | 157 (59) | 111 (41) | 47 (59) | 33 (41) |
| • At home (column %) | 155 (99) | 2 (2) | - | - |
| • Out patient clinic (column %) | - | 16 (14) | 30 (64) | 5 (15) |
| • Telephone consult (column %) | 2 (1) | 93 (84) | 17 (36) | 28 (85) |
| Number of visits per person; median (IQR) | | | | |
| • At home | 4 (4-5) | | 0 (0-0) | |
| • Out patient clinic | 0 (0-1) | | 1 (0-2) | |
| • Telephone consult | 1 (0-5.5) | | 1 (0-3) | |

**Table 3.** *Characteristics of 356 home care visits, out-patient clinic visits or telephone consults for 66 patients (first 4 months of follow-up).*

Patients in the nurse-led follow-up group had a overall survival of median 6.3 months [IQR 4.7-7.9] vs. median 6.8 months [IQR 3.9-9.6] (p = .87) in the conventional medical follow-up arm. More patients in the nurse-led group completed the 33 patients (92%) nurse-led group vs. 21 patients (70%) in the conventional medical follow-up group (p = .02).

### Patient and relative satisfaction

Both patients and their relatives in the nurse-led group were more satisfied with their follow-up than those receiving the conventional medical follow-up (Table 2a and 2b). Mean overall patient satisfaction at 1½ and 4 months was respectively 8.4±.95 and 8.5±1.03 for the nurse-led follow-up group compared with 7.5±2.02 and 7.1±1.18 for the conventional medical follow-up group (p = 0.02 and < 0.001, respectively). Mean overall relative satisfaction at 1½ and 4 months was respectively 8.0±1.13 and 8.5±.98 for the nurse-led follow-up group compared with 6.8±2.32 and 6.9±2.38 for the conventional medical follow-up group (p = .02 and .01).

At both time points, patients and relatives in the conventional medical follow-up group less frequently agreed on the statement that they had opt for this follow-up strategy when given a choice (p < .001), and they evaluated the conventional medical follow-up as more burdensome (p < .001). According to the visits, patients in the nurse-led follow-up group were more satisfied about the following aspects: care is readily available (at 1,5 month follow-up, p = .01), advices, information and support given by the care-provider (at 4 months follow-up, p < .001, p < .001 and p = .01, respectively), and the involvement of the patient in his or her own care planning (at 4 months follow-up, p < .001). For these items, except for 'care is readily available', patients in the conventional medical follow-up group became less satisfied over time, whereas the scores remained the same in the nurse-led follow-up group.

### Health-related quality of life

HRQoL generally followed the same pattern in both groups on both time points. At baseline, patients in the nurse-led follow-up group, respectively had less symptoms of diarrhoea (mean 9.3±21.98 vs. 18.9±29.92, NS), financial difficulties (mean 6.5±23.66 vs. 16.7±31.26, NS), and had a better cognitive functioning (mean 83.8±21.26 vs. 72.8±27.15, NS). These differences were no longer present during follow-up. Patients in the conventional medical follow-up group were more often depressed (mean 8.5±5.36 vs. 6.4±4.86, NS),



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after 1½ months of follow-up, and in these patients loss of appetite was less common (mean 26.7±33.81 vs. 55.0±40.86, NS) after 4 months of follow-up.

### Health care use

In total, 268 visits were performed in the nurse-led group (157 home visits, 95 telephone consults and 16 referral visits to the out patient clinic), and 80 in the conventional medical follow-up group (35 outpatient clinic visits and 45 telephone consults). Of these visits 157 (59%) and 47 (59%), respectively, were regular visits and 111 (41%) vs. 33 (41%) were extra visits initiated by the patient, the relative, or the nurse/physician (Table 3). In the conventional medical follow-up group more regular visits were replaced by telephone contacts (17 visits (36%) vs. 2 visits (1%) in nurse-led follow-up group). Ten patients (28%) from the nurse-led follow-up group were referred to the outpatient-clinic for a visit with the physician.

Costs of a nurse-led follow-up visit per patient were 38% lower than those of a conventional follow-up visit (€ 89,97 nurse-led visit vs. € 144,48 conventional medical follow-up visit) (Table 4). Overall, within the 4 first months, costs for the nurse-led follow-up strategy were € 336,91 vs. € 144,48 per patient for conventional medical follow-up visits due to a higher volume of visits in the nurse-led group.

On average, patients in the nurse-led follow-up group had a slightly higher number of contacts with the general practitioner compared to patients in the conventional medical follow-up group (nurse-led follow-up median 6 contacts (IQR 2.75-11.0) vs. conventional medical follow-up median 4 contacts (IQR 1.50-7.50); p = .11), and similar number of hospital admissions (nurse-led follow-up median 1 admission (IQR 0.00-1.25) vs. conventional medical follow-up median = 1 (IQR 0.00-1.00); p = .91), within the first 4 months (Table 5).

## DISCUSSION

This study shows that palliative care for patients with upper GI cancer can be provided at home by specialized oncology nurses with high patient satisfaction. Patients as well as their relatives were highly satisfied with this type of nurse-led follow-up. Our findings also document that this strategy is less costly per visit than the conventional medical follow-up strategy, while patients' quality of life and contacts with general practitioner and hospital care are similar to conventional medical follow-up (Table 5).

The higher level of satisfaction is largely determined by the fact that the home visits were perceived as less burdensome compared to the visits to the outpatient clinic. This is probably related to the burden of travel to the hospital, delays in physicians' schedule, and the fact that most patients prefer to receive palliative care at home and prefer to die at home.[22] This could also explain that more patients in the conventional medical follow-up group ended the study before death (30%) than patients in the nurse-led group (8%). Furthermore, we found a difference in travel time between included patients from both groups. This was not the case when we analysed the difference in travel time between the two groups of all 138 randomized patients. Therefore, patients with conventional medical follow-up with a further distance between home and hospital had ended participation in the study earlier after study entry.

The higher level of satisfaction in the nurse-led follow-up group can further be explained by the fact that patients and relatives appreciated the nurses' care more than physicians' care.[23] It has





| | Nurse-led follow-up | | | Conventional medical follow-up | | |
|---|---|---|---|---|---|---|
| | Cost prize 1 visit per patient | Volume; median per patient in this study | Costs | Cost prize 1 visit per patient | Volume; median per patient in this study | Costs |
| Travel costs home visit[1] | € 7,88 = € 0,20 X 37,5 km[5] (x2 for return) | 4 | € 63,04 | NA | NA | NA |
| Time costs travelling home visit | € 18,87 = € 0,51 x 37 min[5] (x2 for return) | 4 | € 150,96 | NA | NA | NA |
| Time costs home visit[2] | € 28,82 = € 0,51 x 56,5 min[5] | 4 | € 115,26 | NA | NA | NA |
| Time costs out patient clinic visit[2] | € 8,93 = € 0,51 x 17,5 min[5] | 0 | € 0.00 | € 129,- per visit | 1 | € 129,00 |
| Time costs telephone consult | € 7,65 = € 0,51 x 15 min[5] | 1 | € 7,65 | € 1,72 x 9 min[5] | 1 | € 15,48 |
| **Total per person** | **€ 89,97** | | **€ 336,91** | **€ 144,48** | | **€ 144,48** |

**[1] Parking costs not included.**

**[2] Inclusive time for direct patient contact, administration and consultation other professionals.**

**[3] Cost a minute (reference value 2009 cost per nurse per hour € 30,50 inclusive holiday pay and social security).**

**[4] Cost a minute (reference value 2009 cost per medical physician per hour € 103,- inclusive holiday pay and social security or cost for outpatient clinic visit € 129,- for 20 minutes inclusive nurse assistant, overhead, accommodation and material)**

**[5] Median per patient in this group.**

**Table 4.** *Costs of both follow-up strategies per person.*





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| | Number of patients (%) at 4 month follow-up | | | Median (IQR) number of contacts/admissions at 4 months follow-up | | |
|---|---|---|---|---|---|---|
| | Nurse-led follow-up | Out patient clinic follow-up | P-value | Nurse-led follow-up | Out patient clinic follow-up | P-value |
| | n = 34* | n = 29* | | n = 34* | n = 29* | |
| General practitioner contact | 33 (97) | 27 (93) | .46 | 6 (2.75-11.0) | 4 (1.50-7.50) | .11 |
| (re)Admission to hospital | 17 (50) | 15 (52) | .89 | 1 (0.00-1.25) | 1 (0.00-1.00) | .91 |

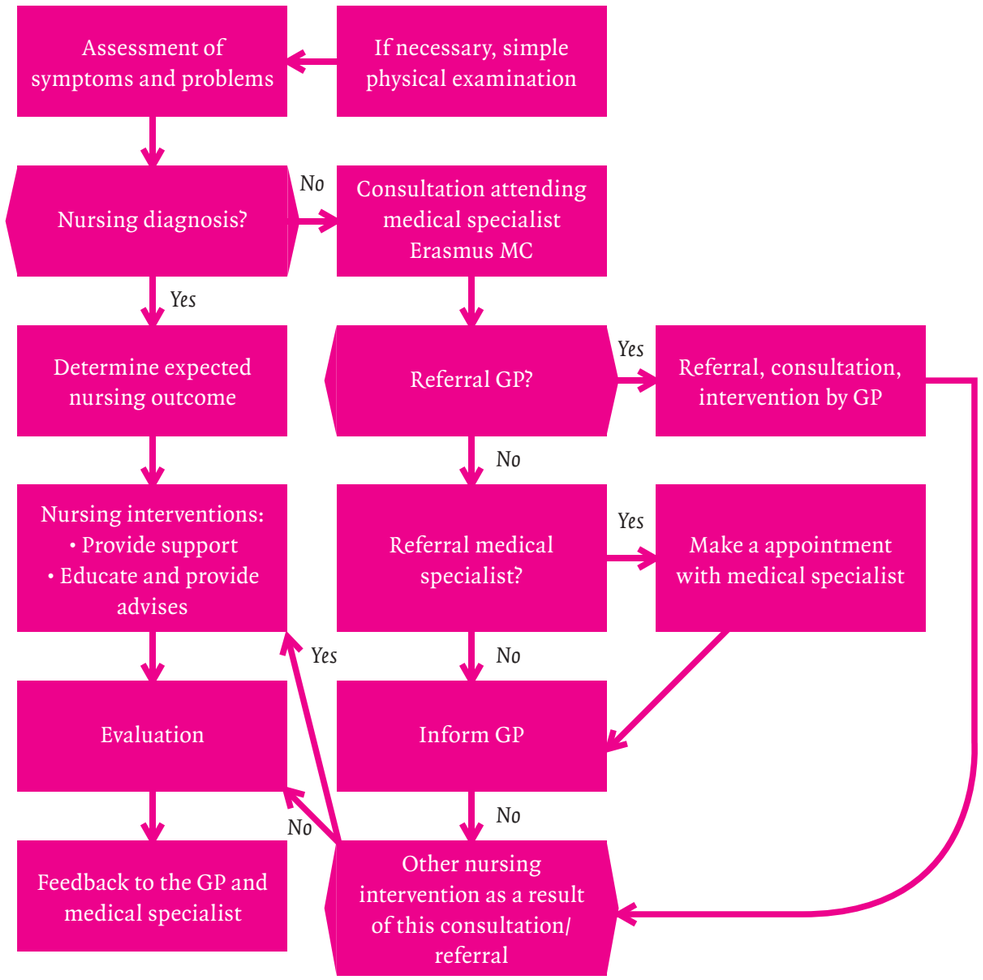
*** 3 patients did not complete a health care questionnaire.**

**Table 5.** *Health care consumption during 4 months follow-up.*

been suggested that quality of care by nurses is better at this disease stage because nurses may deal with broader aspects of health care experience, rather than concentrating solely on treatment of the disease.[12, 23] A high level of satisfaction with nurses' care was found in two reviews on substitution of doctors by nurses in cancer care and in primary care.[24, 25] Chapple et al[26] found that palliative care by nurses was highly valued by the patients, particularly their advice on practical matters, information on their disease, emotional support, advice on symptoms, help with communication and that nurses' help was readily available. In addition, continuity of care in this study was probably better maintained by the nurse. In the outpatient clinic there was a high rotation of junior medical staff, although, some doctors made sure that they always saw the patient themselves. Nevertheless, there are patients who may feel more confident with follow-up given by a doctor.[27] In our study, this involved 14% (n = 9) of the patients refusing participation and 3% (n = 2) of the patients, who preferred at baseline conventional medical follow-up over nurse-led follow-up.

Despite the higher satisfaction in the nurse-led group, there was no difference in quality of life between both groups. It may not be realistic to assume that the quality of life at this stage of the disease would be significantly influenced by a visit from a nurse once a month.[28] Previous studies on the impact of palliative home care teams and coordinating nurses on patients' quality of life[29] and on the effectiveness of nurse-led follow-up for patients with cancer[24, 30, 31] revealed similar results. Corner[32] found in a review that situations where the goals of nurse-led initiatives were to improve quality of care, this outcome was not always achieved. This may have been influenced by the short duration of follow-up given the rapid death of a considerable proportion of patients[33], or by the possibility that the EORTC QLQ-C30 is not sufficiently sensitive to provide relevant information on this level.[34]

The nurse-led follow-up did not interfere with existing standard health care structures. In case the general practitioner had a key role in the provision of palliative care, this was not changed. All GP's received a letter from the study coordinators




**Appendix 1.** *Problem oriented nursing care plan during home visits.*

with information about the study and the randomization procedure. Shortly after that, if the patient was randomized to nurse-led follow-up the nurse contacted the general practitioner. GP's generally appreciated his and consented to the study, even more if they had insufficient knowledge about upper gastrointestinal cancer and/or this specialists' treatments, (such as on aspects of stent placement) and they noted that the nurse was readily available for professional advice and support. So we assume that the nurse-led follow-up seems to complement the general GP follow-up, just as the conventional medical follow-up has done in the past.[35]

Per visit, we found a lower cost price for the visit of the nurse at home in comparison with the cost price of the outpatient clinic visit. However, the total follow-up cost of the nurse-led strategy was more expensive than standard care during the four first months of follow-up. This was mainly due to the fact that patients in the nurse-led group had more regular visits. We assumed that patients in this phase of their disease had a need for close monitoring and support to receive symptom control, and therefore our nurse-led protocol included at least one visit each month. A higher frequency reveals in our study no significant changes in symptom burden or quality of life. It is unclear if the higher level of satisfaction was caused by more visits. Therefore, further research on the frequency and the duration of visits is necessary in a cost-utility study. Because the costs are largely determined by travel time and travel costs, we should also study if the home-based follow-up can be performed by nurses with less travel time and costs, such as community nurses, or by innovative interventions such as telehealth.

Four methodological issues merit discussion. First, missing data may have biased the results. Palliative care research is known to be hampered by methodological challenges related to attrition and missing data due to progressive illness and death. Second, findings may also have been biased by the fact that a quarter of the questionnaires were completed with help of a relative or friend. However, the likelihood of such bias was limited since the form elicited patient reports regardless of who completed it. Third, the information on health care use could have been biased by the extent to which patients were able to remember events. However, we used a diary to immediately update after every event, thus reducing the influence of memory. Fourth, the generalisability of results is unknown. Prior to the 1½ month follow-up 58 patients were lost to follow-up, mainly due to progressive disease with deterioration and death, with related poor quality of life scores. Furthermore, 53% of the patients refusing study participation probably had a poorer performance status as they found participating too burdensome. In addition, we did not include non-Dutch speaking patients in the study given the fact that we needed input by means of questionnaires. Therefore, the result of this study cannot be transferred to all incurable GI cancer patients.

In conclusion, nurse-led follow-up at home resulted in a marked increase in satisfaction with palliative upper GI cancer patients and their relatives compared with conventional medical follow-up at out-patient clinic. The intervention had no significant effect on quality of life and health care consumption, and was less costly. The results suggest that physician-led follow-up is interchangeable for nurse-led follow-up, although it is unclear which frequency for visits is desirable. This information can be useful in developing hospital-based palliative care follow-up programmes improving their palliative care for patients and relatives. Although, patients' choice on preferred way of follow-up remains important.



## REFERENCES


1. Gullo L, Tomassetti P, Migliori M, et al. Do early symptoms of pancreatic cancer exist that can allow an earlier diagnosis? Pancreas 2001;22:210-213.

2. Sun VC, Sarna L. Symptom management in hepatocellular carcinoma. Clin J Oncol Nurs 2008;12:759-766.

3. Siersema PD. New developments in palliative therapy. Best Pract Res Clin Gastroenterol 2006;20:959-978.

4. Linder S, Bostrom L, Nilsson B. Pancreatic carcinoma incidence and survival in Sweden in 1980-2000: a population-based study of 16,758 hospitalized patients with special reference to different therapies. Eur J Surg Oncol 2007;33:616-622.

5. IKNL. Integraal Kankercentrum Nederland (Comprehensive Cancer Center the Netherlands). 2012; http://cijfersoverkanker.nl/; (assessed 18-02-2012)

6. WHO. World Health Organisation. 2002; http://www.who.int/cancer/palliative/definition/en/; (assessed 16-2-2012)

7. Nordin K, Glimelius B, Pahlman L, et al. Anxiety, depression and worry in gastrointestinal cancer patients attending medical follow-up control visits. Acta Oncol 1996;35:411-416.

8. Nordin K, Glimelius B. Psychological reactions in newly diagnosed gastrointestinal cancer patients. Acta Oncol 1997;36:803-810.

9. Teunissen SC, Wesker W, Kruitwagen C, et al. Symptom Prevalence in Patients with Incurable Cancer: A Systematic Review. J Pain Symptom Manage 2007;34:94-104.

10. Uitdehaag MJ. Verschuur EML, van Eijck CHJ et al. Problems and needs in patients with incurable esophageal and pancreatico-biliary cancer: an explorative study. Submitted.

11. Johansson B, Berglund G, Glimelius B, et al. Intensified primary cancer care: a randomized study of home care nurse contacts. J Adv Nurs 1999;30:1137-1146.

12. Anderson WG, Alexander SC, Rodriguez KL, et al. "What concerns me is." Expression of emotion by advanced cancer patients during outpatient visits. Support Care Cancer 2008;16:803-811.

13. Detmar SB, Muller MJ, Wever LD, et al. The patient-physician relationship. Patient-physician communication during outpatient palliative treatment visits: an observational study. Jama 2001;285:1351-1357.

14. Verschuur EM, Steyerberg EW, Tilanus HW, et al. Nurse-led follow-up of patients after oesophageal or gastric cardia cancer surgery: a randomised trial. Br J Cancer 2009;100:70-76.

15. Polinder S, Verschuur EM, Siersema PD, et al. Cost comparison study of two different follow-up protocols after surgery for oesophageal cancer. Eur J Cancer 2009;45:2110-2115.

16. Heedman PA, Strang P. Symptom assessment in advanced palliative home care for cancer patients using the ESAS: clinical aspects. Anticancer Res 2001;21:4077-4082.






M.J. Uitdehaag | Living in the face of death

17. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365-376.

18. Dolan P. Modeling valuations for EuroQol health states. Med Care 1997;35:1095-1108.

19. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-370.

20. Spinhoven P, Ormel J, Sloekers PP, et al. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychol Med 1997;27:363-370.

21. Hakkaart-van Roijen L, Tan S, Bouwmans C. Manual for cost research, methods and standard cost for economic evaluations in healthcare. Updated version 2010. Rotterdam: Insitute of, Erasmus MC; 2011.

22. Murray MA, Fiset V, Young S, et al. Where the dying live: a systematic review of determinants of place of end-of-life cancer care. Oncol Nurs Forum 2009;36:69-77.

23. Viklund P, Wengstrom Y, Lagergren J. Supportive care for patients with oesophageal and other upper gastrointestinal cancers: The role of a specialist nurse in the team. Eur J Oncol Nurs 2006;10:353-363.

24. Lewis R, Neal RD, Williams NH, et al. Nurse-led vs. conventional physician-led follow-up for patients with cancer: systematic review. J Adv Nurs 2009;65:706-723.

25. Laurant M, Reeves D, Hermens R, et al. Substitution of doctors by nurses in primary care. Cochrane Database Syst Rev 2005:CD001271.

26. Chapple A, Ziebland S, McPherson A. The specialist palliative care nurse: a qualitative study of the patients' perspective. Int J Nurs Stud 2006;43:1011-1022.

27. Cox K, Wilson E, Heath L, et al. Preferences for follow-up after treatment for lung cancer: assessing the nurse-led option. Cancer Nurs 2006;29:176-187.

28. Crippa S, Dominguez I, Rodriguez JR, et al. Quality of life in pancreatic cancer: analysis by stage and treatment. J Gastrointest Surg 2008;12:783-793.

29. Salisbury C, Bosanquet N, Wilkinson EK, et al. The impact of different models of specialist palliative care on patients' quality of life: a systematic literature review. Palliat Med 1999;13:3-17.

30. Moore S, Corner J, Haviland J, et al. Nurse led follow up and conventional medical follow up in management of patients with lung cancer: randomised trial. BMJ 2002;325:1145.

31. Faithfull S, Corner J, Meyer L, et al. Evaluation of nurse-led follow up for patients undergoing pelvic radiotherapy. Br J Cancer 2001;85:1853-1864.

32. Corner J. The role of nurse-led care in cancer management. Lancet Oncol 2003;4:631-636.

33. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care 2003;41:582-592.





34. Nordin K, Steel J, Hoffman K, et al. Alternative methods of interpreting quality of life data in advanced gastrointestinal cancer patients. Br J Cancer 2001;85:1265-1272.

35. Meeuse JJ, van der Linden YM, Post WJ, et al. Cancer patients use hospital-based care until death: a further analysis of the Dutch Bone Metastasis Study. J Palliat Med 2011;14:1117-1127.





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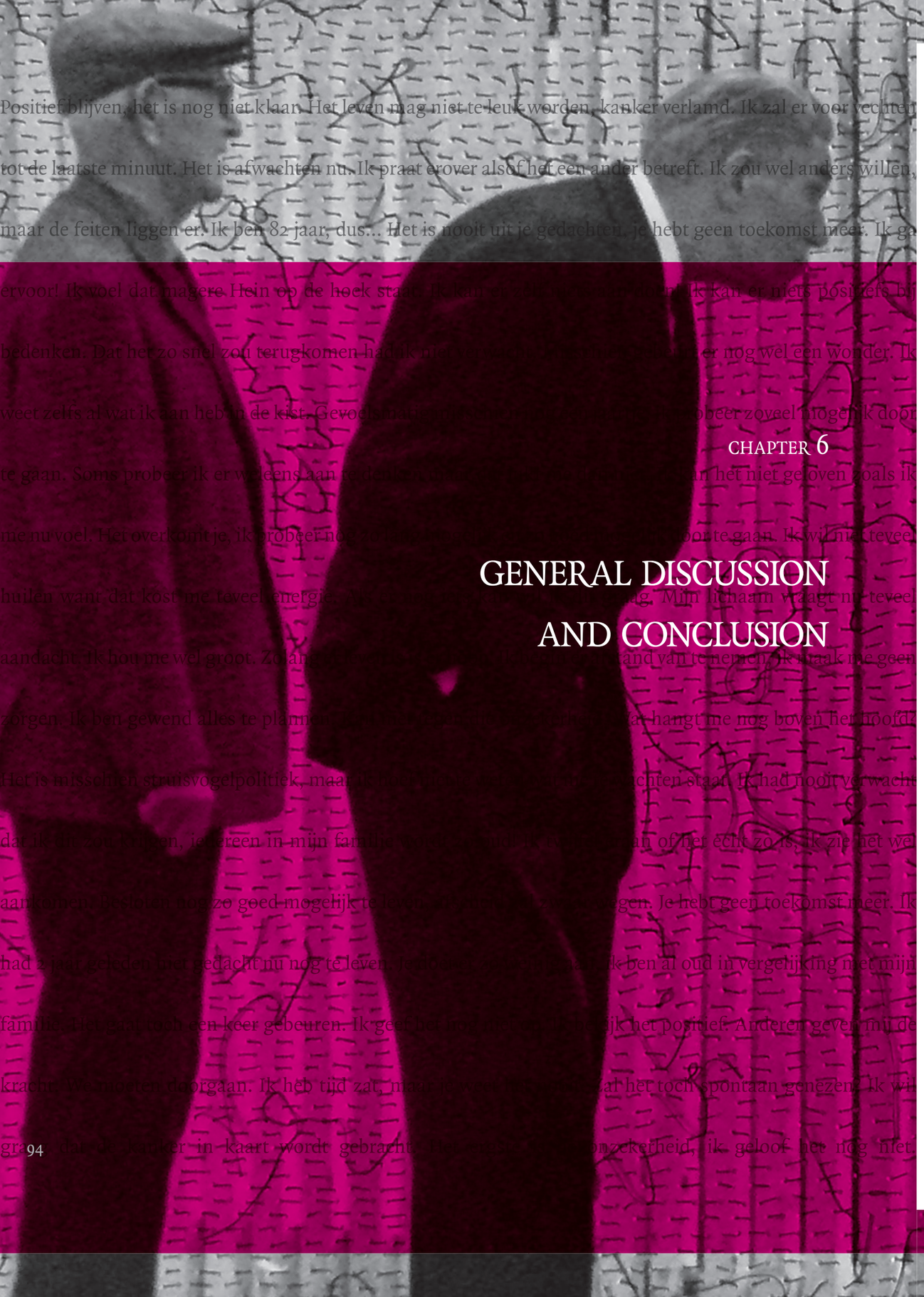


CHAPTER 6

# GENERAL DISCUSSION AND CONCLUSION





## INTRODUCTION

The central aim of this thesis was to explore the main problems and needs of patients with incurable or recurrent upper GI cancer and to study different interventions to maintain or improve their quality of life. Several research questions were addressed:

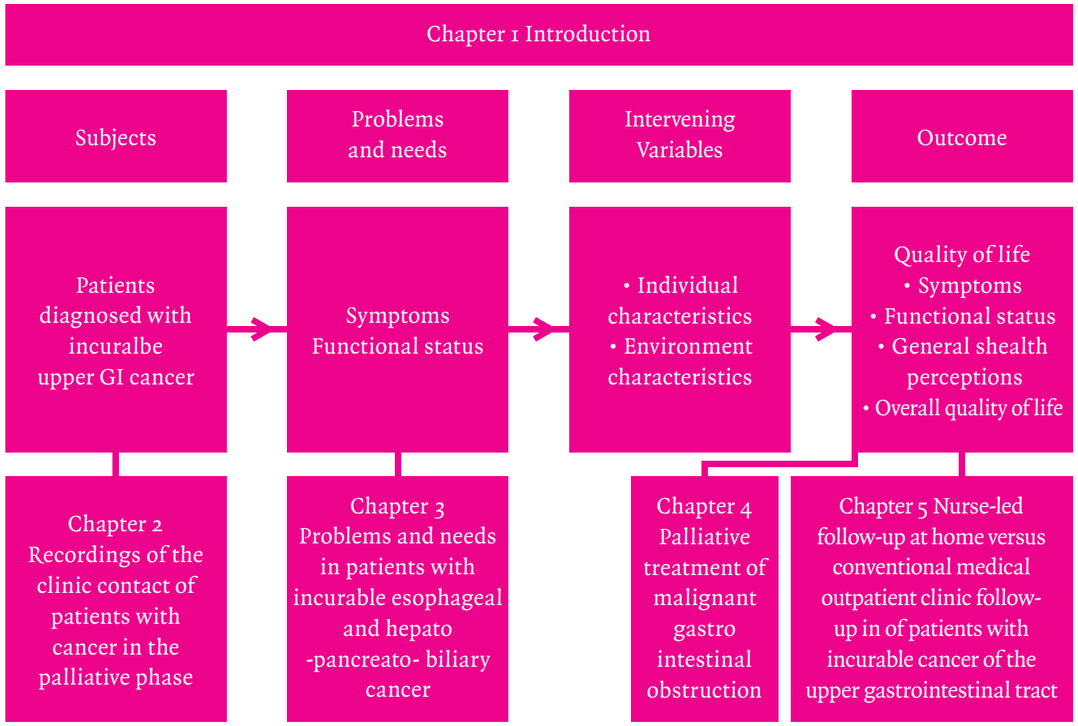
1. Is a CD recording of the consultation in which patients are informed about their new diagnosis of non-curable cancer feasible and useful, and what is the impact on quality of life and the openness to discuss cancer-related issues in the family?
2. What are the main problems and needs for care of patients diagnosed with incurable esophageal or pancreatico-biliary cancer?
3. What are the functional outcomes, quality of life, frequency of re-interventions and complications of three newly developed stents for treatment of malignant upper GI stenoses? These stents were:
   a. the Alimaxx-E stent, a esophageal stent which is fully covered with polyurethane to resist tissue ingrowth and has 20 antimigration struts to prevent migration,
   b. the SX-ELLA stent Esophageal HV, which is fully covered to resist tissue ingrowth and has an antimigration ring to withstand migration,
   c. and the WallFlex enteral stent, a nitinol stent which has looped ends to reduce risk of mucosal injury, and a proximal flared end to minimize risk of stent migration.
4. Is nurse-led follow-up by home visits an acceptable alternative to the standard medical follow-up at the outpatient clinic for incurable esophageal and pancreatico-biliary cancer patients and their relatives?

## MAIN RESULTS

Professionals offer different definitions of the starting point of palliative care. Usually, the care of patients with cancer may be divided conveniently into different phases, each determined by the primary aim of treatment and care: curative, palliative and terminal.[1] Although the dividing lines are not always clear, patients must be given the chance to acknowledge which mode of treatment they are in. For many doctors this is a difficult message to convey, because when a cancer is no longer thought to be curable, the patient's world becomes filled with uncertainty, which usually affects patient's quality of life (QoL). On the other hand, withholding the truth or patients' unawareness seems to have more negative effects on QoL.[2, 3] Cancer patients and their relatives have been shown to appreciate receiving a recording of oncological consultations. However, there is reluctance in providing incurable cancer patients with recordings of their bad news consultation, even though one could hypothesize that this could help in terms of recalling and understanding the information[4, 5], receiving support[5-7], and to feel more empowered.[8-10] Therefore, we studied the impact of such recordings on quality of life and the opportunity to discuss cancer-related issues with others, in incurable cancer patients.

**Is a CD recording of the consultation in which patients receive a new diagnosis of non-curable cancer feasible and useful, and what is the impact on quality of life and the openness to discuss cancer-related issues in the family? (RECORD study)**

To answer this question we performed a pilot study in which seventeen patients with a new diagnosis of incurable oesophageal or head and neck cancer were randomized to receive a CD (n = 10) or no CD (n = 7) of their consultation. Data on feasibility, utility, and quality of life were collected before




consultation and 1 week and 1 month afterwards. No major technical or procedural problems were encountered. Three-quarters of the patients appreciated receiving the CD, which was listened to by 8/10 patients and by 10/10 others in the CD group. After 1 month, two-thirds of the patients in the control group also asked to receive the CD. However, we found a trend towards a poorer quality of life but an improved openness to discuss cancer related issues, in the CD group. These findings require verification in a study with a larger sample size. As an important side finding we discovered that in clinical practice it is difficult to clearly determine what 'the' initially palliative consultation is. Most physicians 'dose' the truth in a process, with each step leading to more or less certainty of incurability, which also is the preference of patients and caregivers.[11] This necessitates that more than one consultation is recorded.

Knowledge of symptom prevalence and intensity and health care needs of patients is important in clinical practice as it enables professional caregivers to focus on these issues and achieve optimal symptom control of patients. Symptom control is paramount in order to allow the patient to achieve the best quality of life possible in the remaining time left. We therefore aimed to explore the specific problems and needs of patients with advanced upper GI cancer.

**What are the main problems and needs for care of patients diagnosed with incurable esophageal or pancreatico-biliary cancer? (pre PACT study)**

A cross sectional study was conducted with 57 patients diagnosed with incurable esophageal or pancreatico-biliary cancer. For the measurement of multidimensional problems and needs we used the Problem and Needs in Palliative Care (PNPC) questionnaire[12] developed in the Netherlands, whereas the EORTC QLQ-OES18[13] and EORTC QLQ-PAN26[14] were used for identification of disease specific problems. We found that these patients experience multiple problems on all domains of the PNPC questionnaire, of which physical, emotional and loss of autonomy (LOA) problems were predominant. Patients expected professional care for physical, emotional, and in a lesser extent for LOA problems. Furthermore, they expected care for anticipated problems that could arise, including a confidential contact person, the assurance that hospitalization is possible when necessary, and availability of emergent care when needed. Inadequate care was received for fatigue, need for written information, fear of physical suffering, the assurance that hospitalization is possible when necessary, and frustration for loss of body functions.

Dysphagia is the predominant symptom in more than 70% of patients with esophageal cancer resulting in weight loss and malnutrition.[15] In the study mentioned above, this problem was well controlled for most of the patients by means of a stent. However, this does not mean that the problem was solved until death. Although, much progress has been made in the last ten years with respect to stent design and stent treatment, current stent treatments still suffer from major problems, including stent migration and stent occlusion. This requires re-interventions in 30% to 50% of patients, mainly due to nontumoral or tumoral tissue ingrowth and overgrowth, stent migration, and, to a lesser extent, food-bolus obstruction.[16-18] We therefore studied several newly developed stent designs with focus on safety and efficacy.

**What is the functional outcome/global quality of life and the amount of recurrent dysphagia and complications of:**

**a. the Alimaxx-Esophageal stent? (Alimaxx study)**

The majority of the currently available metal stents are partially covered to reduce migration risk. However, one of the remaining issues is tissue ingrowth through the uncovered stent parts. Therefore, a new stent design which was fully-covered supplemented with 20 anti-migration struts on the outside of the stent, was developed. We tested this design in 45 patients with dysphagia due to esophageal or gastric cardia cancer. We found that this new stent design provided good symptomatic relief of malignant dysphagia. Twenty-two of 45 patients (49%) with an Alimaxx-E stent developed 28 episodes of recurrent dysphagia, which was caused by tissue overgrowth (n = 7), stent migration (n = 16), food bolus obstruction (n = 4), or a stent that was not fully deployed (n = 1). The median World Health Organization performance status remained stable in the first month (score: symptoms but ambulatory) after stent placement, but slightly deteriorated 6 months after treatment. Placement of an Alimaxx-E stent was safe and was not associated with a higher incidence of complications compared to previous studies with other stents.[16-20] We conclude that although the Alimaxx-E stent is associated with a lower incidence of nontumoral and tumoral tissue overgrowth, the incidence of stent migration was unacceptably high, requiring further adaptations in stent design.

**b. the SX-ELLA stent Esophageal HV? (Ella study)**

Secondly, we tested another fully covered

esophageal stent, supplemented with an antimigration ring plus flare ends with a flip-flop mechanism to withstand migration. This stent design also provided good symptomatic relief of malignant dysphagia. Twelve of forty-four patients with an SX-ELLA stent developed 18 episodes of recurrent dysphagia, which were caused by food impaction (n = 8), stent migration (n = 6), tumor overgrowth (n = 2), stent fracture (n = 1), and an incomplete deployed distal part of the stent (n = 1). Major and minor complications were seen in 18 of 44 patients. Despite the single-wire, braided, low-trauma design, the frequency of hemorrhage and fistula formation was considerable with this stent. This was particularly true for hemorrhage, which was fatal in five patients. So for this stent design we concludes that although it reduced tumoral and nontumoral tissue overgrowth, migration rates occurred at a similar (high) frequency as that observed with other currently available fully covered stents.[17-19, 21, 22] More important, a relatively high complication rate, particularly hemorrhage, was observed. This was probably due to friction from the antimigration ring or the large size of the mid section of the stent. These observations also require further adaptation of the stent.

**c. the WallFlex enteral stent? (Wallflex study)**

Thirdly, we tested a new duodenal stent, made of nitinol in stead of stainless steel, in fifty-one patients with symptomatic malignant gastric outlet obstruction (GOO). This new stent has been constructed to provide an improved flexibility while maintaining lumen integrity, has looped ends to reduce risk of mucosal injury, and has a proximal flared end to minimize risk of stent migration. The GOO score improved, the Body Mass Index decreased, and the World Health Organization performance score improved when the score before stenting was compared with the mean score until death. Global quality of life did not improve. Stent dysfunction was proved in 7 patients (14%), migration in 1 (2%), and tumor overgrowth or ingrowth in 6 (12%). Complications included intermittent pain (n = 2), cholangitis (n = 3) and bleeding (n = 2). Eleven patients (22%) died within 30 days after stent placement: 1 died from untreatable cholangitis, all others from progressive malignant disease, but without clinical signs of biliary or enteral obstruction. We thus concludes that this stent is safe and provides a clinically significant relief of obstructive symptoms until death, without high re-intervention or complication rate.

The poor prognosis of upper GI cancer combined with the multidimensional problems and re-interventions for esophageal, biliary or enteral obstruction that arise in this short period suggested a need for close monitoring and support, instead of the conventional 1-2 monthly hospital follow-up at the outpatient clinic. Therefore, we evaluated a nurse-led follow-up for palliative GI cancer patients by home visits compared with the usual medical follow-up in outpatient clinic in a randomized study.

**Is nurse-led follow-up of incurable esophageal and pancreatico-biliary cancer patients by home visits an acceptable alternative to our usual medical follow-up at the outpatient clinic for these patients and their relatives? (PACT study)**

We designed a prospective, two-arm study of patients with inoperable primary or recurrent oesophageal-, pancreatic- or hepatobiliary cancer. Sixty-nine patients were randomized to either nurse-led follow-up at home (n = 36) or conventional medical follow-up at the out patient clinic (n = 30). Outcome parameters were patient satisfaction, quality of life, and health care consumption. Furthermore, cost-analyses were made to compare both follow-up strategies. On the basis of the main problems experienced by patients with advanced upper GI cancer (Chapter 3), we developed guidelines for the oncology nurse in follow-up. In total, 268 visits were performed in the nurse-led group (157 home visits, 95 telephone consults and 16 referral visits at the out patient clinic) and 80 in the conventional medical follow-up group (35 outpatient clinic visits and 45 telephone consults). Of these respectively 157 (59%) vs 47 (59%) were regular visits and 111 (41%) vs 33 (41%) were extra visits initiated by the patient himself, his relative or the nurse/physician. Both patients and their relatives in the nurse-led group were more satisfied with their follow-up than those receiving routine follow-up. Mean overall satisfaction of patients and their relatives at 1 and 4 months was higher in the nurse-led follow-up group compared with the conventional medical follow-up group. The health-related quality of life generally followed the same pattern in both groups on both time points. On average, patients with nurse-led follow-up had a slightly higher number of contacts with their general practitioner and equal number of hospital admissions within the first four months as patients with standard follow-up. Cost of a nurse-led follow-up visit per patient was 38% lower than those of a standard follow-up visit, although the total costs were higher in the first four months of follow-up due to a higher frequency of regular visits in the nurse-led follow-up group. We thus conclude that nurse-led follow-up at home is an acceptable alternative for these patients and their relatives. Patients who received nurse-led follow-up at home were more satisfied with their visits, whereas their quality of life and healthcare consumption within the first four months remains the same. Nurse-led follow-up was per visit less costly than the conventional medical follow-up, but this was not the case for the total costs which were made in the first 4 months. Further research is necessary to find a good balance between frequency and duration of the home visits (possibly combined with interventions without travel time and costs, such as telehealth) and patients' outcomes on quality of life.



## METHODOLOGICAL CONSIDERATIONS

The studies as presented in this thesis had several limitations. Firstly, the RECORD study was a pilot-study with a small sample size. The results should be seen as an indication for further research as only 17 patients were included and one-third of the patients in the control group (3/10) was not available for follow-up. Secondly, the pre PACT study was a cross sectional study. For a more complete overview of the problems and needs that these patients experienced, a future longitudinal study of cancer patients followed from the start of the palliative phase of a malignancy until death will provide further insight. Furthermore, there is probably an underestimation of certain problems and needs in these types of cancer patients due to the exclusion of patients who were actually too ill to participate in this study and the problems wherefore they were referred to the hospital were mostly well controlled at the time of the survey. Thirdly, in the PACT study 58 patients were lost to follow-up in the first six weeks of follow-up, mainly due to progressive disease with deterioration and inevitable death, with related poor quality of life scores. Furthermore, 53% of those who refused to participate may have had a poorer performance status as they found participation too burdensome. For all three studies mentioned above, the investigator was dependent on the physician if the patient actually was referred for the study. As known from the literature, not all physicians are willing to refer to trials, especially not as this involved patient inconvenience.[23] In our three studies the patients had to be aware or otherwise they were made aware of the palliative

stage of the disease. We assumed that most of the patients in the early stage of the palliative phase were not referred to our studies, as well as the patients who denied this fact. Also, in case of the PACT study, patients for whom the physician saw no reason for longer follow-up in the outpatient clinic were probably not referred.

Only two out of five interventions studies we performed were randomized studies (RECORD and PACT study). For the Alimaxx, Ella and Wallflex study it remains uncertain how the functional outcomes would have been without stent placement or with placement of another stent design because of the absence of a control group.

Our last limitation concerns the missing answers on the questionnaires that had been used in the RECORD, pre PACT and PACT study. These missing data may have biased the results.

## DISCUSSION OF MAIN RESULTS

Within palliative care, QoL is the main patient-oriented outcome of care, which contains five types of measures: biological function, symptoms, functional status, general health perceptions, and overall QoL.[24] Awareness of the stage of the disease could positive influence this outcome in comparison with unawareness.[2] If so, this could be due to several factors. Firstly, patients understand their prognosis and are prepared to make an appropriate decision of care directed towards symptom management, whereas providers can understand the patient's goals, and may be encouraged to offer more supportive care. Secondly, patients who understand their disease status may be better able to manage symptoms. Thirdly, an accurate understanding of prognosis allows patients to prepare themselves and their families for the future, strengthen relationships within the family, and allow for the resolution of various tasks before the patient's death. In our RECORD study we found in the CD-group a trend towards a poorer quality of life one month after the baseline consultation, but an improved openness to discuss cancer related issues. Most of the patients and relatives appreciated to receive the CD, but not everyone. It is important to identify those patients who may benefit from this intervention, and to identify the best moment(s) for this intervention.

Patients with advanced upper GI cancer included in our study experienced multiple, multidimensional problems, mainly physical, emotional and loss of autonomy problems. In the literature mostly physical and specific upper GI cancer symptoms were described untill now. Our results on physical symptoms were comparable with other prospective studies in patients with advanced upper GI cancer[25-27], but we found a low prevalence of disease-specific physical symptoms[25, 28] such as dysphagia and symptoms of obstructive jaundice, and gastric outlet obstruction in our population. Probably, these symptoms were reasonably controlled in our patients at the time of filling out the questionnaires. Further longitudinal research on experienced problems in this specific group of patients will be relevant for the planning and rationalization of palliative care services. Compared to the high frequency as a problem, the expected care for loss of autonomy problems is much lower. It is unknown whether this is due to the current standards of care and subsequent expectations or patients' considering that these problems are untreatable and an inevitable part of the disease at this stage of illness. More care was expected for fatigue, symptoms of fear and frustration, and potential future problems with health care providers. These problems are frequently overlooked by professionals.[29, 30] There are limited interventions for effective treatment of these problems[30, 31], so







additional research is necessary to provide clinically important improvement in the intensity of these problems.

Palliation of relieving dysphagia aims reducing the risk of aspiration, maintaining a patent orogastric pathway and nutritional status, and improving the quality of life. Although several management options have been developed in recent years to palliate dysphagia, the optimum management has not been established. The stents we have studied also had no additional benefit to the current available stents, 2 out of 3 had even more serious problems. To date the two main treatment options for dysphagia in esophageal cancer are placement of a self-expanding metal stents (SEMS), and brachytherapy. Stent insertion provides a swift palliation of dysphagia compared to brachytherapy. However, this difference gradually diminishes over time and, in the long run, brachytherapy appears to provide better dysphagia improvement and improved disease-specific QoL scores along with better general health-related QoL scores.[32] With regards to stent technology, further research is necessary to improve stent patency and to mitigate stent-related complications. Today, there are three future trends on the horizon: 1) drug-eluting esophageal stents in treatment of refractory benign and malignant strictures, which provide mechanical support as well as release of drugs to prevent restenosis by inhibiting tissue hyperplasia[33, 34], 2) a new hanging-type esophageal stent for preventing migration[35], and 3) biodegradable stents, which completely dissolve after approximately six weeks, for use in benign esophageal strictures.

The nurse-led follow-up at home seems to be a preferred alternative for the conventional medical follow-up at the outpatient clinic for most of the patients. The intervention had no negative effect on quality of life and health care costs, and was per visit less costly, although more expensive overall due to the higher number of patient contacts. To keep the costs at least equal to the conventional medical follow-up, the nurse should reduce the number of visits and probably shorten the time of each visit. It is unknown if this negatively affects patient satisfaction and quality of life, this should be studied further in a costs-utility study. Because the costs are largely determined by travel time and visit frequency, we should also study home-based follow-up by nurses with less travel time and costs. Examples are (1) the use of community nurses, although this would probably be more problematic in the Netherlands because of the shifting of costs from secondary to primary care, or (2) telehealth care, health care delivery using interactive, electronic and telecommunications technologies. The evidence on the latter suggests that, despite the challenges, there are numerous examples of good practice in relation to telehealth, palliative and end-of-life care.[36]

This leads to the following recommendations for practice and research:

- A large randomized study investigating the actual effects on quality of life issues of a recording for patients and their relatives with a follow-up time of more than 1 month is needed to identify subgroups of patients that may benefit from this intervention or not, on the short and long term.
- A qualitative component could add strength to a large study also addressing the reasons why patients rate the provision of the CD differently.
- Till that time we recommend that all upper GI cancer patients, regardless of the stage of the disease, are given the opportunity to receive a CD recording of their consultation.
- Patients should be offered all information given by professionals in writing. The already developed leaflets of the Dutch society for Cancer

relief (KWF) can be used for this, supplemented with institution specific or patient specific information in written.

- Proper diagnosis and treatment of symptoms and problems requires a structured and multidimensional approach, whereby in the follow-up of advanced upper GI cancer patients physical, emotional and loss of autonomy problems certainly can not be ignored.
- Symptoms of fatigue, fear, frustration, uncertainty, and loss of autonomy problems must be added to standardized measurements in these patients during follow-up. Further, potential future care possibilities have to be discussed in detail before care is necessary to reduce patients' uncertainty.
- If these symptoms are present, different interventions should be studied in large, multi-centre, randomized studies. The four knowledge centers of palliative care in the Netherlands can play an important role in this.
- Further longitudinal research is needed to explore the relationship between experienced symptoms (clusters) and expecting professional care for these on the one hand, and the stage of the disease on the other hand in advanced upper GI cancer patients.
- New developments and research is necessary to improve the palliation of dysphagia, in a short span of time with a reduced need for additional interventions. Physicians and developers must work together to find new, probably 'outside the box' solutions.
- Until better stents have been developed, we recommend the use of the present, conventional stents such as the Wallstent, Z-stent en Ultraflex.
- Further developments such as telehealth in home-based multidisciplinary, follow-up strategies for patients with upper GI cancer patients, in stead of the conventional medical follow-up at the outpatient clinic, have to be developed and studied in large randomized studies.
- There is a need to find the 'ideal' short questionnaire to measure quality of life in palliative patients by comparisons of current available questionnaires. The ideal questionnaire should easily be implemented into routine practice. In this way, the provision of palliative care can be monitored and we can continue to strive to obtain the best standards of patient care.

In conclusion, this thesis shows that a recording of the consultation in which patients receive a new diagnosis of non-curable cancer as well as subsequent nurse-led follow-up did not improve the quality of life (in terms of a comprehensive concept) of the patients. However, it did have positive effects on feasibility, utility and openness to discuss cancer related issues as well as on satisfaction of patients and relatives. Furthermore, nurse-led follow-up was associated with lower costs per visit and thus could be cost-efficient when the number or duration of visits can be limited in future practice. Furthermore, patients with incurable upper GI cancer experience multiple dimensional problems of which physical and emotional problems were most problematic and most patients express a need for professional care for these. This was however not the case for loss of autonomy problems that are also frequently experienced as problematic. Inadequate professional care was received for symptoms of fatigue, fear, frustration and uncertainty. The Ella and Alimaxx stent are no alternative to the current, conventional stents for the palliation of dysphagia, where the Wallflex enteral stent was for enteral obstruction.







## REFERENCES


1. Ashby M, Stoffell B. Therapeutic ratio and defined phases: proposal of ethical framework for palliative care. Bmj 1991;302:1322-1324.

2. Lee MK, Baek SK, Kim SY, et al. Awareness of incurable cancer status and health-related quality of life among advanced cancer patients: A prospective cohort study. Palliat Med 2011.

3. Fallowfield LJ, Jenkins VA, Beveridge HA. Truth may hurt but deceit hurts more: communication in palliative care. Palliat Med 2002;16:297-303.

4. Scott JT, Harmsen M, Prictor MJ, et al. Recordings or summaries of consultations for people with cancer. Cochrane Database Syst Rev 2003:CD001539.

5. Ong LM, Visser MR, Lammes FB, et al. Effect of providing cancer patients with the audiotaped initial consultation on satisfaction, recall, and quality of life: a randomized, double-blind study. Journal of Clinical Oncology 2000;18:3052-3060.

6. McHugh P, Lewis S, Ford S, et al. The efficacy of audiotapes in promoting psychological well-being in cancer patients: a randomised, controlled trial. British Journal of Cancer 1995;71:388-392.

7. Knox R, Butow PN, Devine R, et al. Audiotapes of oncology consultations: only for the first consultation? Annals of Oncology 2002;13:622-627.

8. Wilkes L, White K, O'Riordan L. Empowerment through information: supporting rural families of oncology patients in palliative care. Aust J Rural Health 2000;8:41-46.

9. Davison BJ, Degner LF. Empowerment of men newly diagnosed with prostate cancer. Cancer Nurs 1997;20:187-196.

10. Gaston CM, Mitchell G. Information giving and decision-making in patients with advanced cancer: a systematic review. Soc Sci Med 2005;61:2252-2264.

11. Deschepper R, Bernheim JL, Vander Stichele R, et al. Truth-telling at the end of life: a pilot study on the perspective of patients and professional caregivers. Patient Educ Couns 2008;71:52-56.

12. Osse BH, Vernooij MJ, Schade E, et al. Towards a new clinical tool for needs assessment in the palliative care of cancer patients: the PNPC instrument. J Pain Symptom Manage 2004;28:329-341.

13. Blazeby JM, Alderson D, Winstone K, et al. Development of an EORTC questionnaire module to be used in quality of life assessment for patients with oesophageal cancer. The EORTC Quality of Life Study Group. Eur J Cancer 1996;32A:1912-1917.

14. Fitzsimmons D, Johnson CD, George S, et al. Development of a disease specific quality of life (QoL) questionnaire module to supplement the EORTC core cancer QoL questionnaire, the QLQ-C30 in patients with pancreatic cancer. EORTC Study Group on Quality of Life. Eur J Cancer 1999;35:939-941.

15. Brierley JD, Oza AM. Radiation and chemotherapy in the management of malignant esophageal strictures. Gastrointest Endosc Clin N Am 1998;8:451-463.

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16. Siersema PD. New developments in palliative therapy. Best Pract Res Clin Gastroenterol 2006;20:959-978.

17. Conio M, Repici A, Battaglia G, et al. A randomized prospective comparison of self-expandable plastic stents and partially covered self-expandable metal stents in the palliation of malignant esophageal dysphagia. Am J Gastroenterol 2007;102:2667-2677.

18. Verschuur EM, Repici A, Kuipers EJ, et al. New design esophageal stents for the palliation of Dysphagia from esophageal or gastric cardia cancer: a randomized trial. Am J Gastroenterol 2008;103:304-312.

19. Conigliaro R, Battaglia G, Repici A, et al. Polyflex stents for malignant oesophageal and oesophagogastric stricture: a prospective, multicentric study. Eur J Gastroenterol Hepatol 2007;19:195-203.

20. Verschuur EM, Homs MY, Steyerberg EW, et al. A new esophageal stent design (Niti-S stent) for the prevention of migration: a prospective study in 42 patients. Gastrointest Endosc 2006;63:134-140.

21. Homs MY, Steyerberg EW, Kuipers EJ, et al. Causes and treatment of recurrent dysphagia after self-expanding metal stent placement for palliation of esophageal carcinoma. Endoscopy 2004;36:880-886.

22. Verschuur EM, Steyerberg EW, Kuipers EJ, et al. Effect of stent size on complications and recurrent dysphagia in patients with esophageal or gastric cardia cancer. Gastrointest Endosc 2007;65:592-601.

23. White C, Gilshenan K, Hardy J. A survey of the views of palliative care healthcare professionals towards referring cancer patients to participate in randomized controlled trials in palliative care. Support Care Cancer 2008;16:1397-1405.

24. Ferrans CE, Zerwic JJ, Wilbur JE, et al. Conceptual model of health-related quality of life. J Nurs Scholarsh 2005;37:336-342.

25. Andreassen S, Randers I, Naslund E, et al. Patients' experiences of living with oesophageal cancer. J Clin Nurs 2006;15:685-695.

26. Labori KJ, Hjermstad MJ, Wester T, et al. Symptom profiles and palliative care in advanced pancreatic cancer: a prospective study. Support Care Cancer 2006;14:1126-1133.

27. Muller-Nordhorn J, Roll S, Bohmig M, et al. Health-related quality of life in patients with pancreatic cancer. Digestion 2006;74:118-125.

28. Krech RL, Walsh D. Symptoms of pancreatic cancer. J Pain Symptom Manage 1991;6:360-367.

29. Hawthorn M. Fatigue in patients with advanced cancer. Int J Palliat Nurs 2010;16:536-541.

30. Roth AJ, Massie MJ. Anxiety and its management in advanced cancer. Curr Opin Support Palliat Care 2007;1:50-56.

31. Olson K, Turner AR, Courneya KS, et al. Possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion in advanced cancer. Support Care Cancer 2008;16:241-249.







32. Homs MY, Steyerberg EW, Eijkenboom WM, et al. Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from oesophageal cancer: multicentre randomised trial. Lancet 2004;364:1497-1504.

33. Jeon SR, Eun SH, Shim CS, et al. Effect of drug-eluting metal stents in benign esophageal stricture: an in vivo animal study. Endoscopy 2009;41:449-456.

34. Lei L, Liu X, Guo S, et al. 5-Fluorouracil-loaded multilayered films for drug controlled releasing stent application: Drug release, microstructure, and ex vivo permeation behaviors. J Control Release 2010;146:45-53.

35. Endo M, Kaminou T, Ohuchi Y, et al. Development of a New Hanging-Type Esophageal Stent for Preventing Migration: A Preliminary Study in an Animal Model of Esophagotracheal Fistula. Cardiovasc Intervent Radiol 2011.

36. Kidd L, Cayless S, Johnston B, et al. Telehealth in palliative care in the UK: a review of the evidence. J Telemed Telecare 2010;16:394-402.



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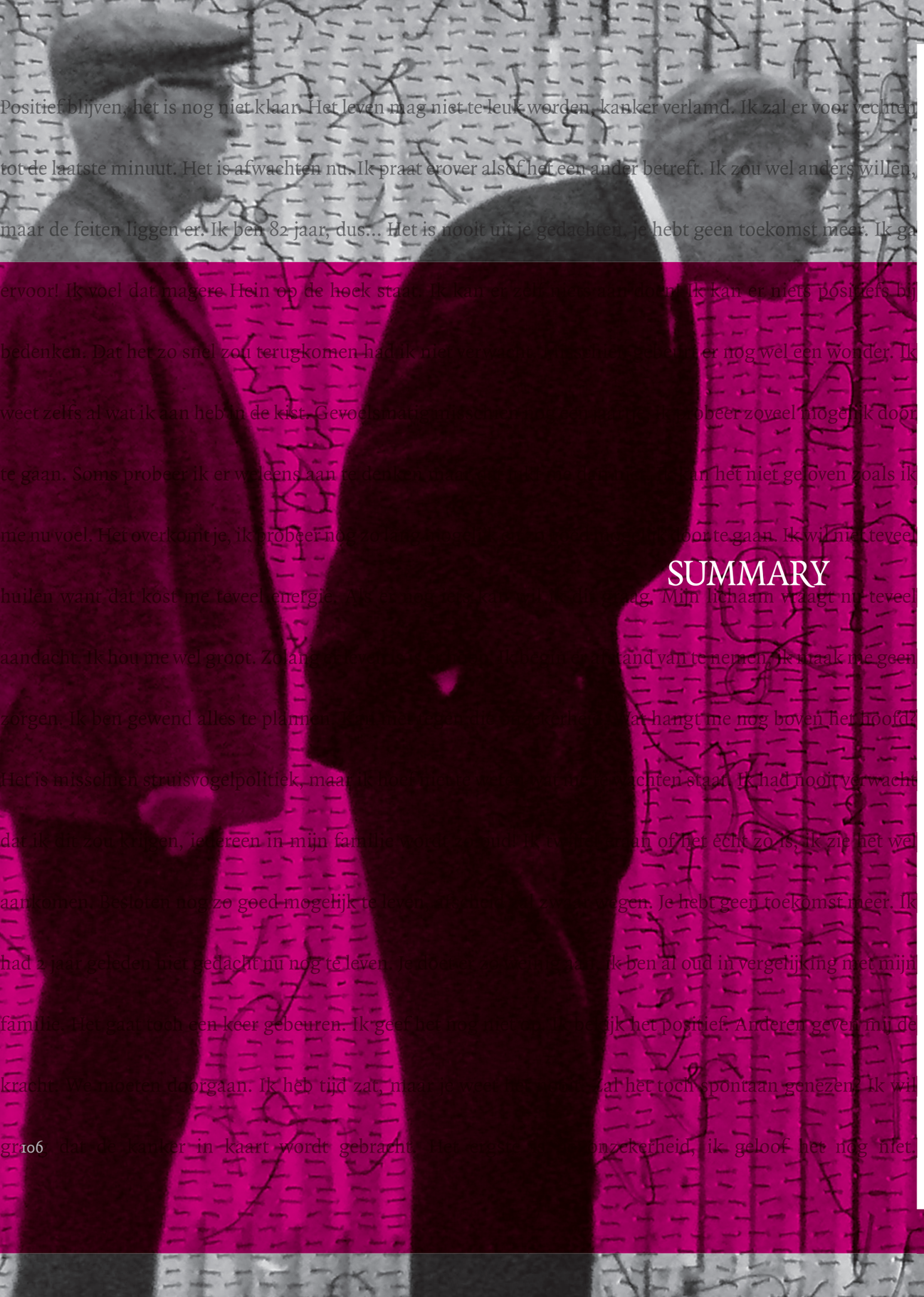


# SUMMARY



This thesis explores palliative care provided to patients with advanced upper gastrointestinal (GI) cancer. The 5-year survival rates for these cancer sites range between 4 and 17%, which implies that many of these patients require palliative care. Considering the fact that there is no uniform management policy aiming at improvement of quality of life (QoL) of these patients and their families, we decided to study different interventions with effect on this primary aim.

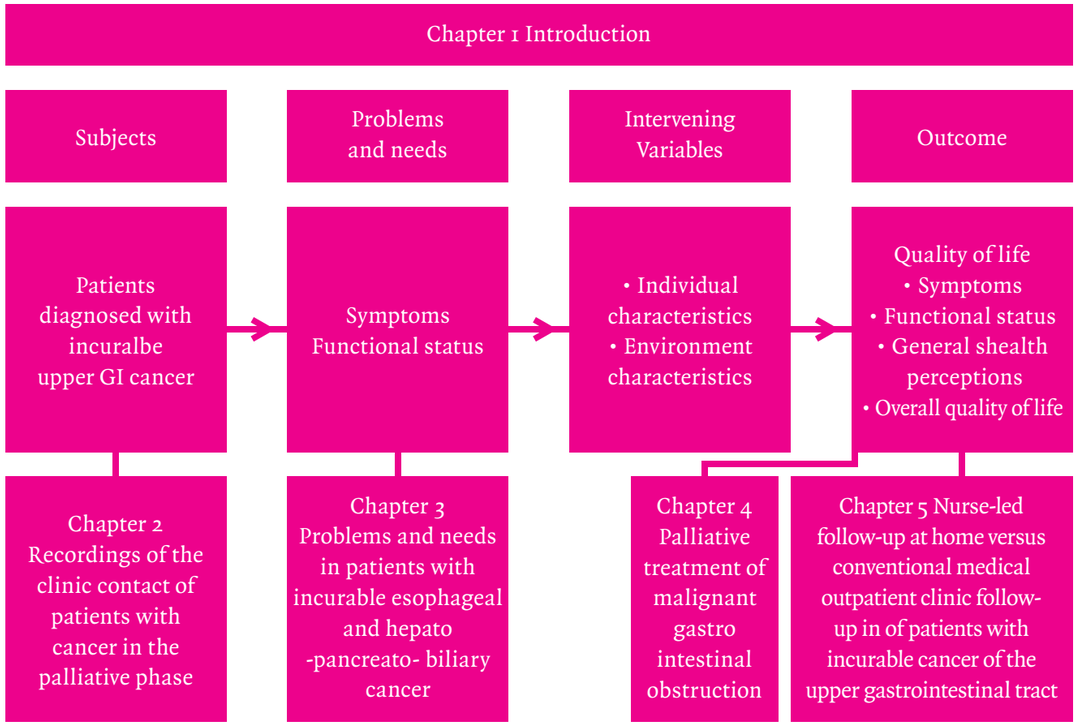
The outline of this thesis is shown in Figure 1. The introduction, **chapter 1**, provides background information on the main subjects of the thesis, i.e., patients with advanced upper GI cancer, the concept of quality of life, and our questions that stand at the basic of it.

The transition from care with curative intent to palliative care marks a drastic change in the life-expectancy of a patient, and thus drastically and negatively affects patient's view of the future. The patient has to adjust to this new situation. In **chapter 2** we present the results of a pilot-study on feasibility and utility of the provision of CD recordings on consultations involving the transition to palliative care for 17 patients with irresectable or recurrent esophageal or head or neck cancer. We found no major technical and procedural problems related to the provision of these recordings and the recordings were well-received and listening by most of our patients and their family. After 1 month we found a trend towards a poorer quality of life but an improved openness to discuss cancer-related issues, in the CD group.

Knowledge of symptom prevalence and intensity, and health care needs of patients with non-curable GI cancer is important in clinical practice as it enables professional caregivers to focus on these issues and achieve optimal symptom control of patients. **Chapter 3** presents the specific problems and needs of 57 patients with advanced upper GI cancer, found in a cross sectional study. They experienced multiple, multidimensional problems, in particular physical and emotional problems. Most patients expressed a need for professional care for these, this was however not the case for LOA problems that are also frequently experienced as problematic. Inadequate care was received for fatigue, need for written information, fear of physical suffering, the assurance that hospitalization is possible when necessary, and frustration because of the inability to do as much as before.

For patients with esophageal cancer as well as for patients with cancer of the periampullary area (head of the pancreas, distal bile duct, papilla of Vater), and with distal stomach or duodenal cancer, dysphagia is known as a common symptom, causing significant distress. Self-expandable metal stents are commonly used for the palliation of malignant obstruction because of inoperable disease. In **chapter 4** the findings of 3 studies on new developed stents are presented, with focus on both safety and efficacy. We found that the Ella and Alimaxx stent were no alternative to the current, conventional stents for the palliation of dysphagia, while the Wallflex enteral stent was a good alternative for enteral obstruction. The Ella stent had an unacceptably high rate of migration (16 times in 45 patients) and the Alimaxx stent a high complication rate (18 times in 44 patients), particularly hemorrhage.

The poor prognosis of upper GI cancer combined with the multidimensional problems and re-interventions for esophageal, biliary or enteral obstruction that arise in this short period suggested a need for close monitoring and support, instead of the conventional 1-2 monthly hospital follow-up at




the outpatient clinic. In **chapter 5** is a new strategy for follow-up for advanced upper GI cancer patients, i.e., nurse-led follow-up by home visits (n = 36) compared with the usual medical follow up in outpatient clinic (n = 30), in a randomized study. On the basis of the main problems experienced by these patients (chapter 3), we developed guidelines for nurse-led follow-up. Patients who received nurse-led follow-up at home were more satisfied with their visits, whereas their quality of life and healthcare consumption within the first four months remained the same. Nurse-led follow-up was per visit less costly than the conventional medical follow-up. However, the total costs for the four months follow-up in this study were higher due to a higher frequency of visits in this group.

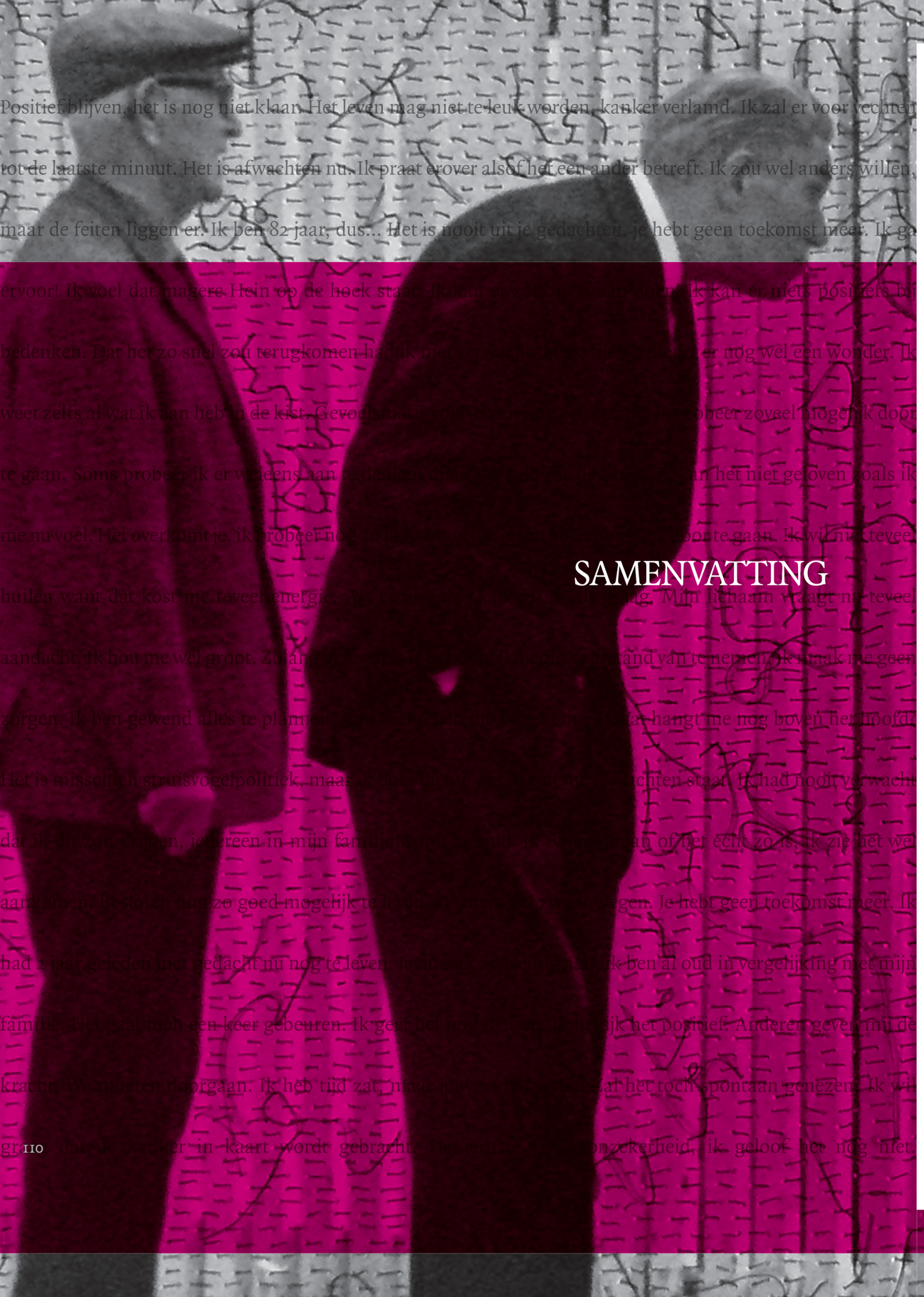
In **chapter 6**, the main results of the thesis are summarized, followed by a reflection on the methodology, the general conclusions concerning the main objectives of the thesis and implications for further research and practice. We recommended the use of CD recordings, Wallflex enteral stent and another strategy of follow-up instead of the conventional in a new policy for advanced upper GI cancer patients of the hospital. The first recommendation had to be studied more in-depth and in a study with a larger sample size. The last recommendation had to be studied further also, preferable in a costs utility study and with the comparison of new strategy such as telehealth.







M.J. Uitdehaag | Living in the face of death



# SAMENVATTING





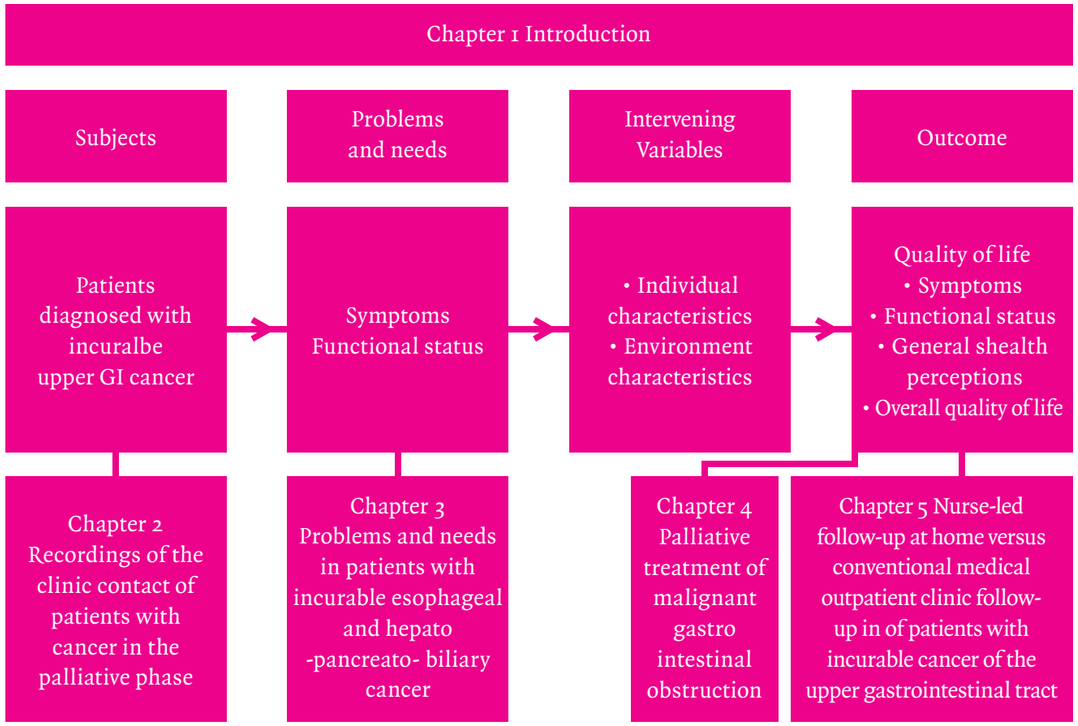
Dit proefschrift bevat diverse studies betreffende palliatieve zorg aan patiënten met kanker in een vergevorderd stadium, in het bovenste deel van het spijswegkanaal. De 5-jaarsoverleving voor deze vormen van kanker is laag en varieert tussen de 4 en 17%. Dit houdt in dat veel van deze patiënten behoefte hebben aan palliatieve zorg. Gezien het feit dat er binnen het Erasmus MC geen uniform beleid was op dit gebied, hebben we besloten om verschillende interventies te bestuderen ter verbetering van de kwaliteit van leven van deze patiënten en hun familie, om deze vervolgens op te kunnen nemen in een nieuw te vormen beleid.

De inhoud van dit proefschrift is weergegeven in figuur 1. De introductie, **hoofdstuk 1**, geeft achtergrondinformatie over de belangrijkste hoofdonderwerpen van het proefschrift: 1) patiënten met kanker in een vergevorderd stadium, in het bovenste deel van het spijswegkanaal, 2) het concept 'kwaliteit van het leven', en 3) de vragen die aan de basis stonden van dit proefschrift.

De overgang van curatieve zorg naar palliatieve zorg betekent een drastische verandering in de levensverwachting en visie op de toekomst van een patiënt. De patiënt moet zich aanpassen aan deze nieuwe situatie. In **hoofdstuk 2** presenteren we de resultaten van een pilot-studie naar de haalbaarheid en het nut van het verstrekken van Cd-opname van het gesprek, waarin deze overgang naar palliatieve zorg wordt verteld door de arts. 17 patiënten met een niet te verwijderen of terugkerende tumor in de slokdarm of het hoofd-hals gebied namen deel. We vonden geen grote technische en procedurele problemen en de opnames werden goed ontvangen en beluisterd door het merendeel van de patiënten en hun naasten. Na 1 maand vonden we een slechtere kwaliteit van leven, maar meer openheid om kankergerelateerde kwesties te bespreken met naasten, bij de mensen die de CD hadden ontvangen.

Het is belangrijk om enerzijds kennis te hebben van de prevalentie en intensiteit van symptomen van patiënten met ongeneeslijke kanker, en anderzijds van de behoeften aan professionele zorg voor deze symptomen. In de klinische praktijk stelt het professionele zorgverleners in staat om zich specifiek op deze symptomen te concentreren en optimale controle van deze symptomen te bereiken. **hoofdstuk 3** beschrijft een dwarsdoorsnede onderzoek naar de specifieke problemen en behoeften aan zorg van 57 patiënten met ongeneeslijke kanker van het bovenste spijswegkanaal. Deze patiënten ervoeren meerdere, multidimensionele problemen, voornamelijk fysieke en emotionele problemen. De meeste patiënten hadden ook behoefte aan professionele zorg voor deze problemen. Dit was echter niet het geval voor problemen ten aanzien van het verlies van autonomie, die ook vaak worden als problematisch werden ervaren. Voor de problemen: 'vermoeidheid', 'behoefte om informatie schriftelijk te verkrijgen', 'angst voor lichamelijk lijden', 'zekerheid dat er een ziekenhuisbed beschikbaar is als dat (acuut) nodig is', en 'frustraties omdat ik minder kan dan voorheen', ontvingen de patiënten onvoldoende zorg op het moment van het onderzoek.

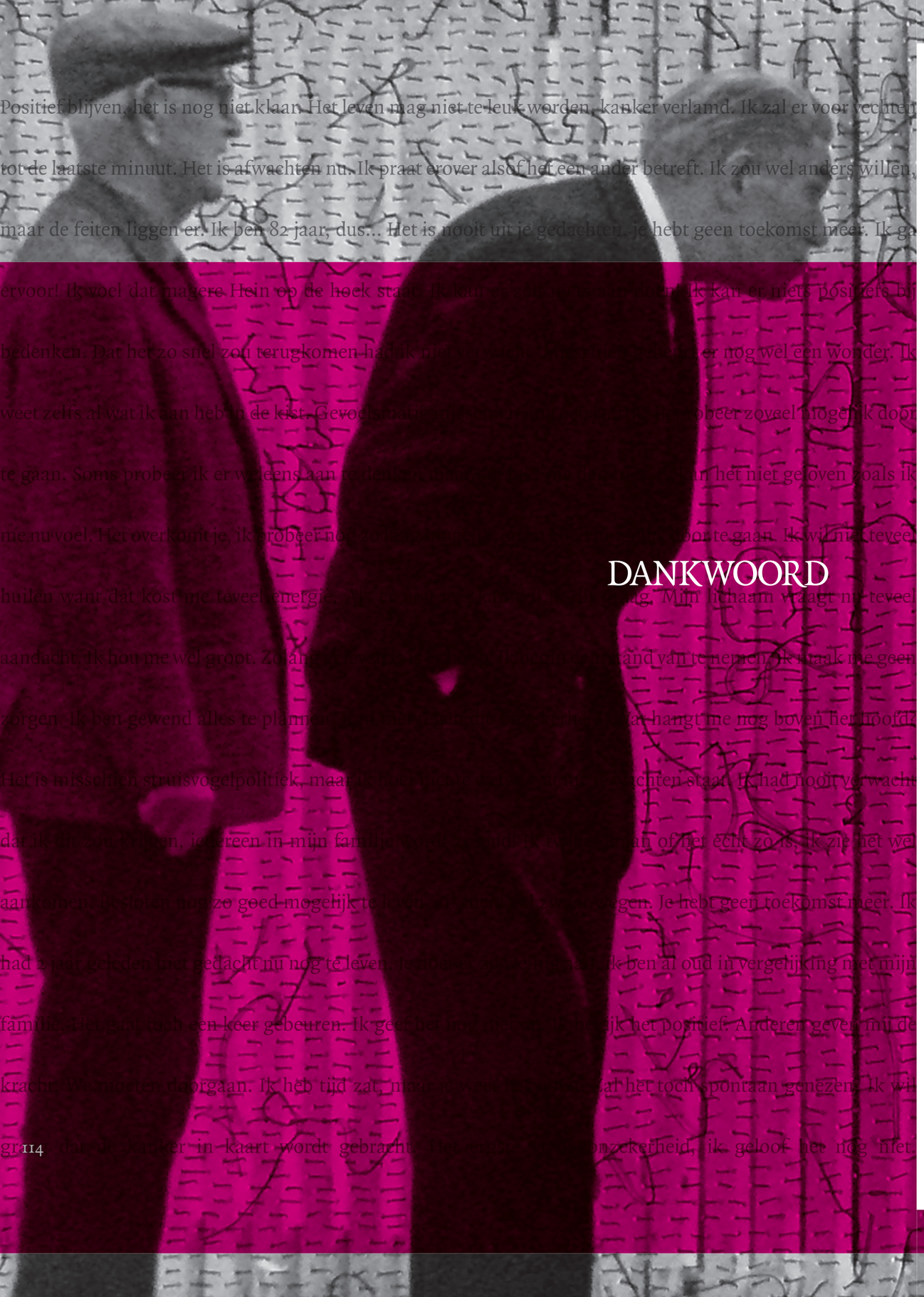
Dysfagie is een vaak voorkomend symptoom bij patiënten met ongeneeslijke kanker van het bovenste spijswegkanaal en kan veel leed veroorzaken. Voor de palliatie van een kwaadaardige obstructie als gevolg van een inoperabele ziekte worden vaak metalen stents gebruikt die uit zichzelf uitzetten. In **hoofdstuk 4** worden de bevindingen van drie studies naar nieuw ontwikkelde stents gepresenteerd, met de focus op zowel de veiligheid als de werkzaamheid van deze stents. We vonden dat de Ella en Alimaxx stent geen goed alternatief zijn voor de huidige, conventionele stents voor de behandeling van dysfagie bij slokdarmkanker,




terwijl de Wallflex enterale stent een prima alternatief was in het geval van een enterale obstructie. Bij de Ella stent was het probleem dat deze vaak migreerde (16 keer in 45 patiënten) en bij de Alimaxx stent het groot aantal complicaties (18 keer in 44 patiënten), in het bijzonder bloedingen.

De slechte prognose van patiënten met kanker van het bovenste spijswegkanaal, in combinatie met de multidimensionele problemen en het aantal re-interventies voor slokdarm-, gal- of enterale obstructie deed ons besluiten de follow-up voor deze patiëntengroep aan te passen. In plaats van de gebruikelijke 1-2 maandelijkse follow-up op de polikliniek ontwikkelde we follow-up strategie aan huis met een frequentere monitoring en ondersteuning. In **hoofdstuk 5** is deze nieuwe strategie, namelijk een 2-4 wekelijkse follow-up door een verpleegkundige aan huis (n = 36) versus de gebruikelijke medische follow-up in de polikliniek (n = 30), onderzocht in een gerandomiseerde studie. Op basis van de belangrijkste problemen van de patiënten met kanker van het bovenste spijswegkanaal (hoofdstuk 3), zijn richtlijnen voor de verpleegkundige follow-up opgesteld. Patiënten die de verpleegkundige follow-up aan huis ontvingen waren meer tevreden over hun controlebezoek, terwijl hun kwaliteit van leven en het gebruik van de huisarts en het aantal opnames in het ziekenhuis gelijk gebleven, in de eerste vier maanden. Verpleegkundige follow-up was per bezoek minder duur dan de conventionele follow-up door de arts. Echter, de totale kosten voor de vier maanden follow-up in dit onderzoek waren hoger voor de patiënten die aan huis controle ontvingen als gevolg van een hogere frequentie van de bezoeken in deze groep.

In **hoofdstuk 6** worden de belangrijkste resultaten van dit proefschrift samengevat, gevolgd door een reflectie op de methodologie, een beschrijving van de algemene conclusies met betrekking tot de belangrijkste doelstellingen van dit proefschrift en de implicaties voor verder onderzoek en praktijk. Drie van de onderzochte interventies raden wij aan om verder te onderzoeken of op te nemen in het nieuw te vormen beleid ten aanzien van patiënten met kanker van het bovenste spijswegkanaal in de palliatieve fase: 1) patiënten de mogelijkheid geven om een geluidsopname te ontvangen van het slecht-nieuwsgesprek, waarin zij vernemen dat zij ongeneeslijk ziek zijn, 2) het gebruik van Wallflex enterale stent bij een enterale obstructie, en 3) het ontwikkelen van een andere strategie van follow-up in plaats van de conventionele medische follow-up in de polikliniek. De eerste aanbeveling moet meer in detail onderzocht worden in een studie met een grotere steekproef. De laatste aanbeveling behoeft ook verdere studie; minder kostbare strategieën moeten worden gezocht, zoals telezorg, en bij voorkeur worden onderzocht in een studie waarbij de kosten en baten (voordelen ten aanzien van kwaliteit van leven) tegen elkaar worden afgewogen.



# DANKWOORD



## FINISH!!

Mijn promotie voelt voor mij als de langste duurloop die ik ooit heb gelopen. Zoals velen weten hou ik erg van duurlopen, het kan voor mij vaak niet lang genoeg zijn. De laatste jaren loop ik vaak duurlopen in de vorm van een non-stop estafetteloop van zo'n 50 uur voor het goede doel. Ik hou van de cadans en het ritme, wat mij het gevoel geeft dat ik dit voor altijd kan volhouden. Het gaat niet om de wedstrijd maar om de uitdaging die ik met mezelf aanga. Ondanks de trainingen vooraf is het altijd weer spannend of ik in staat ben om het vol te houden en mezelf eventueel te overtreffen. Eén ding is wel altijd zeker: ik ben bij de finish een ander mens dan aan de start. En dat is precies wat ik nu ook voel. Wat is er veel gebeurd de afgelopen jaren, wat heb ik veel mogen leren van de vele mensen die ik onderweg heb ontmoet, wat is 'de route' vaak anders gelopen dan verwacht, wat was het soms moeilijk om 'door te blijven lopen' en bovenal wat ben ik ontzettend blij dat ik de finish heb bereikt!

Maar dit was me nooit gelukt zonder al die mensen die (een stukje) met mij hebben meegelopen, de organisatie hebben verzorgd en/of langs de zijlijn hebben gestaan om mij aan te moedigen. Het spannende nu vind ik dat ik niemand vergeet te bedanken aangezien het een 'duurloop' betreft en vooral de mensen aan 'de start en de eerste kilometers' al enige tijd uit het zicht zijn.

Onvergetelijk zijn voor mij natuurlijk de patiënten en naasten die hun medewerking hebben gegeven aan één van de studies in dit proefschrift. Gedurende mijn promotie waren de patiënten en naasten voor mij het goede doel waar ik het voor deed! Ik hoop dat de resultaten positief hebben kunnen bijdragen aan de kwaliteit van leven van deze patiënten en van al die patiënten die nog volgen in de toekomst. Alle patiënten gaven hun medewerking op een keerpunt in hun leven, wat vaak samen ging met onzekerheid, angst en fysieke achteruitgang. Toch waren zij allen bereid om zich in deze fase nog in te zetten voor één van de studies door het invullen van vragenlijsten of het beantwoorden van vragen over de telefoon. Ik vind het zeer bijzonder om te zien hoe mensen omgaan met dergelijke 'life events', ieder op zijn/haar eigen manier. Door de vaak bijzondere contacten werd ik deelgenoot van hun verdrietige, mooie en hoopvolle momenten in deze fase. Velen kunnen de resultaten zoals beschreven in dit proefschrift niet meer lezen, maar dit maakt ze voor mij nog waardevoller.

Een duurloper kan niet zonder een navigator op de fiets, die continue de weg wijst naar de finish. Bijzondere dank ben ik verschuldigd aan de 'navigators' van deze duurloop: mijn promotoren Prof. Dr. Siersema en Prof. Dr. Kuipers. Zij kenden de route en de spelregels van de duurloop en wezen mij het juiste pad. Beste Peter, hartelijk dank voor je begeleiding en de fijne samenwerking, ondanks alle veranderde situaties tijdens mijn promotie heb ik altijd gevoeld dat ik bij je terecht kon en dat je er voor me zou zijn tot aan de eindstreep. Tevens heb je me de 'spelregels' van de voor mij totaal nieuwe wereld bijgebracht. Beste Ernst, na het vertrek van Peter kwam jij meer in beeld voor mij. Hartelijk dank voor je vertrouwen in mij. "Je moet dit afmaken, anders krijg je er spijt van" is wat je vaak heb gezegd. Ik heb me daar aan opgetrokken en ben dan ook erg blij dat de finish nu bereikt is.

In de regel ontmoet je tijdens een duurloop vanzelf een loopmaatje met hetzelfde ritme en dezelfde cadans. Je loopt als vanzelf met elkaar op, en versterkt elkaar. Hannie van Ginkel, een 'loopmaatje' was jij voor mij. Je bezocht alle patiënten thuis in het kader van de PACT studie. Ik bewonder je inlevingsvermogen en authenticiteit, twee eigenschappen waarvan ik zeker weet dat veel patiënten zich daaraan 'gewarmd' hebben in hun laatste levensfase. Dank je wel, dat je meegelopen hebt.

Onderweg kwam ik nog meer ‘loopmaatjes’ tegen die even met me opliepen, Prof. Pruijn en Prof. Dr. de Boer, en Dr. van der Velden. Beste Jean, Maarten en Lilly-Ann, ik vond het heerlijk jullie te ontmoeten, zorgverleners met oog en hart voor het psychosociale van de mens. Ik kijk met een fijn gevoel terug op onze samenwerking en de inspanningen rondom de RECORD studie.

In een duurloop in teamverband hoef je (gelukkig) niet alle 50 uur zelf te rennen, je teamleden nemen het af en toe van je over. Als ik aan rust toe was namen mijn collegae Dr. Verschuur en Dr. Jeurnink ook als vanzelfsprekend deze rol op zich. Els en Suzanne, jullie waren altijd weer bereid alle activiteiten over te nemen, zodat de studies gewoon gecontinueerd konden worden tijdens mijn vakantie. Ik voelde me erg verantwoordelijk voor een goede voortgang, maar aan jullie liet ik het altijd vol vertrouwen over. Ook dank aan mijn collega Paul van Putten, die bereid was de PACT studie over te nemen na mijn vertrek uit het Erasmus MC.

Na een rustpauze zorgen de chauffeurs dat de lopers weer zo snel mogelijk op de wisselplek komen om het stokje over te nemen van hun teamgenoten. Daar kon het rennen weer beginnen. Dank aan ‘mijn chauffeurs’ in deze duurloop; de secretaresses, verpleegkundigen en specialisten uit het Erasmus MC. Monica Seijbel, Carla Capel, Marijke Smits Schouten, Helma van Dijk en Chulja Pek, Dr. Gaast, Dr. van Zuylen, Dr. Eskens, Dr. Spaander, Prof. Dr. van der Rijt, Prof. Dr. Tilanus en Prof. Dr. Yzermans, jullie brachten mij altijd weer op juiste plaats waar ik verder kon, namelijk bij de patiënten en naasten die wilde meewerken aan de studies.

Gedurende een duurloop wordt er achter de schermen veel werk verricht door allerlei mensen die niet altijd zichtbaar zijn, maar er wel voor zorgen dat het geheel vlekkeloos blijft verlopen. In dit verband wil ik heel graag Wendy, Carla, Marion en Bernadette, en de medewerkers van het trialbureau hartelijk danken voor de vele ‘kleine’ regeldingen onderweg.

Tijdens een duurloop is het belangrijk om voldoende te blijven drinken. Op vaste plaatsen staan waterposten om bij te tanken. Jitske Bruinix, jij was voor mij de ‘waterpost’ waar het water altijd klaar stond. Tijdens mijn ‘schrijfperiode’ kon ik altijd op je rekenen, elk artikel zat weer flitsend snel in mijn mailbox, zodat ik altijd weer door kon. Hartelijk dank hiervoor.

En dan natuurlijk al de mensen die aan de zijlijn hebben gestaan tijdens de ‘duurloop’.

Mijn kamergenoten van het 1e uur: Wim Leemans en Martijn ter Borg, altijd behulpzaam, in voor gezelligheid en een grote steun voor mij bij voornamelijk computer gerelateerde problemen. Wim, dat je zelfs terug kwam om me te helpen met de CD opnames voor de RECORD studie, heb ik bijzonder gewaardeerd. Na hun vertrek stonden Jurriën Reijnders en Arjun Koch ‘langs de zijlijn’. Maar ook alle andere collegae onderzoekers en assistenten die daar hebben gestaan, wil ik bedanken. Met plezier kijk ik terug op de borrels uit de beginperiode en natuurlijk de ski vakanties.

Toen ik al een heel eindje op weg was stonden mijn collegae van het kenniscentrum palliatieve zorg en het Integraal Kankercentrum Nederland langs de zijlijn. Het rennen viel me op dat moment al zwaarder. Allen dank voor jullie interesse naar mijn vorderingen in deze ‘duurloop’. Zonder de anderen te kort te willen doen wil ik Ellen de Nijs in het bijzonder bedanken, ik vond het zo ontzettend lief van je dat je me aanbood ‘een stukje mee op te lopen’, door te helpen met het invoeren van data. Dank je wel.





Masseurs zijn onontbeerlijk tijdens een non-stop duurloop. Zij voeren de vermoeidheidsstoffen zoals melkzuur af, waardoor spierpijn zoveel mogelijk wordt voorkomen en je goed kunt blijven functioneren. Tijdens mijn promotie zijn dit de mensen geweest die me altijd een warm hart toedragen en met veel enthousiasme ook hebben uitgekeken naar de finish! Allereerst mijn loopmaatjes uit het echte leven; Peter, Kris, Herman, Wil, Saskia O, Saskia F, Tineke en Michiel. Met jullie heb ik al de nodige meters gerend waarbij ‘deze duurloop’ ook vaak het onderwerp van gesprek was. Dit voelde voor mij ook altijd alsof jullie een eindje met me mee liepen, en zoals jullie ook allemaal weten gaat het dan altijd weer beter. Daarnaast ook dank aan Miranda, Thirza, Marcel en Will. Dank jullie wel, voor jullie luisterend oor en aanmoedigingen. Will, het spijt me zo dat je de finish niet fysiek kunt meemaken, maar voor mij ben je er op een andere wijze zeker bij op 14 juni!

Een goede catering is onontbeerlijk om de finish te halen. ‘Krachtvoer’ ontving ik van mijn buurvrouwen Madeleine, Francis en Vroukje. Eindelijk is het dan zo ver, hé! Dank voor jullie vele aanmoedigingen tijdens onze etentjes.

Het lopen van een duurloop vergt een goede voorbereiding en training vooraf. Trainers geven je hierbij adviezen en tips, en leggen daarmee de basis voor de duurloop. Gedurende de loop zelf zijn zij vaak op afstand aanwezig. Dit gold ook voor mijn familie die het geheel met interesse vanaf een afstandje hebben gevolgd, en mijn geestelijke moeder Laura, die in de geest altijd bij me was. Dank voor de basis die jullie me hebben gegeven en me tot dit mooie eindresultaat heeft gebracht.

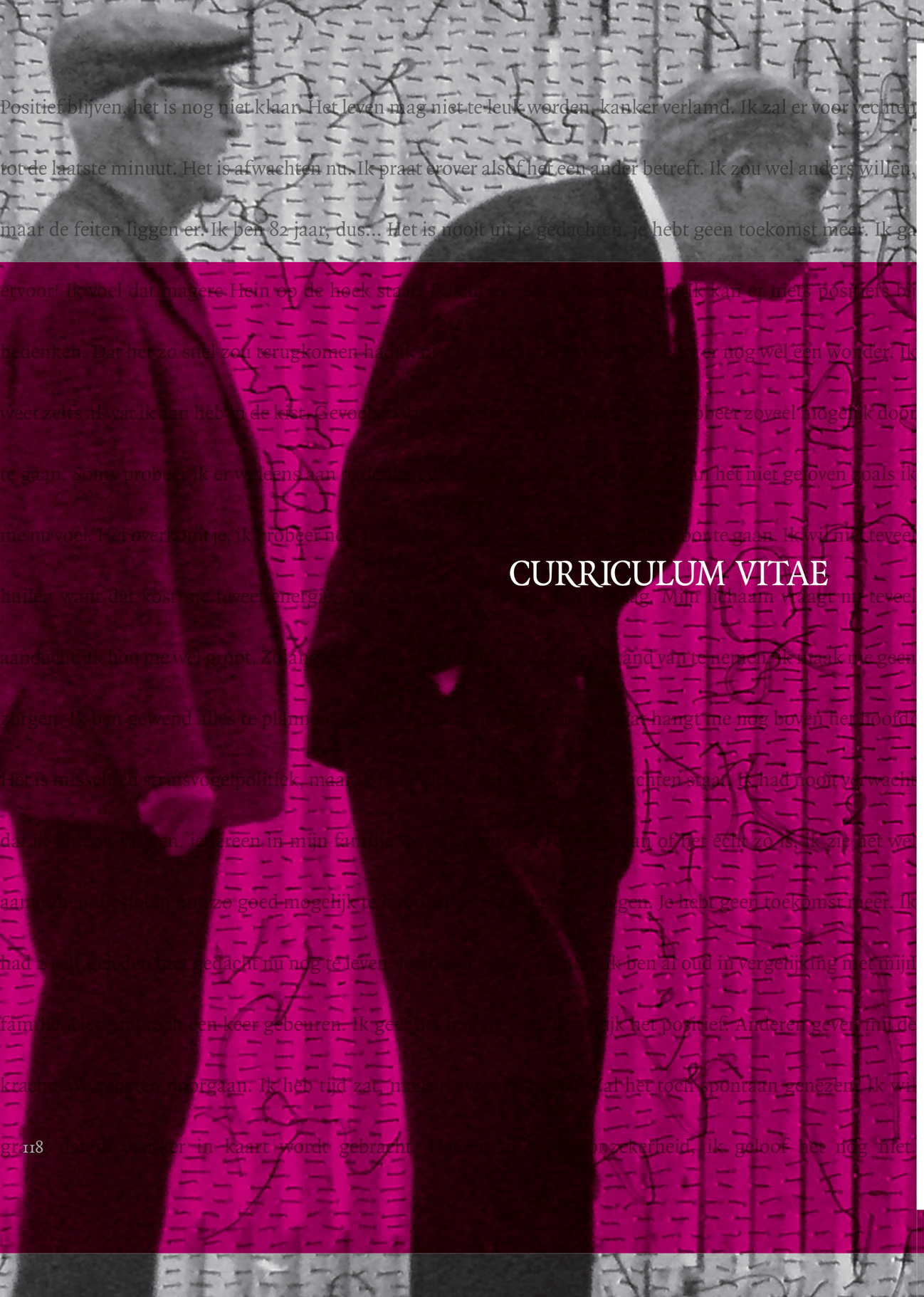
Arnold, Jeroen, Yvonne en Erik van 100.nl, jullie vingen me op aan de finish met een warme, mooie jas, met strik! De strijd met mezelf was geleverd en jullie hebben dit alles wonderschoon verpakt. Ik heb bewondering voor de manier waarop jullie werken en zal de middag dat ik bij jullie zat om de gehele lay-out te bespreken nooit meer vergeten. De gehele ‘duurloop’ passeerde de revue en we werden geïnspireerd tot het maken van een CD. Ik ben heel blij dat het eindproduct zo mooi is vereeuwigd door jullie.

Zoals bij elke lange duurloop, het venijn zit hem in de staart! Dat was ook hier zeker het geval toen er in de zomer 2011 onverwachts een hoge berg beklommen moest worden, die in eerste instantie uit het parcours was verwijderd. De moed zakte me in de schoenen... Lieve Gert, mijn zielsmaatje, zonder jou was het me werkelijk nooit gelukt om die berg te beklimmen, jij was voor mij het dweilorkest dat je laat meerennen op de maat van de muziek en al het andere even doet vergeten. Helende muziek. Je liet me zelf lopen maar was altijd aan mijn zij, ja, een rennend orkestje dus... Je weet niet half hoe je me van steun bent geweest. Je was voor mij een masseur, cateraar en bovenal loopmaatje tegelijkertijd. Met jou is één plus één alles en twee min één niets.

Dank jullie wel, dat jullie er allemaal waren!



M.J. Uitdehaag | Living in the face of death



# CURRICULUM VITAE





Madeleen Uitdehaag werd geboren op 29 januari 1968 te Essen (België) en groeide op in Nispen (West Brabant). Zij behaalde haar MAVO diploma aan de Maria MAVO te Roosendaal. Daarna heeft zij diverse opleidingen gevolgd; in-service opleiding tot A-verpleegkundige in het RK/Jacobus Ziekenhuis te Dordrecht/Zwijndrecht (1986-1990), opleiding HBO-Verpleegkunde aan de AVANS Hogeschool te Breda (1991-1995) en de studie Verplegings-wetenschappen aan de Universiteit van Utrecht in Utrecht (1997-2000). Gelijktijdig met de 3 laatstgenoemde studies werkte zij als verpleeg-kundige in het RK/Jacobus Ziekenhuis te Dordrecht/ Zwijndrecht (1986-1991) en het Franciscus Ziekenhuis te Roosendaal (1991-2001). Vanaf 2001 maakte zij de overstap naar het onderwijs als docent Verpleegkunde aan de HBO-V. Eerst 3 jaar aan de AVANS Hogeschool te Breda (2001-2004), gevolgd door 1 jaar aan de Hogeschool van Amsterdam te Amsterdam (2004-2005).

In juni 2005 is zij als promovendus begonnen op de afdeling Maag-, Darm- en Leverziekte van het Erasmus MC te Rotterdam en heeft zij diverse onderzoeken opgezet en uitgevoerd op het gebied van de palliatieve zorg (zie dit proefschrift).

Sinds 2009 is zij deels werkzaam als onderzoeker bij het kenniscentrum palliatieve zorg te Utrecht, en deels werkzaam als adviseur richtlijnen bij het Integraal Kankercentrum Nederland. Binnen deze twee banen heeft zij diverse subsidieaanvragen geschreven en aan diverse (gesubsidieerde) projecten gewerkt. Ondermeer aan de totstand-koming van een veertigtal richtlijnen voor de palliatieve zorg, een online registratiesysteem voor de registratie van symptomen en aanverwante problemen bij kankerpatienten in de palliatieve fase, en een onderzoek naar knelpunten binnen de palliatieve zorg ervaren door verpleegkundigen en verzorgenden (PALVER project). Binnen de beroepsvereniging V&VN Palliatieve zorg is Madeleen sinds 2007 actief als bestuurslid en voorzitter van de wetenschapscommissie. In haar vrije tijd houdt zij van hardlopen (bij voorkeur lange duurlopen voor het goede doel), piano spelen, een mooi boek lezen en wandelen met haar vriend(en).

# PHD PORTFOLIO

*Summary of PhD training*

*Name PhD student: M.J. Uitdehaag*
*Erasmus MC Department: Gastroenterology and hepatology*
*Research School: Erasmus University Rotterdam*
*PhD period: 2005 - 2012*
*Promotor(s): Prof. Dr. E.J. Kuipers, Prof. Dr. P.D. Siersema*





| | Year | Workload (ECTS) |
|---|---|---|
| **General academic skills** | | |
| • Biomedical English Writing and Communication | 2006 | 4.0 ECTS |
| • English High-Intermediate 1 (B2.1) | 2007 | 3.0 ECTS |
| **Research skills** | | |
| • Methodology (Clinical trials-CPO) | 2006 | 0,4 ECTS |
| • Database search | 2008 | 0,2 ECTS |
| • Cursus kwalitatieve analyse | 2011 | 0,6 ECTS |
| **In-depth courses (e.g. Research school, Medical Training)** | | |
| • Pain relief in advanced cancer patients | 2006 | 0,2 ECTS |
| • Autumn symposium Quality of life (CPO) | 2008 | 0,4 ECTS |
| **Oral presentations** | | |
| • NPTN congres (Pre PACT) | 2006 | 1,0 ECTS |
| • AGORA onderzoekersbijeenkomst (Pre PACT) | 2007 | 0,4 ECTS |
| • Pancreatic pathology in current practice, Boekarest (Nurse-led follow-up) | 2007 | 1,6 ECTS |
| • Vlaams Nederlands onderzoeksforum palliatieve zorg (RECORD) | 2009 | 1,0 ECTS |
| • Vlaams Nederlands onderzoeksforum Palliatieve zorg (SYMPAL) | 2010 | 1,0 ECTS |
| • NPTN congres (Symptomen bij ouderen) | 2010 | 0,6 ECTS |
| • Palliatief Team Midden Nederland (PTMN) congres (VESCO) | 2010 | 0,6 ECTS |
| **Poster presentations** | | |
| • European Association for Palliative Care Congress, Budapest (PACT) | 2007 | 1,0 ECTS |
| • Nederlandse Vereniging voor Gastro-enterologie voorjaar (Wallflex stent) | 2007 | 0,2 ECTS |
| • Digestive Disease Week, Washington (Pre PACT) | 2007 | 1,0 ECTS |
| • Digestive Disease Week, San Diego (Alimaxx stent) | 2008 | 1,0 ECTS |
| • Digestive Disease Week, Chicago (SX-Ella stent) | 2009 | 1,0 ECTS |
| • European Association for Palliative Care Congress, Vienna (RECORD) | 2009 | 1,0 ECTS |
| • European Association for Palliative Care Congress, Glasgow (V&VN) | 2010 | 0,6 ECTS |
| **International conferences** | | |
| • 10th EAPC Congress (Budapest) | 2007 | 0,8 ECTS |
| • Digestive Disease Week (Washington) | 2007 | 1,0 ECTS |
| • 11th EAPC Congress (Vienna) | 2009 | 0,8 ECTS |
| • 6th EAPC Research Congress (Glasgow) | 2010 | 0,8 ECTS |
| • 12th EAPC Congress (Lissabon) | 2011 | 0,8 ECTS |
| • 7th EAPC Research Congress (Trondheim) | 2012 | 0,8 ECTS |

| | Year | Workload (ECTS) |
|---|---|---|
| **Seminars and workshops** | | |
| • How to get published? | 2006 | 0,1 ECTS |
| • GCP course | 2007 | 0,4 ECTS |
| • The CECo New Perspectives on evaluation in palliative care workshop | 2010 | 0,4 ECTS |
| **Other** | | |
| • Erasmus Liver Single Topic | 2005 | 0,4 ECTS |
| • Nederlandse Vereniging voor Gastro-enterologie najaar | 2005 | 0,6 ECTS |
| • Nederlandse Vereniging voor Gastro-enterologie voorjaar | 2006 | 0,6 ECTS |
| • 3e IBDay | 2006 | 0,4 ECTS |
| • Nationaal congres palliatieve zorg | 2006 | 0,6 ECTS |
| • Symposium V&VN Palliatieve Zorg (voorjaar en najaar) | 2007 | 0,4 ECTS |
| • 1e Nationale Voedingscongres | 2008 | 0,4 ECTS |
| • Symposium V&VN Palliatieve Zorg | 2008 | 0,4 ECTS |
| • Nationaal congres Palliatieve zorg | 2008 | 0,6 ECTS |
| • Avondsymposium V&VN oncology | 2009 | 0,1 ECTS |
| • Eerstelijns congres palliatieve zorg | 2009 | 0,4 ECTS |
| • Oncologiedagen voor verpleegkundigen | 2010 | 0,4 ECTS |
| • Symposium V&VN Palliatieve Zorg | 2011 | 0,4 ECTS |
| • V&VN bestuursscholing | 2011 | 0,4 ECTS |
| • KWALON najaarsconferentie | 2011 | 0,4 ECTS |
| • Oncologiedagen voor verpleegkundigen | 2011 | 0,4 ECTS |





M.J. Uitdehaag | Living in the face of death

**Madeleen Uitdehaag** werd geboren op 29 januari 1968 te Essen (Belgie) en groeide op in Nispen (West Brabant). Zij behaalde haar MAVO diploma aan de Maria MAVO te Roosendaal. Daarna heeft zij diverse opleidingen gevolgd; in-service opleiding tot A-verpleegkundige in het RK/Jacobus Ziekenhuis te Dordrecht/ Zwijndrecht (1986-1990), opleiding HBO-Verpleegkunde aan de AVANS Hogeschool te Breda (1991-1995) en de studie Verplegingswetenschappen aan de Universiteit van Utrecht in Utrecht (1997-2000). Gelijktijdig met de 3 laatstgenoemde studies werkte zij als verpleegkundige in het RK/Jacobus Ziekenhuis te Dordrecht/Zwijndrecht (1986-1991) en het Franciscus Ziekenhuis te Roosendaal (1991-2001). Vanaf 2001 maakte zij de overstap naar het onderwijs als docent Verpleegkunde aan de HBO-V. Eerst 3 jaar aan de AVANS Hogeschool te Breda (2001-2004), gevolgd door 1 jaar aan de Hogeschool van Amsterdam te Amsterdam (2004-2005).

In juni 2005 is zij als promovendus begonnen op de afdeling Maag-,Darm- en Leverziekte van het Erasmus MC te Rotterdam en heeft zij diverse onderzoeken opgezet en uitgevoerd op het gebied van de palliatieve zorg (zie dit proefschrift).

Sinds 2009 is zij deels werkzaam als onderzoeker bij het kenniscentrum palliatieve zorg te Utrecht, en deels als adviseur richtlijnen bij het Integraal Kankercentrum Nederland. Binnen deze twee banen heeft zij diverse subsidieaanvragen geschreven en aan diverse (gesubsidieerde) projecten gewerkt. Ondermeer aan de totstandkoming van een veertigtal richtlijnen voor de palliatieve zorg, een online registratiesysteem voor de registratie van symptomen en aanverwante problemen bij kankerpatienten in de palliatieve fase, en een onderzoek naar knelpunten binnen de palliatieve zorg ervaren door verpleegkundigen en verzorgenden (PALVER project).

Binnen de beroepsvereniging V&VN Palliatieve zorg is Madeleen sinds 2007 actief als bestuurslid en voorzitter van de weten-schapscommissie. In haar vrije tijd houdt zij van hardlopen (bij voorkeur lange duurlopen voor het goede doel), piano spelen, een mooi boek lezen en wandelen met haar vriend(en).

**www.madeleenuitdehaag.nl**

*Erasmus Universiteit Rotterdam*

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