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Vos, M.S.

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Denial and Quality of Life in Lung Cancer Patients

Martina S.Vos

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Denial and Quality of Life in Lung Cancer Patients

ACADEMISCH PROEFSCHRIFT

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aan de Universiteit van Amsterdam

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Promotor(es): Prof. dr J.C.J.M. de Haes
Prof. dr. J.C. van Houwelingen

Co-promotor(es): dr. H. Putter

Overige leden: Prof. dr. E.H.D. Bel
Dr. A.M.M. Kolk
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Prof. dr. W. van Tilburg

Faculteit der Geneeskunde

*Yesterday, upon the stair
I saw a man who wasn't there
He wasn't there again today
I wish, I wish, he'd go away.*

William Hughes Mearns, 1899

Contents

Chapter 1	Introduction	9
Chapter 2	'Doctor, I don't want to know': an investigation of denial in lung cancer patients <i>Nederlands Tijdschrift voor Geneeskunde</i> , 2001, 145 (50), 2409-12.	15
Chapter 3	Denial in Cancer Patients, an explorative review <i>Psycho-Oncology</i> 2007;16: 12-25	25
Chapter 4	The Denial of Cancer Interview: development and first assessment of psychometric properties in lung cancer patients	49
Chapter 5	Denial in lung cancer patients, a longitudinal study <i>Psycho-Oncology</i> 2008; 12: 1163-1171	71
Chapter 6	Denial and physical outcomes in lung cancer patients, a longitudinal study <i>Lung Cancer</i> (2009), doi 10.1016/j.lungcan.2009.04.003	89
Chapter 7	Denial and social and emotional outcomes in lung cancer patients: the protective effect of denial <i>Submitted</i>	107
Chapter 8	Summary and general discussion	123
Appendix	Joint analysis of multiple longitudinal outcomes: application of a latent class model <i>Statistics in Medicine</i> 2008; 27: 6228-6249	139
Samenvatting		165
Dankwoord		171
Epiloog		177
Curriculum Vitae		179

Chapter 1

Introduction

INTRODUCTION

We live in an era of communication. Speaking about one's actions, opinions, and feelings has become a daily standard for many people. This is reflected in the rapid expansion of internet, the mobile phone and considerable number of talk shows, for example.

Communication has also become an important issue in modern healthcare.

Doctor-patient communication is one of the competencies in which medical trainees have to qualify.^{1,2} By law doctors have to inform their patients about diagnosis, treatment options and prognosis. Most cancer patients appreciate such disclosure and want to be fully informed.³

The question arises whether this provision of information improves patient outcomes. In a recent paper, 90% of the investigated lung cancer patients correctly recalled their physician's information about the diagnosis, but only 49% was able to recall the information regarding the goal of treatment, even when this goal was curative. Patient satisfaction was higher with information about diagnosis and treatment procedures than with information concerning the treatment goal ($\geq 73\%$ vs. $\leq 41\%$, respectively).⁴

Could it be possible that some patients do not want to be fully informed? Lagarde et al.⁵ found that following esophagectomy, 30% of patients did not want their physician to initiate the discussion about prognosis. Information preferences declined as information became more specific and more negative.

After the information has been given, can patients still deny what they have been told about diagnosis, treatment and prognosis? And if they do so, how many patients cope through denial? Does denial change over time and do these patients feel and function better or worse as time goes by? These questions are at the centre of this thesis and will be addressed in the different chapters.

Denial

"Denial is, and always has been, a fuzzy and complex concept which has acquired many meanings and connotations, depending upon the context in which it has been invoked as an explanation. In trying to propose an all-purpose definition, one is immediately confronted with a multiplicity of theoretical issues that relate to the underlying processes".

This characterization of denial by Goldberger⁶ refers to the comprehensiveness of the concept of denial. For the purpose of our study, the context was limited to cancer patients, and we could fall back on the term 'denial of illness', which has been well-known in the literature since 1953.⁷ In 1998 Muskin et al.⁸ even proposed to define "Maladaptive Denial of Physical Illness" as a new diagnosis in the DSM IV. In reaction to this suggestion, Appelbaum⁹ argued that denial is a ubiquitous phenomenon that is usually beyond the range of psychiatry. Whether denial in cancer patients is a normal phenomenon or a sign of psychopathology will be discussed in this thesis.

To do justice to the different ways in which cancer patients try to escape from the burden of the facts and feelings related to their illness, an encompassing concept of denial, such that the different underlying processes of denial could be classified, was needed. The definition according to Hackett and Cassem^{10,11} met these requirements: “the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects”. The advantage of this definition is that it covers related denial-like mechanisms such as avoidance, disavowal, suppression, self-distraction, etc. In addition, this definition covers conscious as well as unconscious denial, making it highly suitable for our purposes since the measurement of unconscious processes is a disputable matter.^{12,13,14}

Lazarus¹⁵ emphasises that denial is a process, saying that “we are dealing with flux” and that “denial is not a single act but a highly diverse set of processes that respond to different external and internal conditions”. Denial can change in one person over shorter or longer times and in different contexts, and the level of denial can move on a continuum from no denial to extreme denial. This challenges any investigator wanting to assess denial. The evolution of denial over time and the possible changing level of denial are discussed in this thesis.

Lung cancer

Lung cancer is the second most common cancer and accounts for the most cancer-related deaths in both men and women worldwide. Since 1987, more women have died each year from lung cancer than from breast cancer. Death rates among men decreased by 1.3% per year between 1994 and 2004. Female lung cancer death rates are approaching a plateau after continuously increasing for several decades.¹⁶ The 1-year relative survival for lung cancer has increased slightly from 35% during 1975-1979 to 41% during 2000-2003, largely due to improvements in surgical techniques and combined therapies. However, the 5-year survival rate for all stages combined is only 15%. The survival rate is 29% for cases detected when the disease is still localized, but only 16% of lung cancers are diagnosed at this early stage.

This well-known poor prognosis possibly explains the shock that accompanies the sudden change in life perspective for most men and women when lung cancer is diagnosed. They become the ‘lung cancer patients’ in our hospitals. They have to trust and build up relationships with strangers such as chest physicians, surgeons, radiotherapists and oncology nurses. Involuntarily, they have to make major decisions about treatment options and adapt their daily agenda because of hospital visits. How do they cope?

Our decision to investigate denial in lung cancer patients is based on a number of considerations. Firstly, psychosocial studies in lung cancer patients are limited. Compared to breast cancer, for example, considerably less attention has been paid to the psychosocial aspects of lung cancer. This might be due to the poor prognosis and the taboo surrounding lung cancer due the patient’s

own role as a smoker. To be able to support lung cancer patients during their disease process we need greater insight into their ways of coping. Secondly, we assumed that lung cancer patients might have more reason to deny than other cancer patients because of 1) the poor prognosis which leaves them limited time to adapt; 2) the dyspnoea, which limits functioning and may be frightening; and, possibly, 3) shame and stigma which may create the need to hide the painful reality.

Research questions and study design

Based on the considerations concerning denial and lung cancer described above, the objective of this study was to investigate:

1. the prevalence of denial in lung cancer patients
2. the influence of background characteristics on the prevalence of denial
3. the existence of recognizable patterns of denial in the course of the disease in this patient group
4. the relation between the observed patterns of denial and the quality of life in lung cancer patients.

These items were analysed empirically using data collected from a group of 195 newly-diagnosed lung cancer patients over time.

The collected data of the patient group were used to test the psychometric properties of the Denial of Cancer Interview (DCI) and to find answers to the research questions.

Outline of the thesis

This thesis comprises eight chapters. The order of the chapters reflects the chronology of the research project.

In the pilot phase of the study we interviewed a number of lung cancer patients to explore their thoughts and feelings and to find out whether they were willing to cooperate. Three of these patients are described in **Chapter 2**. These case reports illustrate the patients we have in mind when describing the phenomena of denial.

In **Chapter 3** the research literature concerning denial in cancer patients is reviewed. This explorative review represents the different concepts and the prevalence of denial in cancer patients. The relationship between denial and background characteristics and the influence of denial on quality of life is also discussed.

In the absence of a well-accepted instrument, we have developed the Denial of Cancer Interview (DCI) to investigate denial of illness in lung cancer patients, with the intention of measuring denial according to the comprehensive definition given by Weisman and Hackett. In the DCI, the patients' reports of their illness situation as well as the expert's clinical impression are addressed. In **Chapter 4** the development and the first psychometric analyses of the

instrument are described. The DCI is presented in **Addendum A**. The frequencies of the items of the Patient Assessment Scale are given in **Addendum B**.

Based on the assessment of denial using the DCI, the mean level of denial of lung cancer patients at four time points is described in **Chapter 5**. The impact of sociodemographic characteristics and illness-related variables on denial are also presented in this chapter.

Patterns of denial over time and how these relate to patient-rated physical outcome is presented in **Chapter 6**. The effect of denial on patient-rated social and emotional outcomes is described in **Chapter 7**.

Finally, a summary of the different chapters followed by a general discussion is presented in **Chapter 8**.

In the **Appendix**, the statistical method of joint analysis of multiple longitudinal outcomes as used in this study is described in detail.

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Chapter 2

'Doctor, I don't want to know': an investigation of denial in lung cancer patients

Martina S. Vos and Hendrikus H. Berendsen

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SUMMARY

Three patients with lung cancer, a man aged 68, a woman aged 69 and a man aged 52, denied the nature or the severity of their disease in three different ways: temporary denial to evade acute emotional shock, full-blown persistent denial, and unjustified optimism respectively. The psychological mechanism of denial may become operational in patients confronted with an overwhelming disease. A less pronounced denial of medical information provided by physicians can be recognised in many patients. It may also be noticed in how individuals or groups of people sharing the same unbearable reality face up to the facts. Denial may be helpful in (temporarily) circumventing a serious problem but when the disease is serious, it may interfere in relationships with partners, relatives and friends. Denial must be differentiated from organicity, e.g. anosognosia in cerebral damage, by patient ignorance, or by vague communication from the medical community. A direct and blunt confrontation of denial may result in adverse effects due to a defensive mechanism being aggravated. Slowly providing the patient with pieces of information whilst taking into account his or her reaction, may provide a clue for gradual conformation to the medical reality.

INTRODUCTION

Some patients with a serious disease give the impression that they prefer not to know how serious their condition is. They appear to hide their head in the sand; they are in denial. The term 'denial' instinctively brings to mind a negative association. The trend nowadays is to face your problems full on. However, sometimes these problems are huge and unsolvable. To avoid collapsing under the burden of acknowledging that these problems cannot be solved, people use methods to undo the torment. One such method is denial of the problem. The intention of denial, be it conscious or unconscious, is to avert unbearable suffering and nullify threatening information. Denial is found both within the field of medicine and beyond. In our hospital pulmonologists diagnose lung cancer in about 120 patients each year. A few of these patients strongly deny their disease. Others only deny it in the beginning or try to avoid the severity of the consequences of their disease by being 'wrongly optimistic', as described by The et al.^{1,2} Denial can be adaptive, but also harmful. A mild degree of denial after a serious disease has been diagnosed can be a helpful form of protection against overwhelming emotions. Some patients, however, present us with difficult dilemmas as we will demonstrate below. In the case histories the patients are anonymous. We will start by describing the cases leading up to the denial, and discuss the further course of events later on.

THE CASES

Patient A, a 68-year-old man, is healthy and fit. Since retiring he spends most of his time on his yacht. He has crossed the Channel several times, together with his wife, and is now preparing for a trip to the Mediterranean Sea. As he has been coughing for a few weeks he asks his family doctor for a course of antibiotics so that he will be fit to leave. The family doctor listens to his lungs and, to make certain, orders a chest x-ray. The radiologist sends the patient straight to the pulmonologist as there is a spot visible on the x-ray which is highly suggestive of a malignancy. The pulmonologist discusses this with the patient and his wife and explains which investigations will need to be carried out the following week to establish the nature of the disease. 'I don't want to know about this', says the patient, 'I don't feel at all sick and now you're telling me I have lung cancer'.

Patient B, a 69-year-old woman comes for an interview with the psychiatrist (M.S.V.), accompanied by her daughter. In preparation for a study into the association between denial of disease and quality of life in lung cancer patients, the psychiatrist has asked the pulmonologists to refer patients who were prepared to participate in an open interview. A prerequisite to participation in the interview was that the patient had been informed of the diagnosis.

The patient explains that there is nothing wrong, as she had thought. There had really been no need for her to go to hospital, as she isn't sick. They had

even checked her liver but not found anything. The patient answers questions quickly, but with short replies. The daughter agrees, explaining that she had been worried but now she also feels somewhat reassured. Mother and daughter leave the office in high spirits, wishing the interviewer a good weekend. Stunned, the interviewer goes to the pulmonologist's office, saying a little indignantly: 'I thought you were only going to send patients with lung cancer?' 'That patient does have lung cancer', replies the pulmonologist. 'And most likely with liver metastases, although the pathologist couldn't find any malignant cells in the puncture fluid. We may have just missed it with the needle. I explained this to the patient and her daughter.'

Patient C, 52 years of age, is a businessman. He hasn't always been financially successful. He is very happily married, has three healthy children in the prime of their lives. He describes himself as self-taught. He has seen a lot, and this has taught him to relativise and not to be too quickly impressed by money or power. He has been found to have small-cell lung carcinoma. Before he starts his courses of chemotherapy he tells everyone who's willing to listen that now he has lung cancer, but that next year he will be running the New York marathon. As proof that he will be cured, he refers to the horoscope that his mother had drawn up when he was born which predicts that he will live to be a 100 years old.

THE BENEFITS AND DISADVANTAGES OF DENIAL

These cases represent three examples of the different disguises in which denial can present in the consultation room. Doctors also make use of denial, for example when playing down the situation. With statements such as 'You have a little lump, but we'll irradiate it and you'll be back to your old self', the anxious patient is seen to heave a sigh of relief. Rightly so, says Wagener:³ 'Denial does not appear to be a problem as long as it does not interfere with the treatment or appropriate medical planning. A doctor should not rob the patient of their essential defence mechanisms'.

Denial can have a useful, protective function for everyone in daily life, not just for our patients. If we were to be constantly aware of all our fears (for example, what might happen to our loved ones) and dangers (such as plane crashes, drug package inserts), we would no longer be able to live and work.

If a person's denial is too strong, the protective effect may be accompanied by harmful side effects. One well-known example is the postponing behaviour of a woman who goes around for months with a lump in her breast thinking 'it will pass', reducing the chance of successful treatment.

Another negative effect of denial is that it may hamper communication. It is not easy to discuss a treatment plan with a patient who does not want to accept that he/she is ill. If the patient refuses an examination or treatment and this goes against medical norms, the doctor is faced with a dilemma. Should the doctor respect the denial because the patient seems to feel the need to pro-

tect him/herself against fears or threatening information, or should he/she try to break through the denial with the intention of drawing up a treatment plan?

THE CONCEPT OF 'DENIAL'

The literature describes denial from various different theoretical viewpoints. Opinions are strongly divided on what does and does not count as denial. The original psychoanalytical definition of denial by Anna Freud in 1936⁴ referred to an unconscious psychotic defence mechanism against external influences. In the decades that followed, the debate focussed on whether denial is only a defence mechanism against external threats or also one against inner conflicts, and whether denial is a conscious or unconscious defence mechanism and, in particular, whether denial is a sign of a pathological disorder or simply a healthy system of defence.⁵⁻⁸ Many researchers consider denial to be an unconscious defence mechanism and suppression to be either conscious or semi-conscious.⁹⁻¹²

The DSM-IV¹³ provides the following definitions of the three terms below:

- suppression: intentional avoidance of thoughts about disturbing problems, wishes, feelings or experiences;
- repression: expulsion of disturbing wishes, thoughts or experience from the consciousness, where the feeling component may remain conscious, detached from its associated thought content;
- disavowal: refusal to acknowledge a painful aspect of the external reality or subjective perception, while this aspect is obvious to others.

The commonly-used term 'denial' can be considered a collective term for these definitions; a general term for various ways to avoid painful facts or feelings.

The term 'denial of illness' is also used in the literature alongside denial as a 'neurotic' defence mechanism. The most well-known researchers in the field of denial of illness are Hackett et al. who found that, in stable individuals with no history of psychopathological disorders, denial is the most commonly used defence mechanism in response to a cardiac infarction.¹⁴ Their definition is as follows: 'denial is the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects'. On the basis of their research, they conclude that denial in the acute phase following a cardiac infarction protects against panic and depression, and their study even found that deniers had a lower mortality rate.

In addition to individual denial, collective denial also exists. Two forms of collective denial can be identified:¹⁵ official denial and cultural denial. Official denial refers to denial initiated, formed and maintained by governments, for example to cover up famine or political murders. Cultural denial tends to refer to the unwritten agreements about what should not be remembered or known publicly or within a certain group, for example the holocaust denial movement. The realisation that denial takes place at many levels helps to view the

cancer patient's denial in the consultation room within a broader setting and generates greater understanding for this context.

PITTFALLS

If a doctor has the impression that a patient is denying his/her disease or the consequences of this disease, it is advisable to investigate whether the denial involves a psychological mechanism. Below we discuss three pitfalls whereby denial may be incorrectly considered a defence mechanism in the patient.

Organicity. In neurological diseases anosognosia can arise. This is an inability by the patient to recognise a loss of function in part of his/her body due to brain damage. Patients with memory problems or those who are delirious may forget what they have been told. Investigation of the cognitive functions is desirable in this case.

Ignorance. It is important not to diagnose denial on the basis of a general impression of a patient. It is important to investigate whether the patient has been well-informed about the disease to rule out denial due to ignorance.

The influence of the medical stronghold. The ability of doctors to induce or maintain denial should not be underestimated. Using vague language or switching to a positive topic too quickly after presenting the bad news can deny the patient the opportunity to realistically assess the severity of his/her situation. Although it is desirable to offer a patient hope, this should not be at the cost of the actual facts. Most patients benefit more from openness, so that they themselves can determine how they are going to deal with it and how long this is going to take. The patient who incorrectly believes him/herself to have excellent chances of recovery because the doctor suggested as much, may be badly disappointed or feel let down if it appears that the 'promises' cannot be fulfilled. In this respect, The points to the tendency of doctors to answer patients' questions about the long-term outlook in terms of a short-term perspective.¹

FOLLOW-ON OF CASE HISTORIES

Patient A. In the case of patient A, who was responding mainly to the acute shock, the pulmonologist suggested postponing further investigations and giving the couple time to come to terms with the shocking information. Two weeks later the patient did indeed want further investigations, but he indicated that he definitely did not want chemotherapy even if it was the only treatment opinion. When the patient was found to have large-cell lung carcinoma with no detectable metastases, he decided to undergo surgery. After the operation the patient remained in pain for months, which he found difficult. One year after the operation he felt good enough to make the sailing trip to the Mediterranean Sea after all.

This patient displayed a short phase of 'conscious denial'. Once he was able to organise the threatening information and took the decision making about potential treatment into his own hands, he was more capable of handling his disease and his relationship with the doctors.

Patient B did not want to make another appointment with the pulmonologist and did not want to undergo liver puncture again. The pulmonologist handed her case over to the family doctor, who made a number of home visits. He did not confront her with the severity of her disease but when her symptoms worsened he tried to tell her that she was suffering from lung cancer which could no longer be cured. She persisted in her denial. The daughter, who by this time was well-informed about her mother's condition, agreed with the family doctor that they would leave her mother alone as her mother had never been one to discuss her feelings. Although the daughter found it difficult not to be able to discuss the imminent death with her mother, she decided to respect her mother's position on the matter. The daughter cared for her mother until the end, and knowing she was supported by the family doctor made it bearable not to talk about the subject.

In this example denial has both adaptive and harmful sides to it. The patient has protected herself, but at the cost of not having the opportunity to say goodbye to her daughter who would have liked to have been able to do so. It can be difficult for those close to the patient not to have the opportunity to talk honestly about their sadness or the patient's imminent death. Weighing up the different interests of those involved can be a precarious task for the doctor.

Patient C remained cheerful and optimistic up to the end of his chemotherapy. On the chest x-ray the tumour appeared to shrink further after each course, so the pulmonologist saw no reason to explain again that the disease was definitely incurable. There would always be an opportunity for that later down the line. In this case the denial appears to have manifested itself in the form of barely realistic optimism which did, however, benefit the patient's quality of life. After the chemotherapy courses the patient moved abroad. We have no further information about the course of his disease.

DISCUSSION AND CONCLUSION

When dealing with a patient who is in denial, a prerequisite is respect for the protective function of denial. Wagener points out that patients appear to consciously deny the severity of the disease during the treatment phase and that attempts by care providers to prompt the patient to resign him/herself to his/her fate understandably earn criticism.¹⁶

If the doctor is of the opinion that it is in the interest of the patient and his/her relatives to nonetheless discuss the situation about which the patient is in denial, a well-considered approach tailored to the patient and those close to him/her is required. Direct confrontation of the denial is generally counterproductive, and may in fact strengthen the patient's defence mechanism and result

in a loss of trust. This does not mean that doctors, nurses or relatives should simply go along with the denial. A satisfactory compromise is to show understanding for the way in which the patient is dealing with his/her disease, but to continue asking questions in a calm and patient manner and, on the basis of the patient's reaction, continue providing information. It is important that there is agreement on the selected approach within the treatment team and to inform others involved in the patient's care at the hand-over about the information provided to avoid the patient and his/her family receiving different or contradictory information.

In this paper we wish to show that 'denial' is a wide-ranging term which describes the various different mechanisms we all use to stave off unbearable events or emotions. This defence mechanism, particularly when temporary, can be a useful and protective way to avoid being flooded with overwhelming emotions and to gain some time to become accustomed to unpleasant events. In the case of rigorous denial, however, there is insufficient acceptance of the reality and communication can become impaired. This impaired communication can be detrimental to those involved. It is the doctor's role to assess whether or not it is possible to break through the denial. If he or she decides it is in the interest of the patient and his/her relatives to break through the denial, he/she should respect the protective function of this defence mechanism and carefully 'challenge' the patient to surrender the denial to some degree.

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Chapter 3

Denial in Cancer Patients, an explorative review

Martina S. Vos and Hanneke C.J.M. de Haes

SUMMARY

Denial is a clinically relevant concept in cancer patients. It has been investigated and discussed extensively. The definition of denial, however, has been subject to different theoretical trends over time. From a psychoanalytical viewpoint, denial is a pathological, ineffective defence mechanism. On the other hand, according to the stress and coping model denial can be seen as an adaptive strategy to protect against overwhelming events and feelings.

In this explorative review the different concepts and the prevalence of denial in cancer patients are described. The relationship between denial and background characteristics and the influence of denial on quality of life are reviewed also.

The prevalence of denial of diagnosis in cancer patients varied from 4% to 47%, denial of impact occurred 8% to 70% and denial of affect was found in 18% to 42% of patients. Elderly cancer patients were more likely to manifest denial. Cultural background seemed to play a role in the prevalence of denial in cancer patients. Neither the type of cancer nor gender seemed to be related to denial. At the most, men might be more likely to deny during the terminal phase. In a limited number of longitudinal studies, a gradual reduction in denial was found over the course of the illness.

The effect of denial on physical and social functioning remained unclear while the effect of denial on psychological functioning seemed to depend on the concept of denial used. Distractive strategies were found to reduce distress, whereas passive escape mechanisms turned out to decrease psychological well-being.

Future research on the prevalence and the (mal)adaptive properties of denial in cancer patients has to be based on a clear concept, longitudinal designs and careful recording of background variables.

INTRODUCTION

Denial of illness is a well recognised phenomenon in clinical practice, and was studied in different disease contexts. Denial in cancer patients has been extensively investigated and discussed in the literature since Avery Weisman's famous article entitled "On Dying and Denying".¹ When searching for a clear definition of denial as to understand what is going on in the minds of cancer patients who 'deny', one finds oneself in a jungle of complex and multiform concepts in both the literature and clinical practice. Moreover, whether denial is an effective or ineffective mechanism in somatic illness remains unclear. To clarify the variety of concepts and the impact of denial in clinical oncology practice, the present review aims to address:

1. The prevalence of denial given the different conceptual approaches
2. The role of background characteristics
3. Patterns of denial over time
4. The consequences of denial for quality of life in cancer patients.

The psychoanalytical view

The concept of denial originated from psychoanalytic theory. Anna Freud² elaborated the concept of denial as an unconscious defence against painful and overwhelming aspects of external reality, contrary to other defence mechanisms which serve to protect the ego against instinctual demands. She limits denial to young children and psychotic patients. Based on her conceptualisation, denial was viewed as a pathological phenomenon for years. The Kris Study Group of the New York Psychoanalytic Institute³ decided that denial primarily was an ineffective defence mechanism operated against danger, an affect, an instinctual impulse, a superego command, or a percept, whether external or internal.

The cognitive, stress and coping model

Influenced by the cognitive, stress and coping theories, the original psychoanalytical definition of denial was shaped up from a maladaptive defence mechanism into a concept frequently used in daily life to express different ways of escaping consciously or unconsciously from painful events or feelings. Whether denial is to be considered maladaptive depends on its 'costs and benefits'.⁴

Dorpat⁵ and Horowitz^{6,7} both integrated psychoanalytical theory and cognitive psychology, stressing the self-protective function of denial. They emphasised that denial can be a normal, though temporary response to overwhelmingly stressful and disruptive situations. Miceli and Castelfranchi⁸ similarly showed how irrational reasoning can be 'clothed' in rational arguments as the normal functioning of the mind, which both permits and constrains denial.

Thus, cognitive theory views denial as an avoidance strategy with adaptive properties.

Denial of Illness

Denial has been addressed in physically ill patients since the end of the nineteenth century, with the initial focus on the unawareness of physical symptoms in neurological patients.^{9,10} Janis¹¹ stated that ‘denial’ was misused as an over-inclusive concept covering both psychotic and normal processes. He tried to clarify the character of denial by proposing a continuum, placing denial of clear cut facts (e.g., denying one’s partners death after the funeral) at one extreme and denial of ambiguous situations (e.g. patients ignoring the probability of getting bad news), at the other. He introduced the term ‘minimisation’.

In his review on denial of illness, Goldbeck¹² underlined the importance of the context of denial and, like Janis, recommended expressing denial along a continuum. He concluded that despite pejorative connotations, empirical research supports the notion of adaptive properties of denial.

Denial in cancer patients

Denial in cancer patients was discussed in two reviews.^{13,14}

Moyer and Levine¹³ presented an extensive review of the measurement instruments used in oncology research. They underlined that interviews and clinical ratings, behavioural measures, and indirect measures tend to rely on what individuals do not admit or do not do, whereas self-report checklists tend to rely on and accept at face value what individuals are aware of and are willing to acknowledge. Different types of assessments therefore measure different types of denial. The authors summarised that in oncology “the theoretical and operational definitions that have described denial reveal a lack of consensus as to whether denial is unconscious versus conscious, a trait versus a state, indicative of psychological disturbance versus a normal response to serious illness, or a broad versus a narrow concept”. In addition they suggested that comparable constructs such as avoidance, distancing, minimising, suppression, repressive coping and defensiveness were developed to reframe the negative value judgements associated with the term denial.

Salander and Windahl¹⁴ summarised the use of ‘denial’ in clinical oncology from a psychoanalytic perspective: “Within the field of psychosocial cancer research, ‘denial’ to some comprises its essence in psychoanalytic theory as an unconscious repudiation of reality”. They proposed a reconceptualisation which distinguishes between three different processes: avoidance, disavowal and denial.

Thus both reviews emphasised the lack of consensus regarding the definition of denial and its effects.

METHODS

A literature search was conducted to categorize the different concepts of denial in cancer patients. References were obtained by searching in PubMed using keywords 'denial', 'repression', 'suppression', 'avoidance' and 'minimising' combined with cancer or oncology. The references of the papers retrieved were also screened. Studies concerning denial-like mechanisms in cancer patients related to prevalence, background characteristics, the course of the disease and function were selected. Given the limited availability of evidence and the necessity to explore the field, no selection was made on the basis of research quality.

Forty research papers published during the period 1959-2005 were found, in which very different operationalisations and assessments of denial were used (table 1). We divided the studies in three categories: 1. denial of diagnosis (DD) 2. denial of impact (DI) 3. denial of affect (DA) and, 4. behavioural escape (BE). The choice of this division was made because of the use of the first three types of denial by previous researchers,¹⁵⁻²⁰ referring to what the patient denies. We added the category behavioural escape, because this item was assessed as part of avoidant coping in some questionnaires.

Obviously overlap between the categories was inevitable. In 23 studies the concept of denial used covered two or even three of the categories.

RESULTS

The category denial of diagnosis comprises 19 studies in which (part of) the assessment was focused on rejection of knowledge about the illness (table 1). Denial of impact was measured in 29 of the 40 studies. Ten studies assessed denial of affect and in four studies behavioural escape was found.

The prevalence rates of the different types of denial

The prevalence of the different types or composites of denial was given in 21 studies (table 1). The description of results varied from straightforward percentages to proportional scores of the coping repertoire.

The prevalence rates of *denial of diagnosis* in 13 studies varied from 4.3%²¹ to 46.7%.²² Interestingly the same measurement was used in the two extreme studies. In two studies^{23,24} the most explicit assessments of denial of diagnosis were found, with prevalence rates of 29% and 38.3%.

The prevalence of *denial of impact* was rated in 14 studies and varied from 8%²⁵ to 70%.²⁶ In four studies literal wording of denial of impact was used,^{21,22,27,28} with prevalence rates of resp. 33.3%, 42.7%, 24.6% and 15.4%.

In five studies prevalence rates of *denial of affect* were found, varying from 17.9%²⁸ to 42%.¹⁸ In the two studies in which denial of affect was assessed with the Ways of Coping Questionnaire prevalence rates were 19%²⁵ and 34.2%.²⁹

In two studies^{25,30} *behavioural escape* was measured by the Ways of Coping Questionnaire. In the first no one used behavioural escape-avoidance as a primary method of coping. In the other high escapism was found in 38%, but not as the primary method of coping. These studies lack comparability as they analyzed their results in different ways.

Table 1 *The concepts of denial and the prevalence*

<i>Author(s) + year</i>	<i>Measurement instrument</i>	<i>Denial of diagnosis (DD)</i>	<i>Denial of impact (DI)</i>	<i>Denial of affect (DA)</i>	<i>Behavioural escape (BE)</i>	<i>Prevalence</i>
AitkenSwan & Easson1959	Interview	“the doctor didn’t say it was cancer”				19%
Weisman & Worden 1976	Interview	Blocking information				10%
Cassileth et al. 1980	Information Style Questionnaire	Information preferences, e.g. “whether or not it is cancer”				5,9 %
Silberfarb et al. 1991	Physicians-completed handicap rating scale	Frequently, usually or completely unaware of illness				8%
Lampic et al. 1994	MAC	“I don’t believe I had cancer”				16%
Chocinov et al. 2000	Interview : prognostic awareness	e.g. “What do you understand about your illness?”				no awareness: 9,5%; partial awareness: 17%
Leigh et al. 1980	Health awareness questionnaire	Did not know diagnosis	Self-reported seriousness of the illness			29% Illness not very serious: 70%
Thomas et al. 1988	Interview	Refusal to accept the diagnosis	Illness not serious, conviction of complete cure			DD+DI: 54.4%
Carver et al. 1993	(brief) COPE	Denial: “I’ve been refusing to believe that is has happened”	Self-distracted: “I’ve been turning to work or other activities to take my mind off things”			
Culver et al. 2002						
Stanton et al. 2002						
Kershaw et al. 2004					Alcohol and drug-use	

Table 1 *continued*

<i>Author(s) + year</i>	<i>Measurement instrument</i>	<i>Denial of diag- nosis (DD)</i>	<i>Denial of impact (DI)</i>	<i>Denial of affect (DA)</i>	<i>Behavioural escape (BE)</i>	<i>Prevalence</i>
Chakravorty et al. 1993	Watson's interview	"refuses to accept to have cancer"	'Admits that the diagnosis is cancer ... but denies or minimizes the implications'			DD: 46.7% DI: 42.7%
Nordin and Glimelius 1997	MAC Impact of Event Scale	"I don't believe I had cancer"	Avoidance : denial of meanings and consequences of the event			DD: 13% DI: 20%
Roy et al. 2005	MAC revised	"I don't really believe I have cancer"	"I don't dwell on my illness"			DD: 38.3% DI: 65.8%
Meyerowitz et al. 1983	Personal opi- nion survey Likert scale		E.g.: "Breast cancer causes always death – never causes death"			
Manuel et al. 1987	Interview		Avoidance ↑ / approach ↓ 'not spending much time thinking about cancer or its conse- quences'			34.3%
Ward et al. 1988 Kreitler et al. 1993						
Zachariae et al. 2004	Weinberger repression questionnaire		Low on dis- tress and high on defensiveness			31.3% 40.6%
Morris et al. 1992	Appraisal of cancer diagnosis		E.g. 'believes that the diag- nosis will not have adverse conse- quences'			49.1% 24.6%
Osowiecki & Compas 1998 Manne et al. 2000	Impact of Event Scale		Avoidance e.g. "I try to remove it from my memory"			

Table 1 *continued*

<i>Author(s) + year</i>	<i>Measurement instrument</i>	<i>Denial of diag- nosis (DD)</i>	<i>Denial of impact (DI)</i>	<i>Denial of affect (DA)</i>	<i>Behavioural escape (BE)</i>	<i>Prevalence</i>
Brown et al. 2000 Butow et al. 2000	Psychological Adjustment to Cancer		'.. cancer is not impacting on social, work and family life and is not a sub- stantial cause of anxiety or distress'			
Burgess et al. 1987	Appraisal of cancer diagnosis		'Thinking very little about it and not con- sciously devis- ing mental strategies for dealing with it'	'... to block out feelings associated with it'		
Heim et al. 1993	Bernese Coping Modes		'minimizing or denying the illness / not undertaking necessary medical action'	'Not admitting feelings ade- quate to situation'		
Dunkel- Schetter et al. 1992; Stanton &Snider 1993; Manne 1994	Ways of Coping-CA		Cognitive escape avoid- ance: e.g. 'hoped a mira- cle would happen'	Distancing: "I tried to keep my feelings from interfer- ing with other things too much"	Behavioural escape avoid- ance: "tried to make myself feel better by eating, drink- ing, smoking..."	DI: 8% DA: 19% BE: -
Reynolds et al. 2000	Interview, similar to Ways of Coping Questionnaire		Avoidance: e.g. 'go on as if every thing will be okay'	Suppression emotion: e.g. 'try to keep others from knowing about your illness'	Escapism: e.g. 'try to get away from it by doing relaxing things'	DI: 34.4% DA: 34.2% BE: 38%
Filipp 1992	Trier Skalen zur Krankheits- bewältigung			Threat Minimisation + intrapsychic, presumably emotion- focuses cop- ing responses,		

Table 1 *continued*

<i>Author(s) + year</i>	<i>Measurement instrument</i>	<i>Denial of diag- nosis (DD)</i>	<i>Denial of impact (DI)</i>	<i>Denial of affect (DA)</i>	<i>Behavioural escape (BE)</i>	<i>Prevalence</i>
Friedman et al. 1992; McCaul et al. 1999; Hack & Degner 1999 / 2004	Coping response inventory			Avoidance: "kept feelings to myself"	Behavioural avoidance: "drinking more"	
Watson et al. 1984	Interview	'Refuses to accept that she has cancer.'	'Admits that the diagnosis is cancer .. but denies or minimizes the implications'	'Admits to cancer and accepts the implications but minimizes the extent to which she is distressed by this knowledge'		DD: 4.3% DI: 33.3% DA: 16.7%
Wool 1986	Interview	"..I just have this pain in my chest"	'Expressing the expectation of cure despite progressive physical decline'	Not being upset		
Orr 1986	Interview	Saying the tumour is benign	Denial of cancer-related information Self-report: very healthy/ quite healthy/ very sick	Avoidance of feelings, e.g. statements about not being afraid or affected		DD: 8% DI: 18 % DA: 42% Self-rating: "Very healthy": 60%
Erbil et al. 1996	Omega Vulnerable Rating Scale	No correct perception of the threat of illness	Denial of implications	Avoiding pronouncing the word cancer		DD: 54.8% DI: 15.4 % DA: 17.9%

The role of background characteristics

The question arises whether illness-related factors and demographic variables are related to the need to protect oneself against painful facts or feelings. For example, younger generations may be less likely to deny than older ones due to a growing openness about feelings over recent decades. On the other hand, elderly people could also be less likely to deny because they more readily accept that death is inevitable.

The prevalence of denial and type of cancer

The prevalence of denial might be related to the type of cancer. For example, Silberfarb et al.³¹ suggested that lung cancer patients might deny because of the self-induced nature of the disease.

Denial was related to type of cancer in two studies.^{25,27} In the first no difference of denial (DI, DA, BE) was shown between breast cancer and other cancer sites. Morris et al.²⁷ found 30% deniers (DI) in the lymphoma and 15% in a breast cancer group.

Denial and gender

The relationship between gender and denial in cancer patients was investigated in eight studies (see table 2). Some researchers expected men to deny more frequently,²⁵ whereas others hypothesized they are less likely to use avoidance coping strategies.³² In three studies in which denial of diagnosis was assessed^{23,33,34} men denied more than women. In one study³⁵ no difference was found.

Men rated lower in one,³⁶ and higher on denial of impact in another.²³ No difference was found in the combination of denial of diagnosis and denial of impact in one study.³⁷ and with respect to denial of impact and affect and behavioural escape in two studies.^{25,32}

Results are therefore inconclusive, although some comments can be made. In two studies^{23,34} men denying their diagnosis turned out to have a worse prognosis. Leigh et al.²³ explained the gender differences they found as a result of hampering communication between physicians and male patients. Thomas et al.,³⁷ suggested that surgical staff assuming that men are better at coping with bad news may have informed them of their poor prognosis at an earlier stage: a sudden awareness of likely death could then lead to denial.

Dunkel-Schetter et al.²⁵ explained the absence of gender differences by selection bias: patients recruiting from self-help groups might result in under-representation of avoidant men. Friedman et al.'s³² hypothesis that male patients would use less avoidance coping, on the other hand, was based on studies in healthy samples.^{38,39}

Denial and age

The relationship between age and denial was investigated in seven studies (table 2). In five studies younger patients denied less than elderly. These covered denial of diagnosis³⁵ ($p < 0.05$), denial of impact⁴⁰ ($p < 0.05$),⁴¹ ($p < 0.05$), denial of affect⁴² ($p < 0.01$) and a composite of these three types.⁴³ In one study no difference was found in denial of diagnosis and of impact.³⁷ In one denial of impact and denial of affect were similar, whereas younger patients showed more behavioural escape.²⁵ Cassileth et al.³⁵ reported that older patients tended to say things such as: "I need as little to worry about as possible", whereas younger patients make remarks such as "Ignorance is fear". In contrast to the secrecy associated with cancer diagnosis in previous

decades, younger patients are also more likely to inform friends about their diagnosis than elderly patients.

As in five studies the same trends were found in terms of age difference, the conclusion that younger patients are less likely to deny than older ones seems justified.

Marital status, education and religion

Few studies investigated the relation between denial and marital status, education and/or religion. Four studies reported no effect of marital status on denial of impact.^{25,37,41,44,45} Chochinov et al.,³⁴ however, unexpectedly found that greater denial of diagnosis in terminally ill patients corresponded with being married: they suggested family members may collude with the denial of prognosis in a deeply distressed loved one.

In one study,²⁵ patients with a lower level of education were more likely to use denial of impact ($p < 0.01$) and denial of affect ($p < 0.001$). No difference was found in the two other studies.^{34,41}

Finally, Wool¹⁶ concluded that 'religious beliefs' were not associated with people's denial, while Dunkel-Schetter et al.²⁵ found that denial of impact was significantly associated with a Christian religious preference ($p < 0.001$).

Ethnic and cultural background

In all studies ($n = 5$, Table 2) investigating the relationship between denial and ethnic and/or cultural background a significant effect was found.

Erbil et al.²⁸ compared Belgian and Turkish patients: Belgians were found to hold a more correct perception of their disease (53% vs. 34%), and displayed less denial of impact (13 vs 19%), but more to denial of affect (21% vs. 14%). The authors underlined the possible role of cross-cultural differences in information transmission; Belgian patients received more explicit information about illness and treatment than Turkish patients.

Butow et al.⁴⁵ found that Australian women were less likely to minimise the impact of their cancer than non-Australian women ($p=0.005$). They suggested that adoption of such a coping style may be sanctioned in some cultures. Reynolds et al.³⁰ found no difference in denial of impact between black and white patients. Black patients, however, were more likely to rely on denial of affect, whereas whites displayed more behavioural escape. Culver et al.⁴⁶ found that Whites and African Americans reported less denial of impact compared to Hispanics in the U.S. ($p < 0.05$). Roy et al.²⁴ found the British Asians were more likely deny diagnosis. A higher proportion of British Caucasians, on the other hand, coped by denial of impact.

A comparison of the studies carried out by Chakravorty et al.²² and Watson et al.²¹ is also of interest. Whereas Chakravorty et al. found that 47% of the patients denied having cancer ('total denial') and 43% denied the implications of the disease, Watson et al., found prevalence rates of only 4% and 33% for these items using the same measurement instrument. The most evident differ-

ence between these two studies was the location of the studies (Bombay and London), and hence the cultures (Indian versus English).

Although these studies offer little explanation regarding possible influences or confounders, such as the information about diagnosis and prognosis given by the doctors, it can be concluded that ethnic and/or cultural background influences the prevalence of denial in cancer patients.

Table 2 *denial, type of tumor and demographic variables*

<i>Authors + year</i>	<i>Type of cancer</i>	<i>Sample size</i>	<i>Denial Categories^a</i>	<i>Socio demographic Characteristics and results</i>
Aitken-Swan 1959	Mixed	231 ♂ 40%	DD	<i>Gender:</i> Men < women
Cassileth et al. 1980	Mixed	246 ♂ 40.2%	DD	<i>Gender:</i> n.d. ^b <i>Age:</i> Younger < elderly
Leigh et al. 1980	Mixed, radiotherapy	100 ♂ 40%	DD+DI	<i>Gender:</i> Men > women
Wool 1986	Breast	Deniers: 20 Non-deniers 30	DD+DI+DA	<i>Age:</i> younger < elderly <i>Religion:</i> n.d.
Thomas et al. 1988	Colorectal cancer/ stoma surgery	T1: 68 T2: 52 T3: 36	DD + DI	<i>Gender:</i> n.d. <i>Age:</i> n.d. <i>Marital Status:</i> n.d.
Ward et al. 1988	Hodgkin, non-Hodgkin, breast	67 ♂ 13.4%	DI	<i>Age:</i> Younger < elderly
Dunkel-Schetter et al., 1992	Mixed	668 ♂ 22%	DI, DA, BE	<i>Gender:</i> DI , DA, BE: n.d. <i>Age:</i> DI , DA : n.d. BE: Younger > elderly <i>Education:</i> DI, DA lower education > higher education B.E.: n.d. <i>Religiosity:</i> DI: believers > non-believers, DA,BE: n.d. <i>Marital status:</i> DI, DI: n.d. BE: Living alone > married
Filipp 1992	Mixed	T 332 ♂ 46.4%	DA	<i>Age:</i> DA: Younger < elderly

Table 2 *continued*

<i>Authors + year</i>	<i>Type of cancer</i>	<i>Sample size</i>	<i>Denial Categories^a</i>	<i>Socio demographic Characteristics and results</i>
Friedman et al. 1992	Mixed	94 ♂ 33%	DA, BE	<i>Gender: n.d.</i>
Morris et al. 1992	Breast and Lymphoma	B 105 L61	DI	Breast < lymphoma
Erbil et al. 1996	Mixed radiotherapy	296 B: 172 T: 124	DD, DI, DA	<i>Ethnic Background (Belgium vs. Turkey):</i> DD: B < T DI: B < T DA: B > T
Nordin & Glimelius 1997	GI	127; ♂ 51%	DI	<i>Gender: Men < women</i>
Butow et al. 2000	Metastatic breast cancer	99	DI	<i>Ethnic background: Australian-born < non Australian born</i> <i>Marital status: n.d.</i>
Chochinov et al. 2000	Mixed, terminal cancer	200 ♂ not given	DD	<i>Gender: Men > women</i> <i>Education: n.d.</i> <i>Marital status: Being married > single</i>
Reynolds et al. 2000	Breast	Black: 442 White: 405	DI, DA, BE	<i>Ethnic background (Black vs. White):</i> DI: n.d. DA: B > W BE: W > B
Culver et al. 2002	Breast	African American: 8 Hispanics: 53 Non-hispanics: 70	DI	<i>Ethnic Background: Hispanics > non-hispanics</i>
Zachariea et al. 2004	Breast	71	DI	<i>Age: younger < elderly</i> <i>Marital status: n.d.</i> <i>Education: n.d.</i>
Roy et al. 2005	Mixed	Asians: 82 Caucasians: 117	DD,DI	<i>Ethnic Background: Asians vs Caucasians</i> DD A > C DI C > A

^a DD = denial of diagnosis

DI = denial of impact

DA = denial of affect

BE = behavioural escape

^b n.d. = no difference

Patterns of denial

Lazarus emphasised that denial is a process, writing: “we are dealing with flux”.⁴ Time can have different meanings in the context of cancer. Firstly, ‘time since diagnosis’ is determined when measuring denial at fixed intervals to establish stability of denial.^{37,47,48,49} Secondly, time can be related to illness stages.⁵⁰ Thirdly, time can be addressed in terms of time until death, i.e., survival time.⁴² In our analysis we looked at denial over time since diagnosis cross-sectionally (data not shown). Given the wide range of results no conclusions could be drawn. Longitudinal designs, however, provide a more appropriate picture of patterns of denial over time.

Longitudinal studies investigating patterns of denial

Seven longitudinal studies relating denial to the course of cancer (Table 3). The study periods varied from 6 months to 3-5 years and time intervals between assessments from 4-6 weeks to 3-12 months.^{15,37,42,46,47,49} Heim et al.⁴⁸ defined time in eight predetermined illness stages and across fixed time intervals. Filipp⁴² carried out a follow back analysis to trace the course of coping in patients who had died.

In three studies denial decreased significantly over time,^{42,46,47} and one study showed a trend in diminishing denial.⁴⁹ One study³⁷ found a gradual reduction in denial amongst males as those men who exhibited signs of denial were dying. Weisman¹⁵ did not observe a specific pattern of denial during the course of the disease, while Heim et al.⁴⁸ established a stable pattern of dissimulation or avoidance during the course of the disease, with an increase in denial during the terminal phase. Although more longitudinal research is needed, this limited number of studies seems to indicate that denial in cancer patients diminishes over time, but increases as death draws nearer.

The effect of denial on quality of life in cancer patients

Although the relevance of denial in clinical practice is undisputed, its effects are extensively debated in the literature. As Lazarus states: “denial can have a positive value under certain conditions and a negative value under others”.⁴ Our search retrieved 26 research papers empirically addressing the relationship between denial and quality of life in cancer patients, 17 of which used a denial measurement instrument with acceptable reliability ($\alpha > 0.60$, Table 4). In two studies,^{51,52} the reliability turned out to be weak ($\alpha < 0.60$) and in one the denial category contained too many items.⁵³ Six studies failed to describe or measure the psychometric qualities, for example when a single item was used.^{21,34,54-57} The results from 17 papers with acceptable reliability for the denial measurement will be described. As customary we subdivided quality of life in physical functioning, psychological functioning and social functioning.

Table 3 Denial over time in longitudinal studies

<i>Authors + Year</i>	<i>Type of Cancer</i>	<i>Sample Size</i>	<i>Type of denial</i>	<i>Design</i>	<i>Pattern over time: results</i>
Weisman 1976	Mixed, newly diagnosed	163	DD	Follow-up-intervals 4-6 weeks, during 6 months	During the 6-months period: 45 % presented a mixed profile, fluctuating between varying degrees of acceptance and denial. 2% persistent deniers
Morris <i>et al.</i> 1977	Breast, newly diagnosed, operable	T1:63 T2:53 T3:45	DI	Months after operation: T1: 3 T2: 12 T3: 24	T1: 16% T2: 11% T3: 7 % A non significant trend of diminishing denial in the course of the disease
Thomas <i>et al.</i> 1988	Colorectal cancer, newly diagnosed	T1: 68 T2: 52 T3: 36	DD + DI	T1: post surgery T2: 3 months T3: 12 months	Stable pattern
Filipp 199	Mixed time since diagnoses 1-840 weeks	T1: 332 T4: 202 T5: 145	DA	Longitudinal follow-through, 2 years. T1-T4 intervals 3 to 4 months, T5: 2 years	Decrease over time $P < 0.01$
Carver <i>et al.</i> 1993	Breast, stage I -II	T1: 59 T2: 59 T3: 56 T4: 52 T5: 52	DD, DI	T1: 1 day presurgery T2: 7-10 days post surgery T3: 3 months T4: 6 months T5: 12 months	DD : Decrease $P < 0.01$ DI: decrease $P < 0.07$
Heim <i>et al.</i> 1993	Breast stage I-IV	74	DI, DA	Prospective longitudinal 3-5 years descriptive. Time in 8 predescribed illness stages	Stable over disease phases, increase in terminal phase
Culver <i>et al.</i> 2002	Breast, stage I-II	131	DD, DI	T1: 2 days presurgery T2: 7-10 days postsurgery T3: 3 months T4: 6 months T5: 12 months	DD: decrease $P < 0.05$ DI: decrease $P < 0.05$

Denial and physical functioning

Denial may lead to the patient experiencing fewer physical complaints, since in non-deniers emotional reactions are likely to amplify noxious physical symptoms. Indeed in three papers the effect of denial on physical functioning was found to be positive.^{40,45,58} Patients in the study of Ward et al.⁴⁰ reported fewer and less severe chemotherapy-induced side-effects. Manne et al.²⁹ reported no relationship between denial of impact and physical symptoms, but a combination of denial of affect and behavioural escape was related to having more physical symptoms in breast cancer patients undergoing adjuvant chemotherapy.

Denial and psychological functioning

Psychological functioning, mostly assessed as distress, was related to denial in 16 studies (table 4 and 5).

In two studies the combination of denial of diagnosis and denial of impact^{46,59} and in one denial of diagnosis⁴⁷ were related to increased distress. Orr,¹⁸ on the other hand, found no relation of distress and denial of diagnosis.

Denial of impact was related to less distress in seven studies^{18,25,29,58,60,61,62} and to increased distress in three studies.^{59,63,64} In two studies no relation was found.^{47,65}

In two studies denial of affect was related to poorer psychological functioning.^{25,65} In Orr's study a positive effect of denial of affect on distress was found and in Heim et al.'s study⁴⁸ denial of impact and affect together caused increased wellbeing. In four studies behavioural escape alone or combined with denial of affect turned out to have a negative effect on psychological functioning.^{25,29,66,67}

Manne et al.⁶⁴ found no effect of denial of illness in patients with early stage cancer and a negative effect in late stage cancer patients. Stanton et al.,⁵⁹ on the other hand, found preoperative avoidance to be related to higher distress at three months, but after one year such a relationship could no longer be detected.

In the studies in which denial of impact was related to improved psychological functioning, the concepts of denial used represent active strategies of realising that one has cancer, but choosing not to let the illness control life, trying to brush the illness aside and instead create a positive outlook (Table 5). Examples of the concepts of denial of diagnosis and denial of affect and behavioural escape found to be related to poorer psychological functioning are: refusing to believe it has happened, hoping a miracle will happen, making oneself feel better by drinking, eating and smoking, giving up the attempt. These strategies can be characterised as passive and having a negative connotation. Patients seek escape by using stimulants, and experience a sense of loss of control, or feel fatalistic and helpless. These strategies share features of depression and seem to be, by definition, maladaptive.

Tabel 4 Denial and quality of life

Author + Year	N= + time of assessment	Type of denial and reliability	Qol or variable of Qol	Results
Meyerowitz et al. 1983	113; time since diagnosis < 3½ yrs no recurrence	DI $\alpha = .81$	<i>psychological functioning:</i> distress	DI $\uparrow$ distress $\downarrow$ $p < .01$
Orr 1986	51; newly diagnosed	DD $R \geq .95$ DI $r = .78$ DA $r \geq .95$	<i>psychological functioning:</i> distress <i>social functioning:</i> social adjustment	DD $\uparrow$ distress n.s. social adjustment $\downarrow$ $p < 0.001$ DI $\uparrow$ distress $\downarrow$ social adjustment $\uparrow$ $p < 0.001$ DA $\uparrow$ distress $\downarrow$ $p < .001$ social adjustment $\uparrow$ $p < .01$
Manuel et al. 1987	35; newly diagnosed	DI $r = 0.90$	<i>psychological functioning:</i> distress	DI $\uparrow$ distress $\downarrow$ $p < .05$
Ward et al. 1988	67; time since diagnosis: 1- 221 months	DI $\alpha = .88$	<i>physical functioning:</i> chemo-therapy induced side-effects	DI $\uparrow$ side-effects: number $\downarrow$ $p = .03$ severity $\downarrow$ $p = .07$
Dunkel-Schetter et al. 1992	668; from newly diag- nosed to sev- eral years ago	DI $\alpha = .79$ DA $\alpha = .78$ BE $\alpha = .74$	<i>psychological functioning:</i> distress	DI $\uparrow$ distress $\downarrow$ $p < .05$ DA $\uparrow$ distress $\uparrow$ $p < .05$ BE $\uparrow$ distress $\uparrow$ $p < 0.001$
Carver et al. 1993	59; newly diagnosed or second opinion	DD $\alpha = .79$ DI $\alpha = .58$	<i>psychological functioning:</i> distress	DD $\uparrow$ distress $\uparrow$ $p < .001$ DI $\uparrow$ distress n.s.,
Stanton & Snider 1993	36; newly diagnosed	DI $\alpha \geq .70$ DA $\alpha \geq .70$ BE $\alpha = 0.51$	<i>psychological functioning:</i> distress	DI $\uparrow$ distress n.s. DA $\uparrow$ distress $\uparrow$ $p < .05$
Manne et al. 1994	43; receiving adjuvant chemotherapy	DI $\alpha = .69$ DA-BE $\alpha = .70$	<i>physical functioning:</i> physical symptoms <i>psychological functioning:</i> distress	DI physical symptoms n.s. DA-BE $\uparrow$ physical symptoms $\uparrow$ $p < .05$ DI $\uparrow$ distress $\downarrow$ $p < .01$ DA-BE $\uparrow$ distress $\uparrow$ $p < .01$

Table 4 continued

Author + Year	N= + time of assessment	Type of denial and reliability	Qol or variable of Qol	Results
Heim et al. 1997	74; newly diagnosed	DI-DA $\alpha \geq .75$	<i>psychological functioning: wellbeing</i>	DI-DA $\uparrow$ distress $\downarrow$ $p < .05$
			<i>social functioning</i>	DI-DA: social functioning n.s.
Osowiecki & Compas 1998	83; time since diagnosis mean 10 weeks, sd=5.84	DI $\alpha = .73$	<i>psychological functioning: distress</i>	DI $\uparrow$ distress $\uparrow$ $p < .001$
Hack & Degner, 1999	70; time since diagnosis: 1,5- 6 months	DA-BE $\alpha = .66$	<i>psychological functioning: distress</i>	DA-BE $\uparrow \rightarrow$ distress $\uparrow$ $p < .01$
Brown et al. 2000	125; metastatic melanoma	DI $\alpha = 0.65$	<i>QOL: physical functioning</i>	DI $\uparrow$ physical functioning $\uparrow$ $p < 0.001$
			<i>Psychological functioning: effort to cope and mood</i>	DI $\uparrow$ effort to cope $\uparrow$ $p < 0.001$ DI $\uparrow$ mood $\uparrow$ $p < 0.001$
Butow et al. 2000	99; time since diagnosis $\pm$ 4 months	DI $\alpha = 0.65$	<i>QOL: Physical + emotional functioning combined</i>	DI $\uparrow$ QOL $\uparrow$
Manne et al. 2000	189; time since diagnosis: 80% < 6 months, 20%: $\frac{1}{2}$ - 13 yrs	DI $\alpha = .80$	<i>Psychological functioning: distress</i>	3 months later: early disease stage: DI: distress n.s. advanced disease stage: DI $\uparrow$ distress $\uparrow$ $p < .001$
Culver et al. 2002	131; newly diagnosed	DD, DI average $r = 0.92$	<i>Psychological functioning: distress</i>	DD $\uparrow$ distress $\uparrow$ $\beta \geq 0.17$ DI $\uparrow$ distress $\uparrow$ $\beta \geq 0.18$
Stanton et al. 2002	70; newly diagnosed	DD+DI $\alpha = .67$	<i>psychological functioning: distress</i>	Preoperative DD+ DI: At 3 months: DD+DI $\uparrow$ distress $\uparrow$ $p < .05$, At 1 year: DD+DI: distress n.s.
Hack & Degner 2004	55; 3 years after baseline	DA+BE $\alpha = .66$	<i>psychological functioning: distress</i>	Baseline DA+BE: 3 years later: distress $\uparrow$ $p < .05$

Denial and social functioning

In two papers the effect of denial on social functioning was studied.^{18,50} One,¹⁸ found avoidance of information to be related to poorer social functioning, while denial of feelings was found to be related to better social functioning. The other⁵⁰ did not find denial of impact and affect to be related to social functioning over time nor at different illness stages.

DISCUSSION

In summary of the findings of this explorative review, three conclusions can be drawn:

Firstly, from a historical point of view the concept of denial developed from psychoanalytical roots with the emphasis on the pathological nature of the phenomenon to become a comprehensive expression for an adaptive strategy for protection against distressing events or feelings. These both pejorative and alleviating connotations are reflected in the variety of concepts of denial used in research and clinical practice over the last decades.

Secondly, the prevalence of denial in cancer patients seems to be related to the concept and the instrument used. Different operationalisations and instruments have been chosen in the different studies. While this is confusing, it does reflect the multiversity of the concept of denial. Besides, conclusions are complicated by the fact that the instruments used do not always have proven validity. When dividing the definitions of denial in four types the overlap between categories, e.g. the overlap between denial of impact and denial of affect could not always be made clearly. This is understandable, since mostly thinking and feeling are connected.

Thirdly, denial seems to be related to demographic variables such as age and ethnic or cultural background. The relationship between denial and gender is still unclear, men possibly are more likely to deny during the terminal phase of illness. Type of tumour does not seem to be related to denial but later disease stages seem to be associated with a higher prevalence of denial. The investigation of the prevalence of denial over time during the course of the disease, however, is complex and requires more attention, particularly by means of longitudinal studies.

Finally, based on this literature review, whether denial influences the quality of life in cancer patients can only be partially answered. Too few studies investigated the effect of denial on physical and social functioning for any conclusion to be drawn.

Psychological functioning is studied more often. The effect of denial on psychological functioning is, at least in part, predicted by the concept used.

Poorer psychological functioning is related to passive escape-strategies. At the same time, more active distractive strategies to create a positive outlook seem to be associated with a reduction in distress. This is in line with the original conceptual distinction described above. In psycho-analytic theory, denial

was considered to be primitive and maladaptive, whereas when viewed as an active coping strategy, it may well be adaptive in severely ill cancer patients.

Based on our explorative review we recommend that future research into the prevalence of denial in cancer patients is based on a clear concept, using a measurement instrument with good psychometric properties with repeated measurements over time, paying particular attention to the terminal phase, and with careful recording of background variables.

Table 5 *The direction of the effect of denial on psychological functioning*

<i>Denial and improved psychological functioning</i>	
Author	Wording of the denial items
Meyerowitz et al. 1983	DI: minimization of cancer's impact
Orr 1986	DI: avoidance of speaking about cancer or death DA: avoidance of negative feelings
Manuel et al. 1987	DI: trying to forget the event or staying away from reminders of it
Dunkel-Schetter et al. 1992	DI: didn't let it get to me, tried to keep my feelings to myself, refused to think about it, made light of it, went on as if it were not happening
Manne et al. 1994	DI: create a positive outlook or detach from the situation
Heim et al. 1997	DI-DA: minimizing, keeping one's poise and self-control, not admitting feelings adequate to situation, discontinuing or not undertaking necessary medical action
Brown et al. 2002	DI: having cancer is not making any difference to my life at all; I try not to let people know about my cancer
Butow et al. 2002	DI: cancer is not impacting on social, work and family life and is not a substantial cause of anxiety or distress.
<i>Denial and poorer psychological functioning</i>	
Dunkel-Schetter et al. 1992	DA: hoped a miracle would happen, prepared for the worst, prayed, went along with fate, slept more than usual, depended mostly on others to handle things BE: Avoided being with people, tried to make myself feel better by eating, drinking, smoking or drug use,
Carver et al. 1993	DD: I've been refusing to believe that is has happened
Stanton & Snider 1993	DA: Tried to keep my feelings from interfering with other things too much
Manne et al. 1994	DA-BE: wished the situation would go away or somehow be over with
Osewiecki & Compass 1998	DI: I try not to think about it, I try to remove it from my memory
Hack & Degner 1999	DA-BE: resigned acceptance, alternative rewards and emotional discharge
Manne et al. 2000	DI: I tried not to think about it, I tried to remove it from memory, I stayed away from reminder of it
late-stage cancer	
Culver et al. 2002	DD: I say to myself: this isn't real/I refuse to believe that it has happened/ DI: I turn to work or other substitute activities to take my mind off things/ I go to movies
Stanton et al. 2002	Composite:
avoidance preoperative distress at 3 months	DD: I say to myself: this isn't real/I refuse to believe that it has happened/I act as though is hasn't even happened DI: I turn to work or other substitute activities to take my mind off things/ I daydream about things other than this, I go to movies BD ^a : I admit to myself that I can't deal with, and quit trying/I give up the attempt to get what I want

Table 5 *continued*

Author	Wording of the denial items
<i>Denial and poorer psychological functioning, continued</i>	
Hack & Degner 2004	DA-BE: feelings that time would not make any difference, the only thing to do
avoidance at the time of	was wait, I realized I had no control, I think that the outcome would be
diagnosis, distress 3 years	divided by fate, I expect the worst possible outcome, I lost hope that thinks
post-diagnosis	ever would be the same, I accept that nothing could be done
<i>Denial and no effect on psychological functioning</i>	
Stanton & Snider 1993	DI: didn't let it get to me, tried to keep my feelings to myself, refused to think
	about it, made light of it, went on as if it were not happening
Carver et al. 1993	DI: I've been going to movies, watching TV, or reading, to think about it less
Manne et al. 2000	DI: I tried not to think about it, I tried to remove it from memory, I stayed
(early stage cancer)	away from reminder of it
Stanton et al. 2002	DD+ DI: composite of mental disengagement, behavioural disengagement and
avoidance preoperative	denial
distress at 1 year	

^a Not included in the denial categories

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Chapter 4

The Denial of Cancer Interview: development and first assessment of psychometric properties in lung cancer patients

Martina S. Vos, Hein Putter, Amber Leurs, Harry G.M. Rooijmans, Hanneke C.J.M. de Haes, Hans C. van Houwelingen

SUMMARY

Based on Weissman and Hackett's comprehensive definition of denial, a semi-structured interview was developed to measure denial in cancer patients. The Denial in Cancer Interview (DCI) covers both the patients' recount of their illness experience and the expert's impression of the level of denial in the patient story. This paper describes the development and first psychometric analyses of the instrument.

The development of the DCI was based on clinical observation, the expert opinion of eight specialised psychiatrists as well as three small pilot studies to assess feasibility. The DCI is composed of two parts: a semi structured interview consisting of nine specific items to be answered by the patient and two items covering the interviewer's clinical impression of the patient's type and level of denial. Follow-up interviews were held at 8, 16 and 32 weeks after the baseline assessment (T2-T4).

To measure the inter-rater reliability, interviews were recorded and rated independently by one interviewer and one of the study's co-workers.

One hundred and ninety-five consecutive newly-diagnosed lung cancer patients were interviewed. The internal consistency of the DCI (Cronbach's α) was 0.84 at first interview and 0.85, 0.82 and 0.83 at T2-4 respectively. The inter-rater agreement was good for the DCI overall and the Patient's Assessment scale, and satisfactory for the clinical impression items. Content validity was supported by clinical observation, in depth open interviewing and expert opinion.

The DCI proved to be a feasible and reliable instrument for measuring denial in lung cancer patients. Further testing in other oncology settings will provide insight in wider applicability

INTRODUCTION

Denial in cancer patients has long been a topic of discussion. There is general agreement on the clinical relevance of the concept of denial as reflected in the numerous publications on the subject. On the one hand, denial may protect a cancer patient against overwhelming feelings of anxiety and despair. If so, denial can be seen as an adaptive coping strategy. The disadvantage of denial, however, may be that communication problems between the patient and family members or caregivers result when those prefer to talk about the illness and its consequences. For instance, physicians may face difficulties when speaking with the denying cancer patient about the planning of treatment. Denial can cause misunderstandings between doctor and patient, e.g. about the seriousness of the illness and the prognosis. Some authors¹ have even suggested that 'maladaptive denial of physical illness' should be included as a new diagnosis in the DSM IV. Therefore, it is important to gain further insight in the phenomenon of denial and better understand the mechanism behind denial in cancer patients.

However, an investigator intending to assess denial in cancer patients is confronted with the multiple interpretations of the concept.^{2,3} Over the years the concept of denial has been defined based on different theoretical, clinical and practical assumptions.⁴ In their review of the assessment of denial in cancer Moyer and Levine⁵ conclude that 'the theoretical and operational definitions that have described denial reveal a lack of consensus as to whether denial is unconscious versus conscious, a trait versus a state, indicative of psychological disturbance versus a normal response to serious illness, or a broad versus a narrow concept'. In the defensive functioning scale of the DSM-IV denial is defined within the disavowal level, meaning that the unpleasant or unacceptable stressors are kept out of awareness: 'The individual deals with emotional conflict or internal or external stressors by refusing to acknowledge some painful aspects of external reality or subjective experience that would be apparent to others'.⁶ The initial definition of Weissman and Hackett contains the multi-formity of the concept of denial in a pragmatic and comprehensive way.^{7,8} They describe denial as covering different elements 'the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects'. Moyer and Levine⁵ present a review of instruments to measure denial in oncology. These include interviews, clinical ratings, self-report instruments, behavioural measures and indirect assessments. The authors underline that interviews, clinical ratings, behavioural measures and indirect measures tend to rely on what individuals do not admit or do not do. On the other hand, self-report checklists rely on and accept at face value what individuals are aware of or are willing to acknowledge themselves. In other words, if wanting to measure denial in a comprehensive manner, as suggested for example in the definition mentioned above, observation and interpretation are needed.

We chose to follow up on the definition of Weissman and Hackett but found no suitable instrument. The Hackett and Cassem Denial Scale,^{7,9,10} based on this definition focuses specifically on hospitalised patients with coronary heart disease. A myocardial infarction is an acute event, in contrast to cancer which tends to develop slowly. Furthermore, the prognosis of some cancer types such as lung cancer is worse than that of a myocardial infarction and cancer treatment is likely to be more physically and emotionally invasive. The same objections rise when considering the Levine Denial of Illness Scale,¹¹ and the Havik and Mæland Questionnaire^{12,13} for assessing denial in oncology patients. Also, several of the instruments available to measure denial in cancer patients are either based on a limited concept of denial,^{14,15} or non-validated¹⁶⁻¹⁸ or employ a single-item measure only.¹⁹ Finally, some measurement instruments are based on coping questionnaires in which one or more denial or avoidance subscales are incorporated, such as the Ways of Coping Inventory,^{20,21} the Ways of Coping – Cancer version with the subscales distraction, cognitive and behavioural escape-avoidance,²² and the COPE²³ with the denial and self-distraction subscales. These instruments are self-report scales, in which denial is one aspect of a coping repertoire. As mentioned above, self-report checklists tend to accept at face value what individuals are aware of or are willing to acknowledge.⁵ Since by definition there are two sides to denial, namely the perception of the denier on the one hand and the external reality apparent to others on the other, the limitations of self-report checklists in assessing denial are evident.

We have assessed denial in lung cancer patients. It seems likely that lung cancer patients have more reasons to deny than other cancer patients because: a) patients may be aware of the role of their smoking behaviour in the development of the disease; Silberfarb et al.²⁴ indeed suggested that lung cancer patients might deny more because of the self-induced character of the illness; b) lung cancer patients often suffer from dyspnoea, which severely limits functioning and may be extremely burdensome and frightening^{25,26} and, c) the 5-year survival rate is relatively low, implying that lung cancer patients have limited time to adapt to the impact of their illness. Whether the level of denial is influenced by these differences is unknown.

In the absence of a well-accepted instrument, we have developed the Denial of Cancer Interview (DCI), to investigate denial of illness in lung cancer patients, with the intention of measuring denial following the comprehensive definition given by Weisman and Hackett^{7,8,10} In the DCI, the patients' recounts of their illness situation as well as the expert's clinical impression thereof are addressed. The aim of this paper is to describe the development and the first psychometric analyses of the instrument.

PATIENTS AND METHODS

Instrument development[†]

To develop the instrument patient questions were generated by clinical observation in lung cancer consultations as well as 10 open interviews with lung cancer patients. The questions were formulated indicating, at face, the patient's denial of facts, feelings or impact of their illness.

Content validity is ensured by representing in the instrument the elements covered in the definition of the concept to be measured.²⁷ It was established by asking the experts' opinion of eight psychiatrists actively involved in oncology to judge the content and the formulation of the items. As stated by Rubinowitz and Peirson²⁸ denial most often is diagnosed based upon findings of a clinical examination and none of the assessment methods is foolproof. Due to the lack of a gold standard we asked thus the expertise of clinical professionals to establish the content validity of our instrument. The agreement of these psychiatrists about the items' relevance for denial was 78% and 86% concerning the wording of the items. Based on these judgements, nine specific items were selected for the first pilot study.

Since, by definition, denial involves a difference between reality and the patient's perception of reality, a third party's assessment of the patient's views and feelings relative to the real situation is needed when rating denial. Therefore, a question covering the interviewer's clinical impression of the type as well as the overall level of denial was involved in the instrument.

The revised list comprising nine specific items to be answered by the patient and two clinical impression expert ratings was tested in three pilot studies with 9, 16 and 14 lung cancer patients, respectively. The feasibility of the instrument proved to be good. The participants did not show any difficulty in answering the questions. In fact, several participants expressed their appreciation of having the possibility to speak extensively about their illness experience. Based on these pilot studies, the nine specific items were adapted if they showed poorer differentiation, lower correlation with the other items or lower inter-rater agreement.

The final composite of items, the Denial of Cancer Interview (DCI), including the questions to be answered by the patient and the interviewer judgement items, is presented in appendix A.

Reliability study

The reliability study was part of a larger study investigating the effect of denial on quality of life in lung cancer.

[†] Data not extensively described. Complete dataset available on request

Design and procedures

Consecutive lung cancer patients were recruited from two pulmonary disease out-patient clinics in The Hague, the Netherlands. Inclusion criteria were: 1) newly-diagnosed primary lung cancer, irrespective of histological type, stage or treatment, 2) age > 18 years, 3) knowledge of the Dutch language and 4) written informed consent. The exclusion criterion was the presence of a serious cognitive disorder.

In the Netherlands doctors are legally obliged to inform their patients about the diagnosis. Still, to further ensure adequate information giving, the chest physicians agreed to explicitly mention the words “cancer” or “malignant tumour” when breaking the bad news. The chest physician or the oncology nurse invited the patient to participate in the study. If the patient consented, the research assistant made an appointment for the interview and sent written information. The patient was asked to sign the informed consent form before the first interview took place.

Four interviews were planned with each patient: within 8 weeks after diagnosis (T1) and at 8, 16, and 32 weeks after the first interview (T2-T4). Three interviewers were involved: the primary investigator (MV, psychiatrist, 98 interviews), a research psychologist (AL, 75 interviews), and a psychosocial therapist (CvdW, 22 interviews).

The instrument: The Denial of Cancer Interview

As described, the DCI is a semi-structured interview consisting of three parts (see Appendix A). The nine specific items to be answered by the patient cover knowledge of diagnosis and prognosis, talking to others, expectations about the effect of treatments, and facts and feelings about the impact of the illness. These items form the ‘*patient assessment scale*’ (PAS). The interviewer scored the answers on three point scales. Sometimes the answers turned out to be unclear at hindsight, explaining the presence of some missing data. Missing data of at most 3 items are imputed by replacing them with the average of the non-missing items. The PAS is scored as the sum-score of these nine items and transformed into a six-point scale (1-6) to make it comparable to the scores of the interviewers’ *clinical impression of the patient’s type* (CIT) and *clinical impression of the overall level of denial* (CIL). The interviewer’s clinical impression of type of denial (CIT) has 6 ordered categories scored as 1-6, running from ‘No denial’ to ‘Unconscious denial’. The interviewer’s clinical impression of the level of denial (CIL) ranges from 1 (= no denial) to 7 (= maximum denial). The three scales are combined to provide the overall DCI score by summing the scores of the three separate scales, resulting in a final scale running from 3-19.

Analysis

The semi-structured interviews were recorded on videotape or audiotape, in case of refusal of the patient to be filmed. During a training phase, the first 44 interviews were rated by all three interviewers and the ratings were compared

and discussed regularly. Consensus guidelines were established regarding the interpretation of patient answers. The scores gathered during this training phase are included in the assessment of consistency and frequency distributions, but have not been used to establish inter-rater reliability.

Simple descriptive statistics are given of all items and (derived) scales.

The structure of the instrument was assessed using the scoring of the interviewer. The consistency of the patient's assessment scale was evaluated 1) by using exploratory factor analysis, 2) by computing Cronbach's α and inspecting the correlation between each item and the sum of the remaining items and 3) by visually checking the ordinal relation between each individual item and the other items. The consistency of the total DCI scale was checked by computing the correlations between the three subscales and by computing Cronbach's α .

The interrater reliability was determined by comparing the scores of the actual interviewer and the control scores of one of the other interviewers. Cohen's kappa was used for the individual items of the PAS and correlations between interviewer and non-interviewer for the DCI and its three components: PAS, CIT and CIL.

RESULTS

Patient characteristics and interviews

Of 244 eligible patients 195 (response = 80%) were interviewed. The interviews lasted 30- 45 minutes. Patient characteristics of these 195 patients are given in Table 1. They did not differ significantly from the 49 patients that refused (data not shown). The numbers of participants at T2 – T4 were 151, 114 and 79, respectively. The overriding reasons for drop-out were death or being too ill.

Table 1 *Patient Characteristics (N=195)*

<i>Characteristic</i>		
Gender	Male	115 (59%)
	Female	80 (41%)
Age	Mean (SD)	65.5 (11.6)
	Range	20-89
Type of tumour	NSCLC	139 (75%)
	SCLC	35 (19%)
	Other	12 (6%)
	Unknown	9
Performance Status (Zubrod Index)	0	58 (30%)
	I	96 (50%)
	II	26 (13%)
	III/IV	14 (7%)
	Unknown	2

Of the 195 interviews at T1, 44 were rated and discussed by the three interviewers. Of the remaining interviews (n=151) 111 (74%) were rated indepen-

Figure 1 *a. Frequency distribution of the sum score for the 159 patients without missing items.*
b. Frequency distribution, for all 195 patients, of the categorized sum score (Patient's Assessment Scale); dark shading represents the 159 patients without missing items, light shading represents the 36 remaining categorized sum scores obtained by imputing missing items.

dently by another interviewer. In the remaining 40 cases recordings had failed because of patient refusal, equipment failure, and errors such as forgetting to push the recording button.

Frequency distribution

The results in this subsection concern all 195 interviews at T1 scored by the interviewer, unless indicated otherwise.

The frequency distribution, number of missing data, mean and standard deviation of the nine items of the PAS are given in Table 2.

One or more items could not be scored in the interviews of 36 patients. Bar charts of the sum score of the other first interviews (n=159) are given in Figure 1a. None of the patients had more than 3 missing items. Figure 1b shows the bar chart of the categorized PAS after imputation of the missing values.

Table 2 Descriptive statistics (n=195) for the nine items of the Patient's Assessment scale (PAS); frequency (percentage) of 0, 1, and 2 scores.

Item	Frequency (percentage)			Number missing	Mean	SD
	0	1	2			
1	179 (92%)	15 (8%)	0 (0%)	1	0.08	0.27
2	163 (84%)	19 (10%)	11 (6%)	2	0.21	0.53
3	58 (30%)	111 (57%)	26 (13%)	0	0.84	0.64
4	23 (12%)	44 (23%)	128 (66%)	0	1.54	0.70
5	131 (67%)	54 (28%)	10 (5%)	0	0.38	0.58
6	145 (78%)	24 (13%)	16 (9%)	10	0.30	0.62
7	124 (72%)	23 (13%)	25 (15%)	23	0.42	0.73
8	86 (44%)	59 (30%)	50 (26%)	0	0.82	0.82
9	70 (37%)	25 (13%)	95 (50%)	5	1.13	0.92

The frequency distributions of the CIT and the CIL as well as the total DCI score are given in Figure 2.

Descriptive statistics of the three elements of the DCI are given in Table 3.

Table 3 Descriptive statistics of all DCI scales (n=195)

Scale	Mean	SD
Patient Assessment Scale (PAS)	5.79	3.00
Categorized PAS	2.75	1.19
Clinical Impression of Type of Denial (CIT)	1.86	1.24
Clinical Impression of Level of Denial (CIL)	1.96	1.01
DCI	6.57	3.01

Figure 2 Frequency distributions of a. the clinical impression of type of denial (CIT), and b. the level of denial (CIL), and c. the DCI (n=195)

Internal consistency

The results in this subsection concern all 195 interviews at T1 scored by the interviewer, unless indicated otherwise.

Patient Assessment Scale

A minimum condition for internal consistency is the ordinality of the relation between the items and the sum score. This was checked by plotting the average

Table 4 *Item-rest correlations and Cronbach's α with item deleted for each of the items in the PAS (n=195).*

<i>Item</i>	<i>Item-rest correlation</i>	<i>α with item deleted</i>
1	0.18	0.57
2	0.33	0.53
3	0.37	0.52
4	0.22	0.56
5	0.14	0.58
6	0.45	0.50
7	0.25	0.55
8	0.21	0.57
9	0.33	0.53
		Overall alpha was 0.58

of the sum of the remaining items against the item values for each item separately. These graphs (not shown) showed monotonic relations and confirmed the conjectured ordinality.

Cronbach's α for the PAS and item-rest correlations are shown in Table 4. The correlations between each of the items and the rest are moderate. When an item is deleted, the values for Cronbach's α remain quite stable and do not differ from the α -value for all items in the sum score. An explanatory factor analysis (not shown) also showed that the correlations between the items are not very high but that no clear subgroups of items could be distinguished. The $\alpha = 0.58$ at T1 justifies the inclusion of the subscale in the DCI.

Clinical impression of Type of Denial (CIT), Clinical Impression of Level of Denial (CIL) and Denial of Cancer Interview (DCI)

Visual inspection (not shown) showed no violation of monotonicity in the relation between CIT and CIL. Correlations of the elements and the final DCI scale are shown in Table 5a and the reliability analysis in Table 5b. Reliability for the DCI was good, with a Cronbach's α value of 0.84 at T1. At T2-4 Cronbach's α was 0.85 (n=151), 0.82 (n=114) and 0.83 (n=79), respectively, indicating good consistency also at follow-up visits.

Table 5a *Correlations of the subscales and DCI (n=195)*

	<i>Type of denial (CIT)</i>	<i>Level of denial (CIL)</i>	<i>Patient's Assessment scale (PAS)</i>	<i>DCI</i>
CIT	-	-	-	-
CIL	0.76	-	-	-
PAS	0.57	0.61	-	-
DCI	0.89	0.89	0.84	-

Table 5b *Item-rest correlations and Cronbach's α with element deleted for each of the items in the DCI*

<i>Instrument element</i>	<i>Correlation</i>	<i>α with element deleted</i>
CIT	0.73	0.75
CIL	0.78	0.73
PAS	0.63	0.85
		Overall $\alpha = 0.84$

Inter-rater reliability

The results of this subsection are based on 111 interviews at T1, scored both by the interviewer and independently by another rater (non-interviewer).

PAS

The agreement between the interviewer and the other scorer for the PAS is shown in table 6. The agreement is satisfactory, with the rater having little effect on the rating.

Table 6 *Agreement between interviewer and non-interviewer for the items in the PAS. Ratings of the interviewer are in the rows, those of the non-interviewer in the columns. Based on 111 interviews at T1 after the initial training phase*

Item 1 (kappa=0.85)				Item 2 (kappa=0.67)				Item 3 (kappa=0.87)			
	0	1	2		0	1	2		0	1	2
0	12	1	0	0	96	2	0	0	29	2	0
1	1	16	0	1	3	4	0	1	2	60	2
2	0	2	78	2	0	2	3	2	0	2	14
Item 4 (kappa=0.92)				Item 5 (kappa=0.93)				Item 6 (kappa=0.65)			
	0	1	2		0	1	2		0	1	2
0	12	1	0	0	81	1	0	0	75	4	0
1	1	16	0	1	0	24	1	1	2	6	6
2	0	2	78	2	0	1	3	2	1	1	8
Item 7 (kappa=0.59)				Item 8 (kappa=0.88)				Item 9 (kappa=0.89)			
	0	1	2		0	1	2		0	1	2
0	57	10	2	0	36	1	0	0	43	0	0
1	3	10	1	1	3	33	2	1	1	8	1
2	2	2	11	2	1	2	32	2	2	3	50

DCI

The correlation between interviewer and non-interviewer for the subscales and the total DCI are given in Table 7. Table 7 also compares the means between interviewer and non-interviewer. As shown a relatively high inter-rater agreement was found for the PAS. The correlation for CIT and CIL is slightly lower, but remains satisfactory.

Table 7 Means (SD) of scales and DCI for interviewer and non-interviewer, and correlation between interviewer and non-interviewer. Based on 111 interviews at T1 after the initial training phase.

Scale	Mean (SD) interviewer	Mean (SD) non-interviewer	Correlation between interviewer and non-interviewer
CIT	1.87 (1.28)	1.95 (1.40)	0.61
CIL	1.96 (1.02)	2.17 (1.14)	0.68
PAS	2.76 (1.14)	2.79 (1.15)	0.89
DCI	6.52 (2.91)	6.84 (3.10)	0.81

CONCLUSIONS AND DISCUSSION

Conceptual approach

Although denial is generally accepted to be a relevant clinical concept, its measurement is fraught with difficulties. Still, if the effects and/or background of denial are to be studied, a reliable instrument is needed. By its very nature, patient's own report is unable to catch the elements of denial that a patient prefers not to acknowledge. We therefore developed an instrument, the Denial of Cancer Interview, DCI, combining patient assessment with the interviewer's clinical impression. The DCI is based on the definition of denial of Weisman and Hackett¹⁰ 'the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects'. The advantage of such comprehensive definition is, that it prevents insolvable discussions concerning the boundaries of the concept of denial. As by definition a denier does not perceive something that others do perceive, a combination of the patient's judgements with an external observation is necessary. Therefore, in the first place, the DCI includes semi-structured items covering patient reports of information, the impact of the illness on daily life or the future and treatment expectations on the one hand. On the other hand, the expert's opinion on the type and level of denial displayed by the patient is asked for.

The development of the DCI was carried out in three phases: a preliminary stage to formulate the items and to find a first basis for (content-) validity, a triple-pilot phase to investigate and improve the feasibility and reliability of the instrument, and finally the testing of the reliability in a large lung cancer patient sample. The instrument turned out to be acceptable to patients, have adequate content validity and showed to be reliable over time.

Feasibility

Patients did not have any problem answering the DCI questions, nor did they object to their answers being recorded. The interviewers made the conditions as comfortable as possible for the patients, e.g., by interviewing them at home

or during chemotherapy in the hospital, depending on their preferences. Although this mode of assessment was fairly time-consuming for the interviewer, it avoided the dropout of patients who may have been only moderately motivated. As the interview largely covers the patients' illness experience, the interview may also be regarded as a general introduction to establishing a counselling relationship if necessary.

Reliability

The reliability of the DCI was tested by measuring the internal consistency and the inter-rater reliability.

All nine specific items contributed more or less equally to the Patient's Assessment Scale (PAS). The final DCI, consisting of three subscales [PAS, Clinical Impression of Type and Clinical Impression of Level of Denial (CIT & CIL respectively)], shows good internal consistency at the four measurement points (T1-T4: $\alpha = 0.84, 0.85, 0.82,$ and 0.83 respectively). The PAS has a slightly lower correlation with the total score than the two other subscales (see table 5a). Nevertheless, we believe it is an essential element of the final scale since it elucidates the patient's perspective which is required for the clinical impression to be scored by the interviewer in the two other scales. The inter-rater reliability of the subscales and the total scale was found to range from good (PAS) to reasonable (CIT and CIL). Overall, these results show the DCI to be a reliable instrument for measuring denial in lung cancer patients.

In fact, The DCI was tested based on assessments carried out shortly after diagnosis and 8, 16 and 32 weeks later. Given that selective non-response may occur over time, internal consistencies might have been different for different measurement points. However, in our study the Cronbach's α remained very good over time.

Content validity

The content validity of the DCI was established in the early phases of its development: first, by clinical observation and patient interviews, secondly, by inviting the expert opinion of psychiatrists working in oncology. While doing the interviews with 195 lung cancer patients over time, the interviewers trained have indeed been able to establish a level of denial in these patients.

It is interesting to note that the type and level of denial turned out to be highly related. The scale addressing the type of denial (see appendix) covers displaying 'No denial, Conscious denial of illness, Denial of affect, Denial of impact, Denial of impact and affect, Unconscious denial'. In other words, this typology represents an order which also seems to indicate an increasing level of denial. This may obviously be due to the interviewers bias but also seems to be clinically understandable.

Limitations of the study

Even though we developed a feasible and reliable instrument to measure denial in lung cancer patients, some study limitations should be mentioned. First, we were unable to ultimately validate the instrument due to the lack of a gold standard for the measurement of denial. As stated by Rabinowitz and Peirson²⁹ denial most often is diagnosed based upon the findings of a clinical examination and none of the assessments methods is foolproof. Our only reference available was the judgement of relevance of the specific items by the psychiatrists working actively with cancer patients.

Second, given the necessity to select the sample in a clinical situation, it is obviously impossible to interview patients who are unwilling to visit their doctor because they ultimately deny having cancer. This may have caused under representation of severe denial in the eventual patient sample and, as a consequence, some bias in the results.

Further research

The DCI was tested in a sample of lung cancer patients. Compared with other types of cancer, lung cancer is associated with special features: a) the awareness of patients of their own role in the development of the disease; b) patients suffer from increasing dyspnoea, and are therefore likely to be severely limited in their functioning,^{25,26} and c) the prognosis is poor.³⁰ Whether these differences will influence the nature and prevalence of denial and the reliability of the DCI when used in other cancer patient groups requires further investigation. When the individual items are examined, it seems plausible that they would be applicable to other cancer patients (see appendix). Item 9, however, which focuses on treatment expectation, is based on the assumption of a poor prognosis, especially for non-operable tumours. Lung cancer patients receiving chemotherapy or radiotherapy who answer that they expect 'complete recovery' are denying the seriousness of their illness. In some other types of cancer, such as chemotherapy for lymphoma, adjuvant chemotherapy for breast cancer patients or curative radiotherapy for head and neck cancer, the aim of the treatment is complete recovery. Item 9 may therefore not be applicable in cancer patients with a good prognosis, although this remains to be proven.

The DCI was tested in a sample of patients just after been diagnosed. Patient delay is likely to be more prevalent in those patients showing significant denial. Ideally, therefore, one would like to study patients prospectively, from the moment they first present with symptoms at the doctor's office, for example in general practice.

The ultimate aim of developing the DCI was to meet the need for a reliable instrument to measure denial, so as to facilitate investigation of the impact of denial on the quality of life in cancer patients. Whether the DCI is also suitable in clinical research, i.e. case finding, also requires further investigation.

Practice implications

The DCI can be used in future studies concerning denial in cancer patients. Particularly, the influence of denial on quality of life in cancer patients has to be investigated in more detail.

Besides, as Lazarus³¹ emphasizes: “denial is not a single act but a highly diverse set of processes that respond to different external and internal conditions” it is important to look at denial at different times in the course of the illness. The results of such investigations will eventually provide insight in denial and its background. They will then help us to adequately address denial in patients and communicate with them.

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DENIAL OF CANCER INTERVIEW (DCI)

DURING THE INTERVIEW: Items 1-9 are part of the PATIENT ASSESSMENT SCALE.

I.

Or: What did the pulmonologist tell you?

 $a.$

What do these results mean for you? Note answer

2.

Score	a. correct diagnosis and treatment	: 0
	b. minimising situation	: 1
	c. nothing	: 2

Note the expressions used by the patient to describe his/her illness.

b.

Who do you talk to about your illness? Note any answer that is given

3.

Or: Some people think about their illness all day, and others do not; what about you?

Score	a. continuously or large parts of day/night	: 0
	b. don't think about it for large parts of the day	: 1
	c. rarely, hardly ever	: 2

C.

Do you think about the cause of your illness? Note answer

4.

Score:	a. no	0
	b. reasonably well	1
	c. well	2

5.

Do you want to know all the details about what is wrong with you?

Score:	a. yes	: 0
	b. not exactly, just roughly	: 1
	c. no or only a little	: 2

d.

Clarify the response by asking what 'all the details' or 'not exactly' means.

6.

What are your plans for the next few months?

Score:	a. future expectation based on understanding of illness	: 0
	b. future expectation based on 'minimising' the illness as much as possible	: 1
	c. future expectation in which the illness has no place	: 2

7.

Are you receiving treatment at present? If yes, which treatment?

score:	a. no treatment
	b. radiotherapy
	c. chemotherapy
	d. waiting for an operation
	e. other (specify)

What do you expect from the effect of this treatment?

Score:	a. realistic expectations	: 0
	b. more positive expectations than those based on the facts, but not complete recovery	: 1
	c. complete recovery	: 2

e.

How do those around you respond to your illness? Describe answer.

f.

And how would you describe your own response? Describe answer.

8.

Does your illness affect your daily life? Please explain.

Score:	a. a lot	: 0
	b. moderately/somewhat	: 1
	c. scarcely/not at all	: 2

9.

Some people say that it is better to think about your illness as little as possible.
Do you agree?

Score	a. no	: 0
	b. somewhat/more or less	: 1
	c. yes	: 2

The sumscore is the sum of the scores 1-9. (*Missing items are replaced by the mean score of the non-missing items, with a maximum of three missing items. Alternatively, the sumscore is 9 times the mean of the non-missing items.*) The resulting score is transformed into a 6 point scale according to the following table.

<i>Sumscore (sum)</i>	<i>Patient's assessment scale</i>
$0 \leq \text{sum} \leq 2.5$	1
$2.5 < \text{sum} \leq 5$	2
$5 < \text{sum} \leq 7.5$	3
$7.5 < \text{sum} \leq 10$	4
$10 < \text{sum} \leq 12.5$	5
$\text{Sum} > 12.5$	6

AFTER THE INTERVIEW: to be assessed by the interviewer

Clinical impression of TYPE OF DENIAL:

1. No denial
2. Conscious denial of illness
3. Denial of affect
4. Denial of impact
5. Denial of impact and affect
6. Unconscious denial

Clinical impression of overall LEVEL OF DENIAL on a scale of 1-7

(1 = no denial, 7 = maximum denial)

ADDENDUM B

PREVALENCES OF THE ITEMS OF THE PATIENT ASSESSMENT SCALE OF THE DENIAL OF CANCER INTERVIEW (DCI)

1. What results did the pulmonologist give you with respect to the tests carried out?

Or: What did the pulmonologist tell you?

		<i>T</i> ₁ <i>n</i> (%)	<i>T</i> ₂ <i>n</i> (%)	<i>T</i> ₃ <i>n</i> (%)	<i>T</i> ₄ <i>n</i> (%)
a. accurate diagnosis	0	179 (93.2)	128 (88.3)	97 (89.0)	61 (83.6)
b. euphemism	1	15 (7.7)	16 (11.0)	12 (11.0)	11 (15.1)
c. not informed	2	–	1 (0.7)	–	1 (1.4)

2. What have you told others about your illness?

a. correct diagnosis and treatment	0	163 (84.5)	122 (80.8)	85 (74.6)	54 (70.1)
b. minimising situation	1	29 (9.8)	17 (11.3)	16 (14.0)	14 (18.2)
c. nothing	2	11 (5.7)	12 (7.9)	13 (11.4)	9 (11.7)

3. Are there times when you do not think about your illness? Or: Some people think about their illness all day, and others do not; what about you?

a. continuously or large parts of day/night	0	58 (29.7)	26 (17.2)	22 (19)	14 (17.5)
b. don't think about it for large parts of the day	1	111 (56.9)	80 (53)	54 (46.6)	39 (48.8)
c. rarely, hardly ever	2	26 (13.3)	45 (29.8)	40 (34.5)	27 (33.8)

4. Are you able to concentrate on other things without thinking about your illness?

a. no	0	23 (11.8)	12 (7.9)	9 (7.8)	5 (6.2)
b. reasonably well	1	44 (22.6)	27 (17.9)	29 (25)	11 (13.8)
c. well	2	128 (65.6)	112 (74.2)	78 (67.2)	64 (80)

5. Do you want to know all the details about what is wrong with you?

		<i>T</i> ₁ <i>n</i> (%)	<i>T</i> ₂ <i>n</i> (%)	<i>T</i> ₃ <i>n</i> (%)	<i>T</i> ₄ <i>n</i> (%)
a. yes	0	131 (67.2)	108 (73)	85 (74.6)	62 (77.5)
b. not exactly, just roughly	1	54 (27.7)	38 (25.7)	25 (21.9)	16 (20)
c. no or only a little	2	10 (5.1)	2 (1.4)	4 (3.5)	2 (2.5)

6. What are your plans for the next few months?

a. future expectation based on understanding of illness	0	145 (78.4)	101 (69.7)	62 (56.9)	54 (71.1)
b. future expectation based on 'minimising' the illness as much as possible	1	24 (13)	26 (17.9)	28 (25.7)	7 (9.2)
c. future expectation in which the illness has no place	2	16 (8.6)	18 (12.4)	19 (17.4)	15 (19.7)

7. Are you receiving treatment at present? If yes, which treatment? a. no treatment. b. radiotherapy c. chemotherapy d. waiting for an operation e. other (specify).

What do you expect from the effect of this treatment?

a. realistic expectations	0	124 (72.1)	91 (65.5)	65 (66.7)	51 (73.9)
b. more positive expectations than those based on the facts, but not complete recovery	1	23 (13.4)	27 (19.4)	15 (14.7)	5 (7.2)
c. complete recovery	2	25 (14.5)	21 (15.1)	19 (15.1)	13 (18.8)

8. Does your illness affect your daily life? Please explain.

a. a lot	0	86 (44.1)	68 (45.0)	34 (29.3)	24 (30.0)
b. moderate / somewhat	1	59 (30.3)	52 (34.4)	47 (40.5)	33 (41.2)
c. scarcely / not at all	2	50 (25.6)	31 (20.5)	35 (30.2)	23 (28.8)

9. Some people say that it is better to think about your illness as little as possible.

a. no	0	70 (36.8)	46 (30.5)	33 (29.2)	24 (30.8)
b. somewhat / more or less	1	25 (13.2)	23 (15.2)	20 (17.7)	13 (16.7)
c. yes	2	95 (50.0)	82 (54.3)	60 (53.1)	41 (52.6)

Chapter 5

Denial in lung cancer patients, a longitudinal study

*Martina S. Vos, Hein Putter, Hans C. van Houwelingen,
Hanneke C.J.M. de Haes*

SUMMARY

Although denial in cancer patients is well-known clinically, few studies investigating the prevalence of denial over time have been conducted.

The objectives of this study are to investigate the level of denial in lung cancer patients over time and the impact of socio-demographic and illness related variables on denial in these patients.

The level of denial was measured in 195 consecutive newly diagnosed lung cancer patients, using the Denial of Cancer Interview. Four assessments were conducted in eight months.

Socio-demographic data were collected during the interviews. Medical data were provided by the chest physicians.

Most patients (86.6%) displayed a low or moderate level of denial at baseline. A small number (3%) showed a high level of denial. The mean level of denial was lowest at baseline and increased over time.

Male lung cancer patients exhibited more denial than did female ones, and younger patients showed less denial than did the elderly. Shortly after diagnosis, patients with a lower level of education denied stronger than higher educated patients, and during the course of illness, both groups showed the same level of denial.

Based on these results the conclusion can be drawn that a certain level of denial has to be considered a normal phenomenon in lung cancer patients, part of the illness process that they undergo.

Whether the level of denial is related to adaptive or maladaptive coping remains to be investigated.

INTRODUCTION

Denial is a most relevant concept in cancer patients. Its clarification is in the interest of patients and physicians, because it is still unclear what it is and how to handle denial in the clinical situation.¹ The definition of denial has been subject to different theoretical trends.^{2,3} The concept is rooted in psychoanalytical theory which emphasizes the pathologic nature of the phenomenon. Over time, however, the term 'denial' has evolved into an all-encompassing expression denoting an adaptive strategy for protecting oneself against events or feelings that cause distress. In clinical studies the concept 'denial of illness' was introduced as a coping mechanism in physically ill patients rather than referring to a general defense mechanism.⁴ Some authors emphasize that denial should be distinguished from concepts like repression, suppression or avoidance.⁵⁻⁸ For clinical purposes investigators prefer to define denial as a broad term covering cognitive strategies minimizing the seriousness of disease.^{4,9,10,11,12}

Lazarus¹³ stressed that denial is a process: "... not a single act, but a highly diverse set of processes that respond to different external and internal conditions." It should not be seen as a discrete 'on-off' phenomenon, but rather as a continuum whereby different levels of denial can be seen in different patients and over time.^{14,15} It is therefore important to investigate denial, not just once, but at various points in time during the disease course. Data regarding denial in cancer patients over time from cross-sectional studies yielded inconclusive results.³ Some longitudinal studies were carried out in breast cancer,^{16,17,18} colorectal cancer,¹⁹ and mixed cancer patient populations.^{20,21} These studies seem to indicate that denial in cancer patients diminishes over time, but increases when death draws closer.

Although lung cancer is the predominant cause of cancer deaths,²² evidence regarding denial in lung cancer patients is limited. At the same time, lung cancer patients likely have more reason to deny than other cancer patients. First, they are usually aware of their own role as smokers in the development of the disease; this may result in stigma and shame. Second, they often suffer from dyspnea, which limits their functioning and may be extremely burdensome and frightening.^{23,24} Third, the 5-year survival rate is relatively low.²⁵ Thus, lung cancer patients have limited time to adapt to the impact of their illness. Indeed, Silberfarb et al.²⁶ suggested that lung cancer patients might exhibit greater denial because of the self-induced nature of their condition.

It is unclear whether socio-demographic or illness related factors are associated with denial in cancer patients. Denial and age seem to be related, but the relation between denial and gender is still unresolved.³

The objective of the present study is twofold: 1) to examine the level of denial in lung cancer patients over time and 2) to investigate the impact of socio-demographic characteristics as well as illness related variables on the level denial.

METHODS

Participants

Consecutive lung cancer patients were recruited from two outpatient lung disease clinics[†] in The Hague, Netherlands, between January 1, 2001 and December 1, 2003. Inclusion criteria were: a) newly diagnosed primary lung cancer, irrespective of histologic type, stage, or treatment; b) age > 18 years; c) diagnosis within the past two months; d) knowledge of the Dutch language; and e) informed consent granted in writing. Exclusion criteria were serious cognitive disorders and the patient being too ill to be interviewed.

The chest physician invited consecutive patients to participate in the study. Patients who agreed received documentation and were asked to sign the informed consent form before the first interview was conducted.

Design

In this longitudinal study, four assessments were planned: the first no more than 8 weeks following diagnosis (T1) and, subsequently at 8, 16, and 32 weeks after the first assessment (T2-T4). Each assessment consisted of a semi-structured interview of 30 to 45 minutes' duration and the completion of written questionnaires.

This research project was approved by the local ethical committees of the two hospitals involved in the study.

Measures

Denial was measured using the Denial of Cancer Interview (DCI), a semi-structured interview based on the definition devised by Weisman and Hackett:^{27,28} "the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects". The DCI is composed of three subscales, one based on nine specific items and two based on overall clinical impression scores. It was proven to have good psychometric properties.¹⁵ The nine specific items to be answered by the patient cover knowledge of diagnosis and prognosis, talking to others, expectations about the effect of treatments, and facts and feelings about the impact of the illness. The two clinical impressions scales cover the interviewer's judgment of the type and the level of denial. The type of denial subscale comprises six categories: no denial/conscious denial/denial of affect/denial of impact/denial of affect and impact/unconscious denial. Unconscious defence is hard to assess and conversion into conscious processes during the has to be taken into account.²⁹ Based on Greer's statement:¹¹ "In clinical practice the important factor is not whether denial is conscious or unconscious, but rather the degree of denial shown....", the second clinical impression subscale consists

[†] Bronovo hospital (B) and Medical Centre Haaglanden (M)

of the assessment of the level of denial ranging from 1 (= no denial) to 7 (= maximum denial). The overall DCI score is composed by summing the scores these three subscales. This results in a continuous scale running from 3 to 19. Reliability at the four assessments shows Cronbach's alphas of 0.82, 0.86, 0.84, and 0.84 respectively.¹⁵ For descriptive purposes, we distinguished between four levels of denial. If a patient showed no denial in response to any item, he/she could, by definition, be considered as “displaying no denial” (score=3). In the absence of available norms, the remaining range of scores (4-19) was divided equally into three categories indicating a low, moderate, or high level of denial (see Figure 1).

Figure 1 *The level of denial at baseline*

Coping was also measured by the Brief COPE,³⁰ which participants filled out after each interview. For the purposes of this paper, we only used the “denial” and “self-distraction” subscales (in our study, $\alpha = 0.73$ and 0.63 respectively).

Socio-demographic factors, such as gender, age, marital status, level of education, and religious beliefs were recorded in the interviews, as were details of current treatment.

Medical data, such as serious cognitive disorder, tumor type and disease stage at baseline, were provided by the chest physicians at the time of all four assessments, along with performance status (ZUBROD-ECOG-WHO).

Statistical Analysis

In the absence of detailed knowledge concerning the effects of denial, sample size calculations were based on the intention to detect cross-sectional correlations between denial and quality of life as low as 0.20, both at baseline and during follow-up visits. To achieve 80% power where true correlation is 0.20, based on a two-sided test of the no correlation null hypothesis where $\alpha = 0.05$, 147 patients are needed. In order to ensure assessment of 147 patients at T2 (while accounting for dropout), 195 subjects were included.

In order to test for differences in patient characteristics between hospitals or eligible and non-eligible patients, Pearson's chi-square test and Armitage's trend test were used for categorical and ordinal variables respectively.

Development of denial over time (DCI as continuous measure) was analyzed using repeated measures ANOVA (random effects model) with random person effects and fixed time and group effects, as well as their interactions. To assess sensitivity of the results to the missing at random assumption standpoint,³¹ pattern mixture models were also set up; however, no substantial difference in results against the random effects models was seen at any time.

All analyses were carried out using SPSS 12.0.1.

RESULTS

Patient Characteristics

The patient sample addressed, along with reasons for ineligibility, are described in Figure 2.

Non-eligible patients did not differ in gender or age and had a lower performance status ($p < 0.001$).

Figure 2 *Eligible and non-eligible patients*

Forty-nine patients (20%) refused to participate in the study. Reasons for refusal, as reported by the patient or the physician, were: “wants to calm down” (n=8), “wants neither treatment nor participation in the study” (n=6), “does not want to talk about the illness” (n=7), “too busy” (n=2), denial of illness (n= 4), too ill to participate (n=3), other/unknown (n=19). Non-responders did not differ significantly from responders in terms of gender, age, and performance.

Characteristics of the study sample are given in Table 1.

Of 195 patients at baseline, 157 (19% dropout), 122 (37% dropout), and 80 (59% dropout) participated at T2 – T4 respectively. The main reasons for dropping out of the study were death or the patient being too ill.

Level of Denial over Time

Most patients displayed a low (65%) or moderate (21.5%) level of denial at baseline, while a small number (3%) demonstrated a high level of denial (see Figure 3).The majority of patients continued to exhibit a low level of denial at subsequent assessments. The number of patients displaying no denial decreases over time (p=0.021).

Table 1 *Patient characteristics at baseline*

	Total N= 195
Hospital	
B	124 (63.6%)
M	71 (36.4%)
Gender	
Male	115 (59.0%)
Female	80 (41.0%)
Age	
> 60 yrs	69 (35.4%)
60-70 yrs	54 (27.7%)
> 70 yrs	72 (36.9%)
Partner	
Yes ^a	137 (70.3%)
No	59 (29.7%)
Children	
No	35 (18.0%)
Yes	159 (82.0%)
Education level ^b	
1	70 (36.8%)
2	53 (27.9%)
3	67 (35.3%)
Unknown	5
Religion	
No	98 (50.5%)
Yes	96 (49.5%)
Unknown	1
Type of tumor and UICC stage	
NSCLC	139 (74.7%)
≤ II	39
≥ III	100
SCLC	35 (18.8%)
limited	18
extended	17
Other/ unknown	21 (6.5%)
Current treatment	
No treatment	35 (18.0%)
Surgery	24 (12.4%)
Chemotherapy	73 (37.6%)
Radiotherapy	47 (24.2%)
Chemo- + radiotherapy	4 (2.1%)
Unknown	1
Performance status Zubrod	
0	58 (29.9%)
I	96 (49.5%)
II	26 (13.4%)
III/IV	14 (7.2%)
Unknown	1

^a Married, living together or having a relationship but living apart^b 1. primary education 2. secondary education 3: college/university

Figure 3 *The prevalence of denial over time*

The mean level of denial, as measured by the DCI, proved to be lowest at T1 and increased thereafter (Figure 4a).

Denial as measured by the Brief COPE two item subscale did not change over time, while the level of self-distraction decreased over time (Table 2).

Table 2 *Denial over time*

DCI	n=195	n=151	n=113	n=80
Observed means (SD)	6.57 (3.01)	7.17 (3.25)	7.17 (3.25)	7.39 (3.30)
Model means (SE) corrected for dropout	6.57 (0.22)	7.25 (0.24)	7.31 (0.26)	7.54 (0.29)
Change over time	<i>P</i> =0.001			
Brief COPE denial subscale	n=187	n=151	n=116	n=79
Observed means (SD)	1.55 (0.79)	1.5 (0.96)	1.41 (0.98)	1.34 (0.67)
Model means (SE) corrected for dropout	1.56 (0.06)	1.5 (0.07)	1.4 (0.08)	1.37 (0.09)
Change over time	<i>P</i> =0.16			
Brief COPE distraction subscale	n=186	n=151	n=116	n=79
Observed means (SD)	1.83 (0.9)	1.7 (0.92)	1.61 (1.11)	1.61 (0.8)
Model means (SE) corrected for dropout	1.85 (0.07)	1.69 (0.07)	1.61 (0.08)	1.64 (0.1)
Change over time	<i>P</i> =0.022			

Note: Observed means are reported with standard deviations, model means with standard errors.

Denial and Socio-demographic Factors

The impact of socio-demographic and illness related factors on denial over time is shown in Table 3 and Figure 4.

Table 3 Denial over time and sociodemographic and illness-related characteristics

Factor	Main effect	Interaction with time
Socio-demographic factor		
Hospital	P = 0.59	P = 0.46
Gender	P < 0.001	P = 0.89
Age	P = 0.028	P = 0.53
Education	P = 0.39	P = 0.011
Partner	P = 0.88	P = 0.67
Children	P = 0.31	P = 0.49
Religion	P = 0.18	P = 0.56
Illness-related factor		
Type of tumor	P = 0.25	P = 0.97
Treatment	P = 0.56	P = 0.45
Performance	P = 0.77	P = 0.69

Male lung cancer patients exhibited more denial over time than female patients ($p < 0.001$, Figure 4b).

Figure 4 The level of denial and sociodemographic characteristics

Younger patients ≤ 60 years of age showed consistently less denial over time than did patients in the 60-70 age bracket and those ≥ 70 years old ($p=0.028$; Figure 4c).

A difference in denial was noted among patients with varying levels of education (factor by time interaction, $p=0.012$). In patients who had completed primary education, the level of denial remained stable over time (Figure 4d). Patients who had completed secondary or college/university education showed less denial at baseline, with an increase at T2 and stable levels afterward.

No relationship was established between having a partner nor having children and the level of denial.

No difference in the mean level of denial was noted between religious and non-religious patients.

Denial and Illness-Related Factors

Levels of denial did not differ between patients with different types of lung cancer, such as non-small cell and small cell lung cancer. Similarly, no difference was noted in levels of denial based on treatment groups or performance status (Table 3).

DISCUSSION

The Level of Denial in Lung Cancer Patients

We studied the level of denial and predictors thereof in lung cancer patients over an eight-months period. First, we found that most patients displayed at least some level of denial. Denial was assessed as defined by Hackett and Cassem: “the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects.” One can thus assume that most patients need to protect themselves from part of the overwhelming reality of being afflicted with lung cancer. This also means that denial should be considered a normal phenomenon, part of the usual illness process that lung cancer patients undergo.

Secondly, the level of denial in our patients significantly increased from shortly after diagnosis to four months later. Between four and eight months, the level of denial remained stable. This finding is surprising when compared to those of other longitudinal studies in which denial diminished over time^{17,21} or remained stable from baseline.^{16,19,32} Such comparison is, however, complicated. In Filipp’s study,²¹ time since diagnosis varied between 1 and 840 weeks. In the study by Morris et al.,¹⁶ a small number of participants demonstrated denial (T1, $n=10$, 16%; T2, $n=6$, 11%; T3, $n=3$, 7%). In the study carried out by Thomas et al.,¹⁹ only male patients exhibited a gradual lessening of denial. This finding was related to increased denial when death was nearby. In another longitudinal study,¹⁸ denial was found to remain stable, with only terminal phase patients demonstrating increased levels. Although our findings are dis-

similar, we believe they are valid since ours is the first large-scale longitudinal study in lung cancer patients.

Thirdly, interestingly, increased denial was demonstrated as measured via the DCI, but not when taking the Brief COPE subscale. In Carver's study¹⁷ among breast cancer patients, denial and self distraction as measured with the COPE dropped significantly between the presurgery period and one year follow-up. When comparing the items of the Brief COPE denial subscale and the DCI, one may conclude that different qualities are assessed. The former contains a small overtone of catastrophization (e.g., "I have been refusing to believe it has happened"), while the latter focuses on assessing a more subtle evasion of worry, fear, and dejection. The Brief COPE self-distraction items assessed "...not to think about the event by focusing on something else". This decrease in self-distraction, as measured by the Brief COPE over the course of the illness, can be explained by patients' becoming accustomed to reality over time, at which point active coping falls off.

The difference in assessment method may also be relevant. The Brief COPE is a self-reporting questionnaire, filled in at face value. The DCI is a semi-structured, in-depth interview, in which participants can refine their answers and, if applicable, demonstrate contradictory feelings: some moments of acceptance and some of denial. These subtle expressions influence the rating on the DCI's two clinical impression scales. Indeed, post hoc analysis of the correlations between the DCI and the COPE subscales denial and self distraction at the four time points indicated that 7 out of 8 correlations were non-significant and one was low (-0.18).

The increase of denial, as measured by the DCI in our study, can be explained based on clinical practice. The initial shock of receiving a lung cancer diagnosis and the immediate need to make decisions about treatment options offer patients virtually no opportunity to deny their illness. After undergoing a shift in perspective, most people try to restore balance to their lives and become accustomed over time to being afflicted with the disease. Denial, characterized as "repudiation of part or all of the total available meaning of an event," can support the notion that life goes on and the impact of the illness may turn out better than was initially expected. Moreover, the permanent realization that one's prospects for the future include pain and dyspnea, and the potential imminence of death, is difficult for the patient to bear. The level of denial expressed reflects a decision to "make the best of things" and disregard the illness and its impact as much as possible.

Denial and Socio-Demographic Background

Gender

Our study revealed that male lung cancer patients consistently exhibit more denial than do female patients. This result is reflected in three previous studies;^{33,34,35} however, researchers in four other studies found no gender differences.^{19,36,37,38} In one study, men scored lower on avoidance,³⁹ while

researchers in three other investigations^{34,35,40} found a correlation between denial and a poor prognosis in men. One explanation suggested is that barriers exist in the communication of doctors and male patients^{19,38}.

One can assume that women in Western culture are more prone to disclosure of their feelings. As Pearlin and Schooler⁴¹ conclude: "... men more often possess psychological attributes or employ responses that inhibit stressful outcomes of life-problems, where women more often employ a response that is likely to result not in less stress, but in more." Since denial is by definition protection against threatening events or feelings, we can infer that women are less able to shield themselves from stressful life events.

Another possible explanation is that all of our study interviewers were female. As the DCI is partly based on the interviewer's clinical impression, a gender oriented bias cannot be excluded. Similarly, in pain research, the interviewer's gender was found to influence the expressed level of patients' symptoms.⁴²

Age

Younger lung cancer patients in our study demonstrated less denial over time than did the older patients. This result is similar to those of previous studies involving patients with other cancer types.^{3,21,38,43,44} In Cassileth's study, younger patients wished to receive "as much information as possible, good and bad" or expressed the opinion that "ignorance is fear." Older patients, on the other hand, tended to say such things as: "I need as little to worry about as possible." It is well-known that elderly are generally less emotionally expressive.⁴⁵ Also, in contrast to the secrecy of previous decades surrounding a cancer diagnosis, younger patients are now more likely to inform their friends of the diagnosis.³⁸

Marital Status and the Presence of Children

In the current study, having a spouse or children did not influence the level of denial over time. This finding corresponds with the results of most previous studies.^{19,36,44,46} Only one study showed a stronger level of denial in terminally ill patients who were married.³⁵

An explanation for these findings could be that denial in lung cancer patients depends on a spouse's character and the nature of the relationship.⁴⁷ On the one hand, it can be assumed that patients try to hide the seriousness of their condition to protect their loved ones, or that family members collude with the patient's denial of a poor prognosis.⁴⁸ On the other hand, the relief of sharing worry and the comfort of a caring partner are factors that may prevent the need for denial. The same assumptions can be made for single patients, in today's individual-centered culture this status is no longer a sign of social deprivation.

Education

Three previous studies investigating the relationship between education and denial provide inconclusive results.^{35,36,44} Similarly, the relationship between education and denial is less evident in our study. Patients who completed primary education exhibited more denial overall, especially shortly after diagnosis. In fact, their level of denial remained stable over time. In patients who completed higher education, the level of denial was low shortly after diagnosis, but increased over time. A possible explanation is that less educated patients may need to shield themselves more, when receiving the overwhelming amount of information about the illness at its onset.

Religious Beliefs

No difference in level of denial was noted in comparing religious and non-religious patients – or Protestant versus Roman Catholic patients – in the current study. These findings are similar to Wool's conclusions.⁴⁹ In Dunkel-Schetter's study,³⁶ however, a correlation with cognitive escape avoidance was seen in patients who were adherents of a Christian religion. The difference between believers' and atheists' life philosophies may have disappeared under the influence of secularization over the past few decades. Given the small numbers of Muslims (n=2, 1%) and Jews (n=1, 0.5%) in our sample, no conclusions can be drawn about other religions.

Illness Related Factors

One could assume that lung cancer patients with a more favorable outlook as a result of surgery would demonstrate less denial than would those with a poor prognosis shortly after diagnosis. Nevertheless, illness related factors did not influence the level of denial displayed by lung cancer patients in our study. A possible explanation for these findings could be that all lung cancer patients "know" about the poor prognosis for this disease, irrespective of treatment options or the absence of physical complaints. This hypothesis, however, would need further investigation.

Study Limitations

Some study limitations need to be mentioned. Firstly, the poor prognosis associated with lung cancer led to the death of many patients during the course of this study, thus potentially causing distortion in results. We therefore chose a random effects analysis, which yields unbiased results when observations are missing in a random fashion.³¹ A sensitivity analysis with different pattern mixture models produced similar results to those of the random effects analysis presented here.

Secondly, lung cancer patients who exhibit strong denial might conceivably not be interested in participating in a study examining how patients cope with the illness. These patients may be overrepresented in the non-responding population. Indeed, among non-responders' 19 patients (7.8%) could show strong denial. When compared with responders demonstrating a high level of

denial (T1, 5 patients [2.6%]), the number of strong deniers does indeed seem to be overrepresented within this group.

Overall Conclusions and Suggestions for Further Research

This large scale study was the first to investigate levels of denial in lung cancer patients over time. The study outcome was that most lung cancer patients displayed some level of denial, which increased over the course of the illness. This outcome warrants the conclusion that in clinical practice denial in lung cancer patients has to be considered as a normal phenomenon, and not as a sign of disturbed coping.

Denial was higher in male lung cancer patients than in females, and lower in younger than in elderly patients. Patients with a lower education level demonstrated more denial shortly after diagnosis than did more educated subjects.

In this study, the number of patients demonstrating strong denial is small and appears overrepresented in the group of non-responders. No conclusions can therefore be drawn about differences between patients with varying levels of denial. Whether strong denial should be considered a sign of inadequate coping or a mental illness has not yet been investigated. The patients in question could conceivably be unwilling to either visit the hospital for diagnosis and treatment, or to participate in a scientific study. General practitioners are, in all likelihood, obliged to care for patients showing strong denial more often than are chest physicians. We therefore recommend involving family physicians in future longitudinal studies concerning the level of denial in cancer patients. Moreover, further research is needed to gain insight into positive and negative effects related to the level of denial in cancer patients.

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Chapter 6

Denial and physical outcomes in lung cancer patients a longitudinal study

*Martina S. Vos, Hein Putter, Hans C. van Houwelingen,
Hanneke C.J.M. de Haes*

SUMMARY

Although denial in cancer patients is often seen in clinical practice, studies relating denial to physical outcomes are lacking. The present study aims to investigate patterns of denial among lung cancer patients and connect these to their physical outcomes. Denial was measured longitudinally in 195 consecutive newly diagnosed lung cancer patients. Four assessments were conducted over an eight-month period. Patient-reported physical outcomes were measured with a generic and disease-specific quality of life measure. Medical data were provided by the patients' chest physicians.

Three patterns of denial over time were identified in lung cancer patients: patients displayed either low, moderate or increasing denial. Male lung cancer patients were found to deny at a moderate level more often. A moderate or increasing level of denial was consistently related to improved patient-rated physical outcomes. Lung cancer patients displaying more denial reported a better overall perception of health and better physical functioning. They complained less about fatigue, nausea and vomiting, appetite loss, dysphagia and pain in arm and shoulder than low deniers. Other symptoms did not differ among denial classes.

Denial in lung cancer patients may well be an adaptive mechanism and has to be respected in clinical practice.

INTRODUCTION

Lung cancer is the most prevalent type of cancer worldwide and the leading cause of cancer-related death in western countries.¹ After diagnosis, lung cancer patients are confronted with symptoms, treatment choices, emotions and existential questions. They may, understandably, protect themselves against the overwhelming facts and feelings associated with this sudden change in life perspective by denying (parts of) the illness and its consequences. Current ethical and psychosocial publications emphasize the need to fully inform patients. Yet, some level of denial was found to be normal in lung cancer patients.²

Whether denial or denial like strategies like avoidance or repression should be considered adaptive or maladaptive has often been discussed but remains uncertain.^{3,4,5} How should an oncologist then handle denial in clinical practice? The relation of denial in cancer patients to psychological functioning was found to depend on the conceptual approach chosen.⁴ The relation of denial to physical functioning in cancer patients has hardly been investigated.

Repressing chemotherapy-patients were found to report fewer physical symptoms than those who did not.⁶ Among breast cancer patients undergoing adjuvant chemotherapy denial of disease impact was not related to physical outcome but behavioural-escaping patients reported more physical symptoms.⁷

Whether denial is adaptive may depend on the disease phase involved. Indeed, a time related pattern has been described: denial was suggested to be adaptive in the short term and maladaptive in the long run.^{3,8,9}

Studies covering denial over time are, however, limited. A literature search retrieved 19 cross-sectional and six longitudinal studies.⁴ The results from cross-sectional studies were inconclusive because of the variety of designs, samples and assessments. Longitudinal studies, in breast cancer,^{10,11,12} colorectal cancer,¹³ and mixed cancer patient populations,^{14,15} seem to indicate that denial diminishes over time, but increases when death draws closer. In our study among lung cancer patients, however, the mean level of denial increased from shortly after diagnosis to four months later and remained stable thereafter.² These studies are generally based on average patient populations. Whether different denial patterns can be distinguished and how these patterns relate to physical function has not yet been investigated.

Studies regarding denial in lung cancer are lacking, even though lung cancer patients may have increased reasons to deny. First, they may feel responsible for the development of their disease through smoking and, consequently, feel shameful and encounter stigma. Secondly, they often suffer from dyspnea, which seriously limits functioning and may be frightening.^{16,17} Finally, given their poor prognosis, lung cancer patients have limited time to adapt to their disease.

The main objective of the present study is to investigate the relation between denial and physical outcomes in lung cancer patients. Research questions are: 1) whether patterns of denial can be distinguished among these patients, 2) how these relate to socio-demographic and disease-related factors, and 3) to physical outcomes.

METHODS

Participants

Consecutive lung cancer patients were recruited from two pulmonary diseases outpatient clinics[†] in The Hague, the Netherlands. Inclusion criteria were: a) being newly diagnosed with primary lung cancer irrespective of histological type, stage or treatment; b) age ≥ 18 years, c) time since diagnosis < 2 months, d) knowledge of the Dutch language, and e) written informed consent. Exclusion criteria were a) serious cognitive disorder and b) being too ill. Patients were invited to participate by their chest physicians. Those agreeing received written information and signed informed consent before being interviewed.

Design

Four assessments were planned for each patient: within 8 weeks following diagnosis (T1) and, subsequently, 8, 16, and 32 weeks later (T2-T4). Each assessment consisted of a semi-structured interview (30-45 minutes) and the completion of written questionnaires. The study was approved by the hospitals' ethics committees.

Measures

Denial was measured using the Denial of Cancer Interview (DCI), a semi-structured interview, based on Weisman and Hackett's definition of denial: 'the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects'.^{18,19} The DCI consists of nine specific items and two clinical impression scores covering the type and overall level of denial. It has proven to have good psychometric properties.²⁰ The reliabilities (Cronbach's α) were 0.82, 0.86, 0.84 and 0.84, at the respective assessments. The interrater reliability (κ) of the DCI was 0.81. Denial is represented on a continuous scale ranging from 3 to 19, with lower scores indicating less denial.

Patient-reported physical outcomes were measured, first, using a generic cancer quality of life measure: EORTC QLQ-C30. The QLQ-C30 incorporates a physical functioning scale, three symptom scales covering fatigue, nausea and vomiting and pain, and single item scales addressing dyspnea, insomnia, appetite loss, constipation and diarrhea, and overall health. Secondly, the EORTC disease-specific lung cancer module (QLQ-LC13) was used, comprising 12 symptom-related questions, covering dyspnea (three items), coughing, hemoptysis, sore mouth, dysphagia, peripheral neuropathy, alopecia, chest pain, pain in arm, and other pain.²¹

[†] Bronovo Hospital and Medical Centre Haaglanden

Medical data (i.e., tumor type, disease stage, and performance status) were provided by the chest physicians. Performance status was rated using the Zubrod-scale.²² Socio-demographic factors (i.e., gender, age, marital status, education level and religion) were collected in the interviews, as was current treatment and smoking history.

Statistical analysis

One of the research questions was whether it is possible to distinguish groups of patients with distinct patterns regarding their evolvement of denial over time. The objective in statistical terms is to identify latent classes of longitudinal denial measurements. This type of models is quite popular in the psychometric literature, where it goes under the name of growth mixture models, latent trajectory classes or trajectory analysis. Within each class, a mixed effects model was assumed, with random person effects and fixed categorical (T1-T4) time effects, and with independent random error. Between-patient and residual variances were restricted to be identical for all classes, while mean vectors (at T1-T4) were allowed to differ between classes. An Expectation Maximization (EM) algorithm was used to identify these latent classes and estimate their probabilities, means and variances.²³ From the EM algorithm, posterior probabilities of class membership were obtained for each patient. For each patient, the highest posterior probability determined the most likely class. Differences between these classes with respect to patient characteristics were assessed by contingency tables with variances adjusted for class membership uncertainty. Physical functioning scales were analyzed using mixed models, with class, time (T1-T4 categorical) and class by time interaction as fixed effects, and with patient intercept as random effect. To account for class membership uncertainty in this analysis, multiple imputation (using M=10 dataset completions) was used (for statistical details see²⁴).

RESULTS

Patient Characteristics

Of 383 newly-diagnosed lung cancer patients 139 were ineligible because of death (n=30), being too ill (n=32), ≥ 8 weeks since diagnosis (n=28), having a language problem (n=15), moving elsewhere (n=8) or other reasons (n=16). Eligible and non-eligible patients did not differ in gender and age.

Of 244 eligible patients, 49 (20%) refused participation. Reasons for refusal were: “wants to calm down” (n=8), “does not want treatment nor study participation” (n=6) “does not want to talk about the illness” (n=7), “too busy” (n=2), denial of illness (n= 4), too ill (n=3), other/unknown (n=19). Non-responders did not differ from responders in gender, age and performance status. Characteristics of the study population are given in Table 1.

Table 1 *Patient characteristics at baseline*

	Total N= 195
Gender	
Male	115 (59.0%)
Female	80 (41.0%)
Age	
> 60 yrs	69 (35.4%)
60-70 yrs	54 (27.7%)
> 70 yrs	72 (36.9%)
Partner	
Yes ^a	137 (70.3%)
No	59 (29.7%)
Children	
No	35 (18.0%)
Yes	159 (82.0%)
Education level ^b	
1	70 (36.8%)
2	53 (27.9%)
3	67 (35.3%)
Unknown	5
Religion	
No	98 (50.5%)
Yes	96 (49.5%)
Unknown	1
Type of tumor and UICC stage	
NSCLC	139 (74.7%)
≤ II	39
≥ III	100
SCLC	35 (18.8%)
limited	18
extended	17
Other/ unknown	21 (6.5%)
Current treatment	
No treatment	35 (18.0%)
Surgery	24 (12.4%)
Chemotherapy	73 (37.6%)
Radiotherapy	47 (24.2%)
Chemo- + radiotherapy	4 (2.1%)
Unknown	1
Performance status Zubrod	
0	58 (29.9%)
I	96 (49.5%)
II	26 (13.4%)
III/IV	14 (7.2%)
Unknown	1
Smoking	
No	9 (4.6%)
Yes	186 (95.4%)

^a Married, living together or having a relationship but living apart^b 1. primary education 2. secondary education 3. college/university

Of 195 patients at baseline, 157 (81%), 122 (63%), and 80 (41%) participated at T2–T4 respectively. Main reasons for dropping out were death and being too ill.

Patterns of denial

Depending on the criterion chosen, a model with three or four classes could be selected; the Aikaike’s Information Criteria (AIC)²⁵ would lead to a four-class model, while the Bayesian Information Criteria (BIC)²⁶ would lead to a three-class model (see Figure 1 for estimated means and 95% confidence intervals [in bold]). Individual data are shown in colors indicating the most likely class for that patient.

Figure 1 *Patterns of denial*

For the three-class model, a clear pattern emerges. The largest class represents patients showing a low level of denial over time (69%, mean DCI=5.34, 95%CI 4.99– 5.69 at T1). The second largest class represents the patients showing a

moderate level of denial over time (19%, mean DCI=11.31, 95%CI 10.65–11.98 at T1). The smallest class starts with a low level of denial and shows increasing denial over time (13%, T1, mean DCI=6.28; 95%CI 5.48 – 7.08, T4, mean DCI=11.89; 95%CI 10.42–13.36). Between-patient and residual standard deviations were estimated to be 0.98 and 1.80, respectively.

The four-class model is harder to interpret. Since the two information criteria favored different models, interpretability was the decisive argument and the three-class model selected. We identified the three classes as ‘low deniers’, ‘moderate deniers’, and ‘increasing deniers’.

Table 2 *Predictors of patterns of denial*

Characteristic		Low deniers	Moderate deniers	Increasing deniers	Test statistic (χ^2)	P-value
Gender	Male	70 (61%)	29 (25%)	16 (14%)	11.93	0.0026
	Female	64 (80%)	7 (9%)	9 (11%)		
Age	≥ 60	54 (78%)	8 (12%)	7 (10%)	7.53	0.11
	60 - 70	34 (63%)	11 (20%)	9 (17%)		
	> 70	45 (63%)	17 (24%)	9 (13%)		
Partner	No	41 (71%)	11 (19%)	6 (10%)	1.09	0.58
	Yes	92 (68%)	25 (18%)	19 (14%)		
Children	No	24 (69%)	6 (17%)	5 (14%)	0.2	0.91
	Yes	110 (69%)	29 (18%)	20 (13%)		
Education level	Primary	44 (63%)	19 (27%)	7 (10%)	8.98	0.06
	Secondary	38 (70%)	7 (13%)	9 (17%)		
	College/ University	49 (73%)	10 (15%)	7 (12%)		
Religion	No	63 (64%)	24 (25%)	11 (11%)	6.44	0.04
	Yes	70 (73%)	12 (12%)	14 (15%)		
Type of tumor	NSCLC	95 (68%)	25 (18%)	19 (14%)	4.09	0.39
	SCLC	22 (63%)	9 (26%)	4 (11%)		
	Other/ unknown	17 (81%)	2 (10%)	2 (10%)		
Current treatment	Surgery	24 (67%)	8 (22%)	4 (11%)	2.1	0.91
	Chemo-therapy	51 (71%)	12 (17%)	9 (12%)		
	Radio-therapy	33 (69%)	8 (17%)	7 (15%)		
	No treatment	22 (63%)	8 (23%)	5 (14%)		
UICC grade	0	39 (65%)	13 (22%)	8 (13%)	0.75	0.94
	I	66 (69%)	17 (18%)	13 (13%)		
	II-IV	28 (70%)	7 (18%)	5 (13%)		
Smoking	No	7 (78%)	1 (11%)	1 (11%)	0.52	0.77
	Yes	127 (68%)	35 (19%)	24 (13%)		

Denial, socio-demographic and disease-related factors

Female ($p=0.0026$) and non-religious ($p=0.04$) patients were more likely to display a low level of denial (see Table 2). Other socio-demographic and disease-related characteristics and smoking history were not related to class assignment.

Denial and physical outcomes

The relation between patterns of denial and physical outcomes is shown in Table 3 and Figure 2.

Table 3 *Denial and Physical Outcomes*

<i>Subscale</i>	<i>Class (P-value) all patients</i>	<i>Class by time interaction (P-value)</i>
EORTC QLQ-C30:		
Physical functioning	0.046	0.68
Dyspnea	0.039	0.21
Pain	0.27	0.70
Fatigue	< 0.001	0.037
Insomnia	0.37	0.54
Appetite loss	0.013	0.35
Nausea and vomiting	0.039	0.23
Constipation	0.16	0.63
Diarrhoea	0.13	0.91
Overall perception of health	< 0.001	0.29
EORTC Lung module:		
Coughing	0.69	0.88
Haemoptysis	0.46	0.62
Dyspnea	0.21	0.38
Sore mouth	0.94	0.83
Dysphagia	0.049	0.99
Peripheral neuropathy	0.31	0.76
Alopecia	0.55	0.57
Pain in chest	0.27	0.80
Pain in arm or shoulder	0.0087	0.28
Pain in other parts	0.40	0.80
Zubrod performance	0.20	0.27

Time by class interaction is tested in a parsimonious way ($df=1$) by adding an extra linear trend term for the class of increasing deniers only.

Lung cancer patients displaying moderate or increasing denial reported better physical functioning ($p= 0.046$), less nausea and vomiting ($p=0.039$), less

Figure 2 Patterns of denial and physical outcomes

appetite loss ($p=0.013$), and less dyspnea ($p=0.0139$). They also reported better overall health ($p < 0.001$). Moderate deniers suffered less from fatigue

than low deniers and increasing deniers reported less fatigue over time (class by time interaction $p = 0.037$).

In disease-specific terms, moderate and increasing deniers reported less dysphagia ($p=0.049$) and arm and shoulder pain ($p=0.0087$). Other symptoms were not different among denial classes.

DISCUSSION

Patterns of denial

In this first large longitudinal study among lung cancer patients, we could identify different patterns of denial over time. Low deniers make up the largest patient group. A smaller group denies at a moderate level from the start. Both groups maintain their original level of denial with time. They display a basic level of denial, seemingly as part of their personal style of dealing with the illness and its impact. A third, small group shows a low level of denial shortly after diagnosis which subsequently increases to a moderate level over time. This finding allows us to differentiate the effects of denial over time.

Physical outcomes

Our main finding is that a moderate or increasing level of denial was consistently related to improved patient-rated physical outcomes. Lung cancer patients displaying more denial reported a better overall perception of health and better physical functioning. They also experienced less dyspnea, fatigue, gastrointestinal symptoms, dysphagia and arm pain. It is worth noting that the differences are substantial. Differences of five points on a scale of 0-100 are generally considered clinically relevant.^{27,28} We indeed found the difference between low and moderate deniers on physical outcome to be over 6 and up to 26 and the difference between low and increasingly deniers to exceed five points.

Thus, denial may be adaptive in lung cancer patients.

How can these results be explained? Symptom experience is, by definition, subjective rather than objective: it consists of symptom occurrence and distress.^{29,30} The level of distress associated with the disease is therefore personal. As described, literature reports concerning the effect of denial on physical health are contradictory. This may result, first, from the use of self-report denial measures in many studies. These have been criticized for being too general.³¹ We based our study on semi-structured interviews conducted by experts in psycho-oncology. These may yield different and more valid results.

Theoretical notions from health psychology have suggested mechanisms underlying the perception and reporting of physical symptoms. Kolk et al³² integrated different theoretical approaches. They described the perception of

physical symptoms as first preceded by peripheral, physiological changes resulting from bodily processes. Next, changes generate information about organ systems but only a small proportion of this information gives rise to awareness and is consciously processed. Awareness also depends on the (selective) attention we pay to these sensations. Negative affectivity was found to lower the detection threshold. Likewise, attention to the body is likely to heighten the processing of physical, internal information rather than external information. The more we focus internally, the more we notice symptoms.³³ Using denial as a coping strategy may influence cognitive processing and lead to reduced internal focusing and thus negative emotions and symptom perception.³⁴ Indeed, Westerman et al³⁵ found that more optimistic lung cancer patients, adopting a protective style, distanced themselves and presented themselves as not suffering from fatigue. It is interesting to note that the effect of denial is more salient when considering generic cancer symptoms than those specific to lung cancer (Table 3). The latter, such as coughing, sore mouth, and alopecia, may be more 'objective' and thus less easily suppressed from awareness. Dyspnea is particularly interesting in this respect. It was found to be lower in the moderate and increasing deniers in the generic EORTC questionnaire, but not in the disease-specific module. Dyspnea was defined as: "a subjective experience of breathing discomfort that consists of qualitatively distinct breathing sensations that vary in intensity".³⁶ The disease-specific question is formulated more concretely: "dyspnea when resting, walking and climbing stairs". This strengthens the assumption that denial is more likely to lower symptom experience when assessed more subjectively.

Some specific symptoms deserve attention. Gastrointestinal symptoms such as nausea, vomiting and appetite loss occur mostly during chemotherapy. Psychological factors, especially anxiety, are associated with nausea and vomiting and with patients' subsequent experience of post-treatment and anticipatory nausea and vomiting.³⁷⁻⁴⁰ Classical conditioning contributes to anticipatory nausea and vomiting, possibly induced by cancer cell cytokine release or stress.^{41,42} It is plausible that a higher level of denial protects against anticipatory reactions.

Studies concerning dysphagia are limited beyond head and neck cancer. Causes of dysphagia can be esophagitis as a side effect of treatment⁴³ or vocal fold motion impairment.⁴⁴ The higher rating of dysphagia in low deniers might reflect the subjective experience of swallowing problems related to psychological stress.^{45,46,47}

We did not find a difference in patient-reported insomnia between different denial classes, even when corrected for the use of sleeping pills. Given the noticeable difference in fatigue between these groups, a difference in the incidence of insomnia would be expected. Our results, however, are in line with other studies that found a discrepancy between subjective and objective sleep disturbances in lung cancer patients.^{48,49}

No difference in the perception of pain was found, except for arm or shoulder pain, even when corrected for the use of analgesics. Pain is common

in lung cancer patients: 75% of patients with advanced disease suffer from pain.⁵⁰ This result is harder to understand. Arm or shoulder pain in lung cancer patients can be caused by a Pancoast tumor or brachial plexus damage due to tumor infiltration or compression.⁵¹ But arm or shoulder pain is also a common symptom in non-cancer patients caused by physical or psychological factors.⁵² The same is true for chest pain.⁵³ Again, this makes it difficult to explain why moderate deniers report less pain in arm or shoulder but not in chest pain.

Sore mouth, peripheral neuropathy and alopecia are chemotherapy and radiotherapy side effects. Ward et al⁶ found repressors report less chemotherapy-induced side effects. However, in line with our results, they found no difference in repressor-reporting of sore mouth, neuropathy and alopecia.

Background factors

It is interesting to note that no effect of disease characteristics on denial was found. As described, denial appears to be a general personal style to cope with the disease rather than directly related to its prognosis or the patient's performance status.

Male lung cancer patients were found to be more likely to deny at a moderate level than female patients (see table 2). This finding is concordant with studies among patients with other cancer types and coronary heart disease.⁵⁴⁻⁵⁷ Traditionally, men are found to be more focused on work-related issues and women on family and health-related matters.⁵⁸ This may explain why men are less attentive to health problems and, thus, move into denial more easily. Moreover, the previously described masculine view that being ill is a sign of weakness, paves the way for their denial.^{59,60} Yet, this finding poses some questions. Are the effects found related to gender rather than denial itself? Unfortunately, routine application of correction for gender to all scales would endanger our findings as it inflates the significance of the relation between denial and outcome, even if gender is not related to the outcome at all. Therefore, we only consider gender to be a confounder if it is directly related to the physical outcome of interest. We therefore compared, post hoc, the marginal significance of gender alone with the marginal significance of denial. If the marginal significance of gender is stronger than that of denial, gender is considered to be a confounder. In line with this reasoning, we indeed found that gender is a confounder for the outcomes nausea and vomiting, and physical functioning (see table 4 for corrected p-values for the outcomes for which confounding might be present after correction). The effects of denial on both physical functioning and nausea and vomiting lose their significance. However, the effect of denial in a joint model with gender has hardly changed in both cases (data not shown). The EORTC-QLQ- reference values of lung cancer patients show the same effects of gender and physical outcome as found in the present study.⁶¹ As it is plausible that these reference groups will also comprise deniers, the conclusion seems warranted that only a small part of the

gender effect on physical outcome can be understood from the indirect effect of gender via denial.

Religious patients were found to deny less than non-religious patients. Interestingly, though, religious patients are in the majority in our group of increasing deniers. However, as the group is rather small these results should be considered with some caution.

Table 4 Denial and physical outcomes, with adjustments for gender

Subscale	Unadjusted marginal P-values		Adjusted P-values	
	Gender	Class	Gender	Class
Physical functioning	0.037	0.046	0.018	0.10
Nausea and vomiting	0.002	0.039	0.004	0.19

Study limitations

Some study limitations need to be mentioned. First, the study has a longitudinal explorative design. Therefore, unfortunately definite conclusions about causality would need further study. Yet, it is obvious that denial can not be manipulated experimentally. Secondly, the possible bias resulting from patient dropping out should be mentioned. Such drop out is unavoidable when studying lung cancer patients longitudinally, but still might influence results. Imputation was used to overcome this problem. Thirdly, the small number of patients displaying a high level of denial is noteworthy. We added the few strong deniers to the class of moderate deniers (Figure 1). Lung cancer patients who exhibit strong denial may indeed be avoiding participating in a study examining how patients cope with their illness. Indeed, these patients seem to be overrepresented in our non-responding population. Based on their reasons for refusal, i.e., not wanting study participation (n=6) or to talk about the illness (n=7), too busy (n=2), and denial of illness (n=4), 19 non-responders (7.8%) might be strong deniers as compared to 5 responders (2.6%). These strongly denying patients are of particular interest and deserve further study.

Conclusions

We conducted the first large longitudinal study among lung cancer patients investigating their level of denial and physical health. Patients turned out to deny either little, moderately or increasingly. Interestingly, we found that patients who denied more reported better physical functioning and less physical symptoms. The implications for clinical practice are that their denial may well be an adaptive mechanism and might have to be respected in clinical practice. By avoiding the confrontation with some of the consequences of their disease and treatment, patients can protect themselves from an uncontrollable reality. It is unclear whether this conclusion applies to strong deniers, whose

coping may interfere with the treatment process. In general, however, the negative views associated with patients not wanting to be confronted with all relevant information could be reconsidered. We may treat patients more adequately if we respect their protective behavior and thus help them to adapt to their illness experience.

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Chapter 7

Denial and social and emotional outcomes in lung cancer patients:
the protective effect of denial

*Martina S. Vos, Hein Putter, Hans C. van Houwelingen,
Hanneke C.J.M. de Haes*

Submitted

SUMMARY

Denial is a well-known phenomenon in clinical oncology practice. Yet whether the impact of denial on patient wellbeing is beneficial or harmful remains unknown. The purpose of the current study is to investigate the relationship between denial and social and emotional outcomes in a large sample of lung cancer patients over an extended time period.

Denial and social and emotional outcomes were measured in 195 newly-diagnosed lung cancer patients. Four assessments were conducted over eight months. The level of denial was measured using the Denial of Cancer Interview. Patient-reported social and emotional outcomes were measured using the EORTC-QLQ-30 and the HADS.

Patients with a moderate or increasing level of denial over time reported better social outcomes (role functioning: $p = 0.0036$, social functioning: $p = 0.027$) and less anxiety ($p = 0.0001$) and depression ($p = 0.0019$) than patients with a low level of denial. The overall quality of life was better among lung cancer patients who displayed either moderate or increasing levels of denial compared with those who displayed low levels of denial ($p < 0.0001$).

A certain level of denial in lung cancer patients can have a protective effect on social and emotional outcomes. Clinicians should take this into account when providing information about the illness and its prognosis.

INTRODUCTION

When patients are told that they have lung cancer, they have to deal with major changes in their life and future perspective. Because of the limited curative treatment options,¹ the diagnosis of lung cancer usually comes as a shock and can throw a patient off stride.² It is conceivable that lung cancer patients may try to protect themselves against this daunting situation by denying at least parts of the illness and its consequences. Indeed, the occurrence of denial in clinical practice is undisputed and a low to moderate level of denial has been found to be a normal phenomenon among lung cancer patients.³

Current practice in the Western world is to fully inform patients about their diagnosis and prognosis. As a consequence, lay people as well as healthcare professionals may try to convince patients to face the full truth of having cancer and to stimulate them to openly discuss their illness experience. Yet whether some degree of denial is adaptive or maladaptive is still under debate.⁴⁻⁷ Such a strategy would be unwise if denial were positively linked to adaptation. Indeed, as Lazarus states: "denial can have a positive value under certain conditions and a negative value under others".⁸ It is therefore important to investigate the impact of denial among cancer patients.

The effect of denial in cancer patients on social functioning was investigated in two earlier studies.^{9,10} In the first, avoidance of information was found to be related to poorer social functioning, while denial of feelings was found to be related to better social functioning. The second study found no relation between denial of the disease impact and related affect and social functioning.

Likewise, different results were found in studies concerning the relation between denial and psychological function. A literature search retrieved 14 studies in which different assessment tools were used and patients with different types of cancer were included. Consequently, results should be compared with caution. Besides, different types of denial were distinguished such as: 'denial of diagnosis', 'denial of affect or emotions', 'denial of the disease impact' and 'behavioral escape'. Denial of diagnosis was shown to relate to poorer psychological functioning in two studies.^{11,12} Denial of the disease impact was related to experiencing less distress in seven studies,^{9,13-18} but more in three other studies^{12,19,20} and the same level of distress in another three.^{11,20,21} Denial of affect and behavioral escape were shown to be related to greater distress in four studies^{16,17,19,21,22} and less distress in another.⁹ In one study the denial of affect and the impact of disease caused improved wellbeing.²³

The effect of denial in cancer patients on psychological functioning may depend on the concept of denial used. Interestingly, studies in which denial of the disease impact was related to improved psychological functioning represented active strategies such as not letting the illness control life, brushing the illness aside and instead creating a positive outlook despite having cancer. In studies where denial was related to poorer psychological functioning, the following concepts were used: refusing to believe 'it' happened (denial of diagnosis), hoping a miracle might happen (denial of affect), and making oneself feel

better by drinking, eating and smoking, or giving up (behavioural escape). Thus, distractive strategies seem to be related to reduced distress, whereas passive escape mechanisms seem to decrease psychological well-being.⁷

Until now, extensive research concerning denial in lung cancer patients has been lacking, yet lung cancer patients may have more reason to deny than other cancer patients. First, lung cancer is related to smoking and patients may feel shameful or stigmatized.^{24,25} Secondly, lung cancer patients often suffer from dyspnoea, which seriously limits functioning and may provoke severe anxiety.^{26,27} Finally, given their poor prognosis and often quickly deteriorating condition, patients have limited time to adjust to the impact of their illness. The objective of the present study is, therefore, to investigate prospectively the relationship between denial and social and emotional outcomes in a large sample of lung cancer patients.

METHODS

Participants

Consecutive lung cancer patients were recruited from two outpatient clinics[†] for lung diseases in The Hague, the Netherlands. Inclusion criteria were: a) being newly diagnosed with primary lung cancer irrespective of histological type, stage or treatment; b) age ≥ 18 years, c) time since diagnosis < 2 months, d) knowledge of the Dutch language, and e) written informed consent. Exclusion criteria were a) a serious cognitive disorder and b) being too ill to be interviewed.

Patients were invited to participate by their chest physicians. Upon agreeing to participate, patients received written information and gave informed consent before the first interview.

Design

Four assessments were planned with each patient: the first within 8 weeks following diagnosis (T1) and, subsequently, at 8, 16, and 32 weeks afterwards (T2-T4). Each assessment consisted of a semi-structured interview lasting 30 to 45 minutes and the completion of written questionnaires.

This study was approved by the ethical committees of the hospitals involved.

Measures

Denial was measured by the Denial of Cancer Interview (DCI), a semi-structured interview, based on the definition of denial by Weisman and Hackett:^{28,29} 'the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects'. The DCI

[†] Bronovo Hospital (B) and Medical Centre Haaglanden (M)

consists of nine specific items and two clinical impression scores covering the type and overall level of denial. It has proven to have good psychometric properties³⁰: the reliabilities (Cronbach's α) at the four assessment times were 0.82, 0.86, 0.84 and 0.84, respectively. Denial is represented on a continuous scale ranging from 3-19, with lower scores indicating less denial.

We previously^{31,32} described that patients in our sample displayed three different patterns of denial over time. 'Low deniers' showed a low level of denial consistently over time. This class was most prevalent (69%, mean DCI=5.34). 'Moderate deniers', showed a stable, moderate level of denial over time; this class was smaller (19%, mean DCI=11.31). The class of 'increasing deniers', starting with a low level of denial and showing increased denial over time (13%, mean DCI at T1= 6.28, mean DCI=11.89 at T4) was the smallest. Consequently, these three patient classes will be presented here as low, moderate and increasing deniers.

Patient-reported social and emotional outcomes were measured with the generic EORTC quality of life questionnaire (EORTC-QLQ-C30) first. The QLQ-C30 incorporates nine multi-item scales of which 1) social outcomes, covering role functioning, social functioning, and financial difficulties, 2) cognitive functioning, 3) emotional functioning, and 4) overall quality of life, are relevant here.

Emotional functioning was also assessed with the Hospital Anxiety and Depression Scale (HADS),³³ a widely used well-validated self-report instrument designed to detect anxiety and depression in the medical setting.³⁴⁻³⁶

Medical data, such as tumor type, disease stage at baseline and performance status (T1-T4), were provided by the chest physicians. Performance status was rated using the Zubrod-scale.³⁷ Sociodemographic factors, such as gender, age, marital status, level of education, and religion were collected in the interviews, as was current treatment and smoking history. Trait anxiety, suggesting a stable tendency to perceive and respond to stressful situations with elevated anxiety levels, was measured with the shortened 10-item version of the State-Trait Anxiety Inventory (STAI T-anx).³⁸

Statistical analysis

In an earlier paper³² three classes of patients were distinguished based on their longitudinal pattern of denial. Posterior probabilities of class membership were obtained for each patient. For each patient, the highest posterior probability determined the most likely class. Differences between these classes with respect to patient characteristics were assessed using contingency tables with variances adjusted for class membership uncertainty. Psychosocial functioning scales were analyzed using mixed models, with class, time (T1,...,T4 categorical) and class by time interaction as fixed effects, and with patient intercept as random effect. To account for class membership uncertainty in this analysis, multiple imputation (using M=10 dataset completions) was used. In order to study a

Table 1 *Patient characteristics at baseline*

	Total N= 195
Gender	
Male	115 (59.0%)
Female	80 (41.0%)
Age	
> 60 yrs	69 (35.4%)
60-70 yrs	54 (27.7%)
> 70 yrs	72 (36.9%)
Partner	
Yes ^a	137 (70.3%)
No	59 (29.7%)
Children	
No	35 (18.0%)
Yes	159 (82.0%)
Education level	
Primary education	70 (36.8%)
Secondary education	53 (27.9%)
College/university	67 (35.3%)
Unknown	5
Religion	
No	98 (50.5%)
Yes	96 (49.5%)
Unknown	1
Type of tumor and UICC stage	
NSCLC	139 (74.7%)
≤ II	39
≥ III	100
SCLC	35 (18.8%)
limited	18
extended	17
Other/ unknown	21 (6.5%)
Current treatment	
No treatment	35 (18.0%)
Surgery	24 (12.4%)
Chemotherapy	73 (37.6%)
Radiotherapy	47 (24.2%)
Chemo- + radiotherapy	4 (2.1%)
Unknown	1
Performance status Zubrod	
0	58 (29.9%)
I	96 (49.5%)
II	26 (13.4%)
III/IV	14 (7.2%)
Unknown	1
Smoking	
No	9 (4.6%)
Yes	186 (95.4%)
STAI	
< 22	144 (77.4%)
≥ 22	42 (22.6%)

^a Married, living together or having a relationship but living apart

specific class by time interaction, mixed models with class, time and “increasing denial effect” were also fitted.

Further details of the statistical analysis are published elsewhere.³¹

RESULTS

Patient characteristics

Of 383 newly-diagnosed lung cancer patients, 139 were ineligible because of death (n=30), being too ill (n=32), ≥ 8 weeks since diagnosis (n=28), a language problem (n=15), having moved house or being treated elsewhere (n=8) or other reasons (n=16).

Of the 244 eligible patients, 49 patients (20%) refused participation. Reasons for refusal were: “wants to calm down” (n=8), “does not want treatment or participation in the study” (n=6), “does not want to talk about the illness” (n=7), “too busy” (n=2), denial of illness (n= 4), too ill (n=3), other/unknown (n=19). Non-responders did not differ significantly from responders in gender, age and performance status. Sample characteristics are given in Table 1.

Of 195 patients at baseline, 157 (19% dropout), 122 (37% dropout), and 80 (59% dropout) participated at T2–T4, respectively. The main reasons for dropping out of the study were death or being too ill.

Denial and social and emotional outcomes

The relation between the denial pattern and social and emotional outcomes is shown in table 2 and in figures 1, 2 and 3.

Social outcomes did indeed depend on the level of denial. Differences in role function ($p=0.036$) and social activities ($p=0.027$) were found, with moderate and increasing deniers displaying a higher level of role function and social activities than low deniers (Figure 1).

Financial difficulties did not depend on the level of denial.

Cognitive function was also independent of the denial pattern.

Emotional outcomes (emotional functioning, [$p=0.0001$], anxiety [$p=0.0001$] and depression [$p=0.0019$]) differed among lung cancer patients displaying different denial patterns. Moderate deniers reported better emotional functioning, less anxiety, and less depression than low deniers (Figure 2). Increasing deniers showed a different evolution of emotional functioning and anxiety over time (class by time interaction: $p=0.035$, respectively $p < 0.001$), experiencing greater distress earlier on and less distress at a later stage.

The overall quality of life was significantly different between classes of denial ($p < 0.0001$). Quality of life was better among lung cancer patients who displayed either moderate or increasing levels of denial.

Table 2 Denial and social and emotional outcomes

Psychosocial outcomes	Class (P-value)	Class by time interaction (P-value)
<i>Social outcome</i>		
– Role functioning	0.036	0.450
– Social functioning	0.027	0.155
– Financial difficulties	0.37	0.984
<i>Cognitive outcome</i>		
– Cognitive functioning	0.066	0.472
<i>Psychological outcome</i>		
– Emotional functioning (EORTC)	0.0001	0.035
– Anxiety (HADS)	0.0001	< 0.001
– Depression (HADS)	0.0019	0.368
<i>Overall quality of life</i>		
– Global Health Status / QOL (EORTC)	< 0.0001	0.199

Figure 1 Denial and social outcomes

Figure 2 Denial and psychological outcomes

Figure 3 Denial and global health status / quality of life

DISCUSSION

Denial and social and emotional outcomes

We studied the impact of denial on social and emotional outcomes in the first large, prospective study among lung cancer patients. Our main and most interesting finding is that patients fare better when they express a moderate level of denial or increase their level of denial after diagnosis over time. Patients showing little denial proved to experience worse social and emotional outcomes, and overall quality of life.

In terms of social outcomes, it is conceivable that those patients who avoid constantly thinking about their illness are also less limited in working or pursuing leisure activities. Thus, their illness may interfere less with family life and social relations.

On the other hand, if family members want to share feelings and concerns about the impact of the illness with the patient, such communication is more difficult if a patient denies. Thus, the benefit of denial for the patient may have an adverse effect on relatives. In a qualitative study, Badr and Taylor³⁹ interviewed spouses of lung cancer patients. Some of them reported constraints in discussing smoking, cancer-related symptoms, prognosis, the emotional impact of the illness and the future of surviving relatives. Family members, however, might also support denial to mitigate their own fears, or resign themselves to the patient's denial out of compassion. In the above-mentioned study, one spouse said: "I try not to talk too much about the cancer so that he feels we still have a normal life".

Surprisingly, cognitive functioning was not affected by the patients' level of denial. We expected concentration to be poorer when a patient is unable to avoid intrusive thoughts. This finding might be explained by the limited, self-reported operationalization of cognitive functioning in the EORTC-QLQ-C30.

Emotional outcomes were found to be strongly affected by the level of denial displayed by lung cancer patients. Patients denying moderately and/or increasingly over time functioned better emotionally. They showed less anxiety and depression. It is worth noting that the differences are substantial. Differences of 5 points on a scale of 0 to 100 are generally considered clinically relevant.^{40,41} We found the difference between low and moderate deniers in emotional function to exceed 12 points and the difference between low and increasing deniers to be over 5 and up to 14 points. In other words, the ability to escape from the reality of the disease appears to be beneficial for the emotional well-being of lung cancer patients. This finding is consistent with results from a study by Westerman et al⁴² who found that small-cell lung cancer patients who distanced themselves from the image of the stereotypical cancer patient reported lower levels of fatigue than patients who expressed pessimistic feelings.

These results may be explained by Taylor's theory of 'positive illusions'.^{43,44} She underlines that focussing on (even unrealistic) positive facts and feelings promotes psychological well-being. In her study with breast cancer patients, she found that illusions of having a sense of mastery over the illness and self-enhancement contributed to successful adjustment.⁴⁵ Based on an extensive literature review she postulates that "...certain biases in perception that have previously been thought of as amusing peccadillo's at best and serious flaws in information processing at worst may actually be highly adaptive under many circumstances".⁴³ Likewise, recent research on selective attention and attention bias among breast cancer and prostate cancer patients offers an explanation for the present results: conscious or unconscious avoidance of cancer-related cues and negative emotions can indeed diminish distress.^{46,47}

A better overall quality of life was reported in our study by patients displaying more denial ($p < 0.001$). Given the previously-described positive relation between denial and physical outcomes³² and the positive effect of denial on social and emotional outcomes, this result is not unexpected.

As described earlier, male lung cancer patients display higher levels of denial than female lung cancer patients³. We therefore checked whether the associations between denial and social and emotional outcomes resulted from confounding by gender. The effect of denial on social/emotional outcomes did not change after correction for gender (data not shown). Thus we can reasonably rule out confounding by gender.

An unresolved question is whether denial should be viewed as part of a person's personality. Should denial be considered a trait or a state? We did not assess personality as such but did measure trait-anxiety at baseline. Post hoc analysis indicated that moderate and increasing deniers showed less trait anxiety ($p=0.016$, see table 3). This finding may indicate that denial is, at least partly, a personality trait; a more stable coping style displayed in difficult situations. Conversely, people with higher trait anxiety may lack the ability to protect themselves with some 'normal' level of denial. Consequently, in line with Hackett and Cassem's²⁹ study of cardiovascular patients, we conclude that moderate or increasing denial in cancer patients should not be seen as a sign

of underlying psychopathology, but rather as a psychological strength in adaptation.

Table 3 Association between STAI at baseline and denial

Characteristic		Low deniers	Moderate deniers	Increasing deniers	Test statistic(χ^2)	P-value
STAI	< 22	100 (69%)	32 (22%)	12 (8%)	8.32	0.016
	≥ 22	35 (83%)	2 (5%)	5 (12%)		

Study limitations

This study has some limitations. First, only few of our patients demonstrated strong denial. Those patients might be unwilling to either visit the hospital for diagnosis and treatment or participate in research. Indeed they seem to be underrepresented in our sample. On the basis of their reasons for refusal, 19 non-responders (7.8%) may be strong deniers compared to 5 responders (T1, 2.6%). Thus, no conclusions can be drawn about the effects of a high level of denial and whether strong denial should be considered adaptive.

Secondly, the number of patients lost to follow up was clearly substantial. Our statistical modelling may have overcome this problem but the overrepresentation of relatively healthy patients in the long term may cause some bias in our results.

Clinical implications

The results of this study raise several clinical questions. Firstly, if a certain level of denial benefits lung cancer patients, does this imply that doctors should not tell the full truth about a cancer diagnosis? The answer is not affirmative, since without adequate provision of information it is not possible to deny having cancer and to deny the impact of the disease. In fact, in most Western countries clinicians are obliged to inform their patients about the diagnosis and prognosis, and most patients prefer being informed realistically and honestly by their doctors.^{48,49} Such information is the starting point for the patient's ability to cope with the disease consequences and for further communication with the doctor. Indeed, most patients prefer their specialist to acknowledge them as an individual and to give them the opportunity to ask questions.⁴⁸ Subsequently, if a patient displays some degree of denial, should we support or challenge this? Given the results of the present study, it seems advisable to respect patients' denial and not to repeatedly confront them with the distressing facts. If a patient seems reluctant to receive detailed information, clinicians should consider how much information is adequate and how to convey their messages. Yet, when denial interferes with decision-making, the doctor is confronted with a dilemma and may have to override the patient's preferences.⁵⁰

Guidelines for the management of serious denial have been developed based on clinical experience.^{4,51-56} Careful exploration of the denial, its context, impact and function can provide the clinician with tools to tailor the information provision process.

Overall, one may conclude that in this era of media-driven self-exposure and urge to openness, patients seem to have to defend the need for a safe niche in which they can find protection against frightening events or keep intense and intimate feelings private. Denial can serve this need and should be respected.

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Chapter 8

Summary and general discussion

INTRODUCTION

In this chapter the major findings of the study are summarized and discussed. The structure of the discussion follows the relevant themes that we have dealt with during the course of the research project: the concept of denial, the scope of the DCI, methodological issues, denial during the course of the illness, considerations concerning patient-rated outcome, gender differences and the implications of the results for daily oncology practice.

SUMMARY

In *Chapter 1* a general introduction is given and the background and outline of the thesis are described.

Chapter 2

Three patients with lung cancer, a man aged 68, a woman aged 69 and a man aged 52, denied the nature or the severity of their disease in three different ways: temporary denial to evade acute emotional shock, full-blown persistent denial, and unjustified optimism, respectively. The psychological mechanism of denial may become operational in patients confronted with an overwhelming disease. A less pronounced denial of medical information provided by physicians can be recognized in many patients. It may also be apparent in the way that individuals or groups of people sharing the same unbearable reality face up to facts. Denial may be helpful in (temporarily) circumventing a serious problem, but when the disease is serious it may interfere with relationships with partners, relatives and friends. Denial must be differentiated from organicity, such as anosognosia due to cerebral damage, patient ignorance, or vague communication from the medical community. A direct and blunt confrontation of denial may result in adverse effects due to aggravation of a defensive mechanism. Slowly providing the patient with pieces of information whilst monitoring their reaction may allow gradual conformation to the medical reality.

Chapter 3

Denial is a clinically relevant concept in cancer patients. It has been extensively investigated and discussed. The definition of denial, however, has been subject to different theoretical trends over time. From a psychoanalytical viewpoint, denial is a pathological, ineffective defence mechanism. On the other hand, according to the stress and coping model denial can be seen as an adaptive strategy to protect against overwhelming events and feelings.

In this chapter the different concepts and the prevalence of denial in cancer patients are reviewed. The relationship between denial and background characteristics, and the influence of denial on quality of life are also described.

The prevalence of denial of diagnosis in cancer patients varies from 4.3% to 46.7%, while denial of impact occurs in 8% to 70% and denial of affect is found in 17.9% to 42% of patients. Elderly cancer patients are more likely to manifest denial. Cultural background seems to play a role in the prevalence of denial in cancer patients. Neither the type of cancer nor gender seems to be related to denial. At most, men might be more likely to deny during the terminal phase. In a limited number of longitudinal studies, a gradual reduction in denial was found over the course of the illness.

The effect of denial on psychological functioning seemed to depend on the concept of denial used. Distractive strategies were found to reduce distress, whereas passive escape mechanisms turned out to decrease psychological well-being.

Future research on the prevalence and the (mal)adaptive properties of denial in cancer patients should be based on a clear concept, longitudinal design and careful recording of background variables.

Chapter 4

Based on Weissman and Hackett's comprehensive definition of denial, a semi-structured interview was developed to measure denial in cancer patients. The Denial in Cancer Interview (DCI) covers both the patient account of their illness experience and the expert's impression of the level of denial in the patient's story. This chapter describes the development and first psychometric analysis of the instrument.

The development of the DCI was based on clinical observation, the expert opinion of eight specialised psychiatrists, as well as three small pilot studies to assess feasibility.

The DCI is composed of two parts: a semi-structured interview consisting of nine specific items to be answered by the patient and two items covering the interviewer's clinical impression of the patient's type and level of denial. Follow-up interviews were held at 8, 16 and 32 weeks after the baseline assessment (T2-T4).

To measure the inter-rater reliability, interviews were recorded and rated independently by one interviewer and one of the study's co-workers.

One hundred and ninety-five consecutive newly-diagnosed lung cancer patients were interviewed. The internal consistency of the DCI (Cronbach's α) was 0.84 at first interview and 0.85, 0.82 and 0.83 at T2-4, respectively. The inter-rater agreement was good for the DCI and the Patient's Assessment scale, and satisfactory for the clinical impression items. The DCI proved to be a feasible and reliable instrument for measuring denial in lung cancer patients. Whether applicable to other cancer populations remains to be studied.

The DCI is presented in addendum A. The frequencies of the items of the Patient Assessment Scale are given in addendum B.

Chapter 5

Denial in cancer patients is a well-known clinical phenomenon, yet few studies investigate the prevalence of denial over time.

This chapter describes the level of denial in lung cancer patients over time, and the impact of sociodemographic and illness-related variables on denial in these patients.

The level of denial was measured by the Denial of Cancer Interview in 195 consecutive newly-diagnosed lung cancer patients. Four assessments were conducted over eight months. Sociodemographic data were collected during the interviews. Medical data were provided by the chest physicians.

At baseline most patients (86.6%) display a low or moderate level of denial and a small number of patients (3%) display a high level of denial. The mean level of denial is the lowest at baseline and increases over time.

Male lung cancer patients deny more than their female counterparts. Younger patients deny less than elderly patients. Shortly after diagnosis lower-educated patients deny more than higher-educated patients, but during the course of the illness both these groups display the same level of denial.

Some level of denial has to be considered a normal phenomenon, part of the illness process for lung cancer patients. Whether the level of denial is related to adaptive or maladaptive coping remains to be investigated.

Chapter 6

Although denial in cancer patients is often seen in clinical practice, little is known about denial over time during the course of the illness. Furthermore, studies relating denial to physical outcomes are lacking. In this chapter patterns of denial among lung cancer patients are described and linked to physical outcomes. Denial was measured longitudinally as described in chapter 4. Patient-reported physical outcomes were measured with a generic and disease-specific quality of life measure.

Three patterns of denial over time were identified in lung cancer patients: patients displayed either low, moderate or increasing denial. Male lung cancer patients were found to deny at a moderate level more often. A moderate or increasing level of denial was consistently related to improved patient-rated physical outcomes. Lung cancer patients displaying greater denial reported a better overall perception of health and better physical functioning. They complained less about fatigue, nausea and vomiting, appetite loss, dysphagia and arm and shoulder pain than low deniers. Other symptoms did not differ among denial classes.

Denial in lung cancer patients may well be an adaptive mechanism and should be respected in clinical practice.

Chapter 7

As mentioned in the previous chapters, denial is a well-known phenomenon in clinical oncology practice. Nonetheless, whether the impact of denial on patients' social and emotional wellbeing is beneficial or harmful remains unknown.

In this chapter the relationship between denial and social and emotional outcomes in lung cancer patients over an extended time period are described. The same sample and longitudinal assessment of denial as described in chapter 5 were used. Patient-reported social and emotional outcomes were measured with the EORTC-QLQ-30 and the Hospital Anxiety and Depression Scale.

Patients with a moderate or increasing level of denial over time reported better social outcomes, and less anxiety and depression than patients with a low level of denial. The overall quality of life was higher among lung cancer patients who displayed either moderate or increasing levels of denial than those with low levels of denial.

Based on these findings, it can be concluded that a certain level of denial in lung cancer patients can have a protective effect on social and emotional outcomes. Clinicians should take this into account when giving information about the illness and its prognosis.

DISCUSSION

Denial

The history and the development of the concept of denial in different psychological schools were presented in chapter 2. How do people view denial nowadays? In the course of our research project we encountered many different points of view from colleagues about the concept. In daily life most people use the term denial with a pejorative charge, as illustrated in the following citation from the New York Times¹: "In the modern vernacular, to say someone is "in denial" is to deliver a savage combination punch: one shot to the belly for the cheating or drinking or bad behaviour, and another slap to the head for the cowardly self-deception of pretending it's not a problem." The author, however, adds: "The psychological tricks that people use to ignore a festering problem in their own households are the same ones that they need to live with everyday human dishonesty and betrayal, their own and others. [...] In this emerging view, social scientists see denial on a broader spectrum — from benign inattention to passive acknowledgment to full-blown, wilful blindness — on the part of couples, social groups and organizations, as well as individuals".

In reaction to this article 55 readers gave their comments. A broad spectrum of opinions was represented in these comments. At one end of the spectrum lie sympathizing and alleviating views: "...Perhaps denial is a person's initial attempt to minimize blame and reconcile themselves to the community. After all, the couples that minimize minor infractions seem to be more likely to have

a good relationship in the long run”, and: “Sometimes what looks like denial to others, should simply be called hope”. At the other end of the spectrum strongly disapproving statements were made: “... denialism has become epidemic in our society. [...] it represents an abnormality, an imbalance, a caustic force that degrades our collective quality of life”.

A similar range of opinions can be found in patients’ and doctors’ views on the definition of denial of illness. Some participants in our study said: “The doctor tells me everything and I appreciate that, because it is wrong to put your head in the sand.” and one patient told us: “I do not want to know anything about my disease. I am a member of the ostrich party.” The different views held by researchers on the concept denial are discussed at length in the literature^{2,3,4,5,6,7,8,9}.

The problem with denial remains the different and even contradictory views on the concept. A deep examination of the meaning of denial can feel like walking in a painting of Escher: following the stairs you gradually realize that you have become trapped in an unfathomable reality.

As it is impossible to encompass the whole variety of viewpoints on denial in one definition, any investigator who needs a research tool of the concept has to make a choice.

We chose Hackett and Cassem’s encompassing definition: “(..) the conscious or unconscious repudiation of part or all of the total available meaning of an event to allay fear, anxiety or other unpleasant affects”.

The advantage of this definition for research purposes is that it covers the whole range from minimization to full disavowal, from facts to feelings and from a little to an extensive level of denial. Besides, the unsolvable question regarding the difference between conscious and unconscious, can be avoided.

An omission in Hackett and Cassem’s definition is that no distinction is made between the necessary two sides of denial: the ‘event’ or the reality that is evident to others, and the denial of this event or its impact by the denier. The DSM IV definition of denial does comprise these two sides: ‘The individual deals with emotional conflict or internal or external stressors by refusing to acknowledge some painful aspect of external reality or subjective experience that would be apparent to others’.[†]

The Denial of Cancer Interview

The DCI, our instrument to measure denial, turned out to be reliable and feasible, yet some remarks should be noted. The concept of denial is multiform. Different and even contradictory views on its appropriateness can be found in the literature. Moyer and Levine¹⁰ underline the lack of consensus on whether denial is unconscious or conscious, a trait or a state, indicative of psychological

[†] This addition is also found in the Wikipedia’s definition: “Denial is a defense mechanism [...] in which a person is faced with a fact that is too uncomfortable to accept and rejects it instead, insisting that it is not true despite what may be overwhelming evidence.”

disturbance or a normal response to serious illness, a broad or a narrow concept. This makes its assessment for research purposes difficult. Given the substantial amount of literature regarding denial in cancer patients, it is remarkable that a valid instrument to measure denial in oncology is lacking. Different attempts have been made, but no instrument was found to survive critical analyses.^{10,11,12} Clearly, there are considerable methodological problems with measuring denial in cancer patients. Connor¹² compared ten different approaches with the aim to measure denial in terminally ill patients: self-report scales, observational assessments and physiological measurements. Two instruments showed reasonable psychometric properties, but neither had yet been tested in physically ill patients. Observational and physiological approaches did not prove to be consistent ways to measure denial. Based on their extensive review of the measurement of denial, including interviews, clinical ratings, self-report instruments, behavioural measures and indirect assessments, Moyer and Levine recommend that future studies explicitly define denial, use multiple measures assessing different modalities and outcomes, measure denial at several times over the course of illness, and take into account aspects of the individual's situation to ensure that denial is not identified erroneously. In the development of the DCI we followed most of their suggestions. Firstly, we explicitly chose the definition of denial established by Hackett and Cassem. Secondly, because the lack of a gold standard makes it difficult to validate a newly-developed instrument, we measured denial with the DCI as well as with the Brief Cope.

Thirdly, the DCI is composed of different modalities: the Patient Assessment Scale and the clinical impression of type and level of denial rated by the interviewer. Fourthly, we measured denial four times over an eight-month period. And finally, because of the elaborated interviews with the patients, we were able to identify denial accurately.

As we assumed that the Brief Cope¹³ subscales of denial and self-distraction would cover aspects of denial that were also addressed in the DCI, we compared these for validity establishment. The Cope denial subscale, interestingly, did not show a correlation with the DCI, and the distraction subscale showed a statistically significant ($p=0.02$) negative correlation with the DCI. The explanation for this finding by the designer of the Brief Cope, Charles Carver (personal communication) is that "The difference comes from the content being assessed. The DCI is after a more subtle, arguably 'truer' sort of denial. The items of the denial subscale of the Brief Cope cover overt denial, with a little overtone of catastrophizing. (...) self-distraction is working not to think about it by focusing on something else." The self-distraction items seem to cover mild, conscious denial or suppression which is rated in the lower range of the clinical impression scores of the DCI. Therefore, a high score on the self-distraction scale of the Brief Cope corresponds with a lower score on the DCI, explaining the negative correlation. These results have to be interpreted with caution, given the moderate internal consistency of the self-distraction subscale ($\alpha = 0.63$ in our study). The conclusion is that our attempt to validate the

DCI by comparison with the subscales of the Brief Cope was not successful and underlines the difference in use of the concept of denial.

The DCI was developed in five phases with lung cancer patients: a face-validity check, three pilot studies and the testing phase. The nine items of the Patient Assessment Scale focussed on illness-related information needs, thinking and speaking about the illness, distraction activities and the impact of the illness on daily life and future planning.

The question is whether the DCI retains its good psychometric properties when used in other cancer patient groups. Looking at the items of the Patient Assessment Scale of the DCI (see addendum A) it seems plausible that they would be applicable to other cancer patient populations. Item 7, however, which focuses on treatment expectations, is based on the assumption of a poor prognosis, especially for non-operable tumours. Lung cancer patients receiving chemotherapy or radiotherapy who indicate that they expect 'complete recovery' are denying the seriousness of their illness. In some other types of cancer, such as chemotherapy for lymphoma, adjuvant chemotherapy for breast cancer patients or curative radiotherapy for head and neck cancer, the aim of the treatment is cure. Thus, to be able to score this item, the patient's answer has to be differentiated according to the realistic treatment expectations for the type of the cancer from which the participant is suffering. Whether the DCI is applicable to cancer patients with a good prognosis remains to be proven.

METHODOLOGICAL ISSUES

The main purpose of this study was to investigate the relation between denial in lung cancer patients and the quality of life over time in the course of the disease. This means that the relation of two series of longitudinal outcomes had to be analyzed. In statistical terms the first aim was to identify latent classes of longitudinal denial measurements. The second objective was to analyze whether this 'longitudinal denial' was related to physical and emotional outcomes, which in turn were also longitudinally assessed.

Some methodological issues have to be considered. Firstly, to be able to measure denial we developed the DCI and tested and adapted the instrument in three pilot studies before the longitudinal study was started. The data of this study were used to analyze the psychometric properties of the DCI. Thus the reliability of the DCI was tested in the same study in which the research questions were investigated.

The second issue concerns the considerable number of drop-outs, inherent to the poor prognosis of lung cancer. We started at baseline with 195 participants (115 men, 80 women) and after eight months we finished with 79 participants (43 men, 36 women), which signifies a dropout rate of 59%. We therefore chose a random effects analysis, which yields unbiased results when observations are missing at random. This means that, in our situation, the

dropout between successive assessments is not directly related to unobserved denial.

The third methodological issue is the small number of patients displaying a high level of denial. It is conceivable that lung cancer patients who strongly deny their illness or do not want to speak about it, will not be willing to participate in a study exploring patients' perception of facts, feelings and impact of the disease, thus creating a bias in our results. Indeed these patients seem to be overrepresented in our non-responding population. Based on their reasons for refusal ("does not want treatment or study participation" (n=6) "does not want to talk about the illness" (n=7), "too busy" (n=2), 'denial of illness' (n=4)), 19 non-responders (7.8%) could be strong deniers compared to 5 responders (T1, 2.6%).

This is a complicated aspect of our study, because without data concerning high denial, we are unable to draw conclusions about the relationships between all the different levels of denial and physical and emotional outcomes.

It is conceivable that an extreme level of denial may cause a delay in diagnosis, withdrawal from medical check-ups and therapy non-compliance.¹⁴ These high-denying patients are probably seen more by their family doctors than by chest physicians. To investigate this patient group, the participation of general practitioners and relatives will be essential.

THE PATTERNS OF DENIAL OVER TIME

Speaking about denial often elicits a reference to Kuebler Ross' stage of grief theory in which denial is supposed to be the first phase.¹⁵ This theory is criticized in the literature and has not proven to be very helpful in daily practice.^{16,17} The results of our study support these critical views. Denial should not be considered as a transitory phenomenon. Based on the analysis of four assessments over eight months in our patient group, an increased level of denial over time was found. Looking at different classes within our patient group, we could distinguish three patterns of denial: low, moderate and increasing. Surprisingly, the level of denial in the low and moderate deniers, the largest groups, remained stable over eight months. This finding raises the question whether in most people denial is a trait, a consistent style of coping in daily life, and only a state, a temporary reaction to a shocking life event, in a small group. As denial has to be assessed before and after the diagnosis of lung cancer to provide an answer, this research question goes beyond the scope of our study.

DENIAL AND PHYSICAL OUTCOME

An important finding in our study is that a moderate or increasing level of denial was consistently related to improved patient-rated physical outcomes.

Lung cancer patients displaying greater denial reported a better overall perception of health and better physical functioning. They also suffered less from dyspnea, fatigue, gastrointestinal symptoms, dysphagia and arm pain. Thus, denial may be adaptive in lung cancer patients. The explanation for these results can be found in theories of symptom perception and selective attention, of which an integrated approach is presented by Kolk and colleagues.¹⁸ They describe the perception of physical symptoms as being preceded first by peripheral, physiological changes resulting from bodily processes. Next, changes generate information about organ systems but only a small proportion of this information gives rise to awareness and is consciously processed. Awareness also depends on the (selective) attention we pay to these sensations. Attention to the body is likely to heighten the processing of physical, internal information rather than external information. The more people focus internally, the more they notice symptoms.¹⁹ Using denial as a coping strategy may influence cognitive processing and may lead to reduced internal focussing. A nice illustration of this theory can be found in the results of the recent clinical study by Mills et al.²⁰ They concluded that inoperable lung cancer patients who completed a weekly patient-held QOL diary reported more deterioration in QOL than patients who received standard care. It is conceivable that each time they fill out the questionnaire, these patients, who suffer from inoperable lung cancer, are confronted with feelings of helplessness and powerlessness knowing that cure is impossible. Not focussing on the painful reality time and again may make it easier to evade these feelings. Whether denial is less adaptive in cancer patients with a favourable prognosis needs further study. Focussing on physical symptoms which are a sign of a curable illness is certainly more to the patient's benefit than delay of consulting a doctor based on denial.

DENIAL AND SOCIAL AND EMOTIONAL OUTCOME

The key finding from our study is that patients fare better when they express a moderate level of denial or increase their level of denial from the moment of diagnosis over time. Patients showing little denial experience worse social and emotional outcomes and reduced overall quality of life.

In terms of social outcomes, it is conceivable that patients who deny having lung cancer or who deny its impact are less limited in working or pursuing leisure activities. Moreover, as lung cancer often raises stigmatizing and guilt-inducing reactions,^{21,22} denial may protect these patients from losing self-esteem and from harm through social interactions caused by negative responses from their environment.

Patient-rated emotional outcomes were strongly related to the level of denial. Patients denying moderately or increasingly over time show less anxiety and depression than low denying patients. This finding is consistent with Taylor and Brown's²³ theory in which they propose that positive illusions are beneficial to mental health. They used a dictionary's definition of illusion: "a percep-

tion that represents what is perceived in a way different from the way it is in reality. An illusion is a false mental image or conception which may be a misinterpretation of a real appearance or may be something imagined. It may be pleasing, harmless, or even useful". In their extensive literature review the authors challenge the common view that the mentally healthy person perceives reality accurately. Taylor and Brown conclude that the association between illusions and a positive mood appears to be a consistent one. Happy people are more likely to have positive conceptions of themselves, a belief in their ability to control what goes on around them and a high self esteem. Furthermore, the ability to care for others and social bonding appear to be associated with positive illusions, which is again consistent with our results on the relation between denial and social outcome in lung cancer patients.

From our explorative literature review we concluded that the effect of denial in cancer patients on psychological functioning depends on the concept of denial used². Studies in which denial of the disease impact was related to improved psychological functioning represented active strategies such as not letting the illness control life, brushing the illness aside and instead adopting a positive outlook in spite of having cancer. In studies in which denial was related to poorer psychological functioning, the concepts used were: refusing to believe 'it' happened, feelings that time would not make any difference, realizing that one did not have any control, thinking that the outcome would be determined by fate, avoiding being with others and making oneself feel better by drinking, eating and smoking. Thus, distractive strategies seem to be related to lower distress, whereas passive escape mechanisms seem to decrease psychological well-being.

In the light of the above, the question arises whether the concept of denial used in our study is one of these distractive strategies, namely creating a positive outlook. Our basic assumption was to use a broad denial concept rather than one which defined denial as an adaptive mechanism from the outset. Looking at the items of the Patient Assessment Scale of the DCI, the rating was based on (rejection of) information provided, (not) thinking and speaking about the illness, making (un)realistic plans for the future, (unrealistic) treatment expectations and (rejecting) the impact of the illness in daily life. These items seem to cover distractive strategies as well as passive escape mechanisms. To find out more about the relation between denial and outlook on life it would be interesting to investigate the relationship of denial with individual items, as well as to compare the PAS with instruments measuring optimism and demoralization in further research.

GENDER DIFFERENCES

The current study shows that male lung cancer patients consistently deny more than female patients. Moreover, the protective effect of denial on patient-rated social and emotional outcomes is stronger for males than for females. The

effects of denial remain significant after correction for gender as a possible confounder. These gender differences in denial and its effects can be explained by results and theories from previous studies.^{24,25} Traditionally, men are found to be more focussed on work-related issues and women on family and health-related matters. This may explain why men are less attentive to health problems and, thus, move into denial more easily. Moreover, the masculine view that being ill is a sign of weakness, paves the way for their denial.^{26,27} Women with lung cancer report concerns regarding psychosocial issues, illness-related symptoms, the future and their family significantly more frequently than men,²⁸ which makes them vulnerable to developing anxiety and/or depression. Sarna²⁹ suggests that the quality of life and demands of illness experienced by women with lung cancer may be different than those experienced by men because of competing household, childcare and other role-related demands. While this may be true, men can have work-related worries and responsibilities as the breadwinner for their family. Thus, in our opinion the different demands facing men and women cannot fully explain the differences in quality of life or mood. We believe that women are less able to protect themselves against worries and negative feelings through denial than men.

The phenomenon of denial is complex and covers emotional, cognitive and behavioural responses to shocking events. Historically, coping and defence mechanisms are considered to be based on social and psychological learning effects and cultural influences.^{30,31} Recent studies in the field of psychoneuroendocrinology focus on sex differences in stress responses and social behaviour.^{32,33} The hypothalamic-pituitary-adrenal axis (HPA) and gonadal steroids and differences in brain structure play a role in psychological reactions and social behaviour. The question whether a neurobiological substrate is responsible for the differences in the use of denial between men and women is challenging and requires further research.

CLINICAL IMPLICATIONS

The current investigation is primarily a descriptive study. Yet, based on the findings some considerations for clinical practice can be discussed.

Firstly, since a certain level of denial seems to be beneficial for lung cancer patients, doctors should take into account the protective role of denial for their patients. This does not discharge clinicians from their duty to inform patients about diagnosis, treatment and prognosis. The process of providing information has to be guided by the patient's verbal and non-verbal responses, to prevent reinforcement of denial strategies.^{34,35} It would be helpful if the doctor were to explicitly mention that they understand the patient's denial and their need to control the underlying fears and worries. To diminish the tension caused by the bad news, the doctor can ask the patient how much information they want and feel they can handle. In this way, doctor and patient create a

close collaboration to help the patient cope with the bad news and the difficult facts and feelings related to the illness.

Secondly, the moderately and increasingly denying patients in our present study were less likely to report that the illness or medical treatment interfered with family life and social activities. The question arises whether the family members agree with the patient's opinion. It is conceivable that family and friends want to share feelings and concerns with the patient about the impact of the illness and maybe prepare for the care the patient will need when the illness gets worse. Such communication can be hampered by the patient's denial.³⁶ Thus, the benefit of denial for the patient may have an adverse effect on their relatives. On the other hand, relatives can also be in denial and may join the patient's disavowal of the threatening facts and feelings. This 'conspiracy of silence' is a well-known phenomenon, originally described by Glaser and Strauss³⁷ in dying patients. When exploring the context of potential patient denial, clinicians should pay attention to the role of family members and, if necessary, support them in their coping process with the patient's illness and denial.

Thirdly, our study shows clearly that a certain level of denial is a common phenomenon in lung cancer patients. The question is, what about doctors? Cousins⁶, who makes a plea for the introduction of the concept of 'healthy denial', states: "In a sense, the physician who treats a terminally ill patient is himself practicing a form of denial". Indeed, Lamont and Christakis³⁸ showed that physicians communicate more optimistic survival estimates than they formulate, and that the latter are even more optimistic than patients' actual survival. It is conceivable that clinicians have to protect themselves against the tragedies of their patients. Being too empathetic can interfere with acting professionally or with their own coping ability. But the opposite behaviour, for example being too aloof, can hamper a doctor-patient relationship based on trust. As a compromise doctors can collude with the patient's denial. The *et al*³⁹ describe collusion in false hope about recovery: "The doctor did and did not want to pronounce a 'death sentence' and the patient did and did not want to hear it". This paper elicited different letters to the editor. In two letters "not knowing" and "false hope" were mentioned as helpful coping strategies to allow patients to lead their lives as fully as possible.^{40,41} The two other letters supported the advice of the authors to break such a cycle of collusion.^{42,43} In our opinion management of denial in cancer patients primarily needs a respectful attitude with regard to the protective effect of the denial. Clinicians should be aware of their own role in the communication with the denying patient. If important medical decisions cannot be made because of the denial, the clinician needs tools to find a middle road between confrontation and support. Careful exploration of the denial, its context, impact and function can help the clinician tailor the provision of information.

To summarize, this study convincingly shows that denial in lung cancer patients is an important phenomenon that deserves attention in clinical prac-

tice. In our era of self-disclosure and nearly boundless openness, we have to realize that some patients need protection against unbearable facts and feelings. A certain level of denial can offer this protection and improve physical, social and emotional outcomes. Clinicians can support these patients by respecting their denial.

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APPENDIX

Joint analysis of multiple longitudinal outcomes:
application of a latent class model

Hein Putter, Tineke Vos, Hanneke de Haes, Hans van Houwelingen

SUMMARY

We address the problem of joint analysis of more than one series of longitudinal measurements. The typical way of approaching this problem is as a joint mixed effects model for the two outcomes. Apart from the large number of parameters needed to specify such a model, perhaps the biggest drawback of this approach is the difficulty in interpreting the results of the model, particularly when the main interest is in the relation between the two longitudinal outcomes. Here we propose an alternative approach to this problem. We use a latent class joint model for the longitudinal outcomes in order to reduce the dimensionality of the problem. We then use a two-stage estimation procedure to estimate the parameters in this model. In the first stage, the latent classes, their probabilities and the mean and covariance structure are estimated based on the longitudinal data of the first outcome. In a second stage we study the relation between the latent classes and patient characteristics and the other outcome(s). We apply the method to data from 195 consecutive lung cancer patients in two out-patient clinics of lung diseases in The Hague, and we study the relation between denial and longitudinal health measures. Our approach clearly revealed an interesting phenomenon: whereas no difference between classes could be detected for objective measures of health, patients in classes representing higher levels of denial consistently scored significantly higher in subjective measures of health.

1 INTRODUCTION

In this paper we address the statistical problem of joint analysis of two series of longitudinal measurements. The typical way of approaching this problem is by applying a joint mixed effects model for the two outcomes. The advantages of this approach are a well-established theory [1] and certified software to fit these models. A number of papers advocating the use of joint mixed effects models in biometry have appeared [2–5]. This approach has a number of drawbacks as well, however. First, a large number of parameters is needed to specify a meaningful model. One would typically need considerably more than twice the number of parameters required for a single outcome, since the correlation of the two measurements at the same time-points as well as the cross-correlation of the two outcomes at different time-points would have to be modeled. The modeling process in this approach is not straightforward, especially with regard to the correlation parameters. Most of the papers dealing with joint mixed effects models for multiple longitudinal outcomes use linear or perhaps quadratic continuous time effects, whereas in our case time is more appropriately modeled as categorical factor [6]. While in principle it is possible to include time as a categorical factor in a joint linear mixed model, the task of correctly modeling the (cross-) correlation parameters then becomes highly involved, and there is a real danger of numerical convergence problems. Perhaps the largest drawback of the joint mixed effects model approach is that, after a final model has been selected and fitted to the data, the results of the model may no longer allow for a clear interpretation. See Fieuws & Verbeke [7] and the discussion for an example of these interpretational problems.

The motivation for the statistical problem and the approach we took is a study on the prevalence of denial in lung cancer patients and its relation with physical and emotional functioning and quality of life. The first objective was to study the evolvement of denial over time and how it is related to patient characteristics. The second question was whether it is possible to distinguish groups of patients with distinct patterns regarding their evolvement of denial over time. For instance, are there groups of patients with increasing or decreasing levels of denial over time or with high and low overall levels of denial, or perhaps a combination of those? The objective here in statistical terms is to identify latent classes of longitudinal denial measurements. This type of models is quite popular in the psychometric literature [8–14], where it goes under the name of growth mixture models, latent trajectory classes or trajectory analysis. The models can be fitted using for instance Mplus [15], Mx [16], or SAS proc Traj [9]. The next question is whether there are differences between these latent classes with respect to patient characteristics. The final question is how denial (longitudinal) is related to a reasonably large number of physical/emotional functioning and quality of life measures (all longitudinal). Thus, we are particularly interested in how two or more longitudinal measurements relate to each other, which is precisely the aspect that is most difficult to model and

interpret using a joint mixed effects model. Especially the combination of the last research questions of this project prompted us to use the latent groups of patients identified in the second question to study differences between these groups with respect to quality of life and physical/emotional functioning.

Although the two-stage approach we took is inspired by the particular application, it can also be motivated in a quite different way. First, in order to reduce the dimensionality of the problem, it is reasonable to assume a latent class joint model for the longitudinal DCI denial and health measure(s) outcomes. In this model one latent class influences both denial and health measures. Then our approach is a two-stage procedure, where in a first stage one part of the model is estimated (the relation between latent classes and denial), and in a second stage the remaining part (the relation between latent classes and patient characteristics and physical/emotional functioning and quality of life). This can be shown to be an estimation procedure that yields consistent estimates. We feel such a two-stage approach is very useful, especially in situations like ours where interest is in relating one pivotal longitudinal outcome to a large number of other longitudinal outcomes. The parameters of the latent class joint model can also be estimated directly using full likelihood, but our approach is more practical here since it avoids the need of completely refitting the joint model (including typically considerable computing time for an EM-type algorithm to converge) for each pair of longitudinal outcomes.

The remainder of the paper is structured as follows. Section 2 describes the project and the data in more detail. Section 3 considers the latent class joint model for denial and the other longitudinal outcomes and discusses the general estimation procedure. Section 4 derives the latent classes with respect to denial, while Section 5 discusses how these latent classes can be used to study the relation with patient characteristics and with quality of life and physical and emotional functioning. Section 6 discusses the results obtained and possible extensions and other applications, and puts our approach into perspective. Technical details concerning the EM-algorithm used to find the latent classes and how to account for uncertain class membership in tests of association are presented in the appendix.

2 THE DENIAL OF LUNG CANCER STUDY

The denial of lung cancer study consists of 195 patients diagnosed with lung cancer. Patients were consecutively recruited from two out-patient clinics in The Hague, The Netherlands. Enrollment took place from January 2001 until December 2003. For more details concerning inclusion and exclusion criteria, recruitment and eligibility, see Vos et al. [6]. A semi-structured interview, called the denial of cancer interview (DCI), was developed, consisting of nine specific items and two clinical impression scores concerning type and level of denial. The measure of the DCI represents by the level of denial on a continuing scale ranging from 3-19, with higher scores indicating higher levels of

Table I *Patient characteristics for the 195 patients in the denial in lung cancer study.*

<i>Characteristic</i>	<i>N</i>	<i>Per cent</i>
Gender		
Male	115	59
Female	80	41
Age		
≤ 60	69	35
60 – 70	54	28
> 70	72	37
Partner		
No	58	30
Yes	137	70
Children		
No	35	18
Yes	159	82
Unknown	1	
Education level		
Primary	70	37
Secondary	53	28
College/University	67	35
Unknown	5	
Religion		
No	98	51
Yes	96	49
Unknown	1	
Type of tumor		
NSCLC	139	75
SCLC	35	19
Other/unknown	21	7
Current treatment		
Surgery	35	18
Chemotherapy	73	38
Radiotherapy	47	25
No treatment	35	18
Unknown	5	
UICC grade		
0	59	30
I	96	49
II-IV	40	21

Partner: 'yes' means married, living together or having a relationship but living apart.

denial. For more details concerning this scale and its psychometric properties, refer to Vos et al. [17]. The DCI was taken at four consecutive time points, $T_1, \dots, T_4$. The first of these time points (T_1) was planned within eight weeks after diagnosis, the following assessments at 8, 16, and 32 weeks after the first assessment (T_2, T_3, T_4 , respectively). Every assessment consisted of a 30 – 45 minutes semi-structured interview as well as written questionnaires. We will provide a detailed report elsewhere on the relation between DCI on the one hand and on several physical and emotional functioning scales and quality of life from the EORTC QLQ questionnaire and the lung module on the other hand. For the purposes of this paper, we report on two anonymized scales, one of which was assessed by the patient him- or herself (this scale is referred to as ‘subjective health’), the other assessed by the treating physician (this scale is referred to as ‘objective health’). The ‘subjective health’ is measured on a scale from 0 to 100, with higher values representing higher subjective health. The ‘objective health’ was measured on a scale from 0 to 4 with lower values representing higher objective health. In order to facilitate easy comparison with ‘subjective health’ this scale was therefore reversed and rescaled from 0 to 100. Both scales were taken at the same time points, T_1, T_2, T_3, T_4 , as the DCI.

For completeness we repeat the patient’s characteristics in Table I.

3 LATENT CLASS MODEL

3.1 The model

The latent class joint model that we consider is represented as a graphical model in Figure 1.

The graphical model is quite similar to that appearing in [18]. As in [18] we assume the existence of a latent class G_i that influences multiple longitudinal outcomes. In [18], the second longitudinal outcome is binary, in our case instead of a single binary longitudinal outcome we are dealing with a reasonably large series of quantitative longitudinal physical/emotional functioning scales. Another difference is that [18] uses a Bayesian approach. Let $\mathbf{y}_i = (y_{i1}, \dots, y_{i4})$, with $y_{i1}, \dots, y_{i4}$ denoting the denial scores at $T_1, \dots, T_4$, and let $(\tilde{\mathbf{y}}_i^1, \dots, \tilde{\mathbf{y}}_i^H)$ denote the H longitudinal health measures, with $\tilde{\mathbf{y}}_i^h = (\tilde{y}_{i1}^h, \dots, \tilde{y}_{i4}^h)$ the h^{th} series of observed health measures at $T_1, \dots, T_4$. Conditionally given the latent class G_i , we assume $\mathbf{y}_i$ and the joint vector $(\tilde{\mathbf{y}}_i^1, \dots, \tilde{\mathbf{y}}_i^H)$ to be independent. Figure 1 suggests that the vectors $(\tilde{\mathbf{y}}_i^1, \dots, \tilde{\mathbf{y}}_i^H)$ are also conditionally independent, given G_i , but this is not a necessary condition. It is depicted like this only to reflect the estimation procedure which considers the physical/emotional functioning scales one by one. The latent vectors ξ_i and $\tilde{\xi}_i^h$ are capturing both fixed and random effects of the longitudinal series. Conditionally given $G_i = g$, the latent vector ξ_i can be represented as

$$\xi_i = \mathbf{X}_i \boldsymbol{\mu}_g + \mathbf{Z}_i \mathbf{b}_i \quad \text{with } \mathbf{b}_i \sim N(0, \mathbf{D}_g) \quad (1)$$

Figure 1 A graphical model representation of the latent class joint model

random effects. The latent vector ξ_i represents the individual mean vector of $\mathbf{y}_i$, which is related to $\mathbf{y}_i$ as

$$\mathbf{y}_i | \xi_i \sim N(\xi_i, \sigma_g^2 \mathbf{R}_i) , \quad (2)$$

where $\mathbf{R}_i$ is a known correlation matrix. We gather the unknown parameters μ_g , $\mathbf{D}_g$, σ_g^2 and the unknown class probabilities π_g for all classes into a single vector $\boldsymbol{\theta}$.

As in [18], patient characteristics Z_i may influence the $\mathbf{y}_i$'s, but the influence of Z_i on $\mathbf{y}_i$ is assumed to act through the latent class G_i only (although in principle patient characteristics could also be incorporated into the fixed effects design matrix $\mathbf{X}_i$). The relation between $\mathbf{y}_i$ and Z_i is given through G_i as

$$f(\mathbf{y}_i | Z_i; \boldsymbol{\theta}, \boldsymbol{\beta}) = \sum_g f(\mathbf{y}_i | G_i = g; \boldsymbol{\theta}) \cdot P(G_i = g | Z_i; \boldsymbol{\beta}) , \quad (3)$$

where $\boldsymbol{\beta}$ is a parameter vector describing the association between Z_i and G_i . For the other longitudinal health measures $\tilde{\mathbf{y}}_i^h$, we will suppress the superscript

h unless confusion may arise. Similar to (1) and (2), $\tilde{\mathbf{y}}_i$ is related to G_i through the latent vector $\tilde{\xi}_i$, such that, conditionally given $G_i = g$,

$$\tilde{\xi}_i = \tilde{\mathbf{X}}_i \mathbf{v}_g + \tilde{\mathbf{Z}}_i \tilde{\mathbf{b}}_i \quad \text{with } \tilde{\mathbf{b}}_i \sim N(0, \tilde{\mathbf{D}}_g) \quad (4)$$

random effects, and

$$\tilde{\mathbf{y}}_i | \tilde{\xi}_i \sim N(\tilde{\xi}_i, \tilde{\sigma}_g^2 \tilde{\mathbf{R}}_i) \quad (5)$$

with $\tilde{\mathbf{R}}_i$ a known correlation matrix. The unknown parameters $\mathbf{v}_g$, $\tilde{\mathbf{D}}_g$ and $\tilde{\sigma}_g^2$ are gathered in the parameter vector $\boldsymbol{\eta}$.

The model we use is quite similar to those proposed in [8–14], where [8–12] impose the somewhat restrictive assumption that conditional on the latent classes, the outcomes at different time points are independent. Each of these papers also relate covariates to the latent classes. Our model is more restrictive in that it only considers normal outcomes. References [10,11] also consider dual trajectories, the only difference with our model then being the conditional independence assumption. Reference [12] is an application of the models in [8,9]. References [13,14] contain our model as special case (but differ from our situation in the large number of longitudinal outcomes that we consider). All of these papers differ in the estimation approach, which is outlined below.

3.2 Estimation approach

The parameters in this latent class model are estimated using a two-stage procedure. In the first stage the latent classes, i.e. their probabilities and the means and covariance structure of $\mathbf{y}_i$ within each class ($\boldsymbol{\theta}$) are estimated based on the longitudinal data of the first outcome, the DCI denial scores. The remaining parameters, relating the latent classes to the patient characteristics and the other longitudinal outcomes, are estimated in a second stage. The $\boldsymbol{\beta}$ parameters relating latent classes to patient characteristics are estimated using (3). Finally, the relation between latent classes and the other health measures ($\boldsymbol{\eta}$) is studied using

$$f(\tilde{\mathbf{y}}_i | \mathbf{y}_i; \hat{\boldsymbol{\theta}}, \boldsymbol{\eta}) = \sum_g f(\tilde{\mathbf{y}}_i | G_i = g; \boldsymbol{\eta}) \cdot P(G_i = g | \mathbf{y}_i; \hat{\boldsymbol{\theta}}), \quad (6)$$

where $\hat{\boldsymbol{\theta}}$ is the estimate of $\boldsymbol{\theta}$ from stage one. Details will be given in Sections 4 and 5. Two-stage estimation is familiar from for instance correlated survival data [19–21], where a first stage is used to estimate baseline hazards and covariate effects from the marginal distributions and where the correlation or copula is estimated in a second stage. For a given number of classes, the two-stage procedure guarantees consistent estimates. The estimates based on the first stage are consistent, since they are based on a closed model with a likelihood known to yield consistent estimates [22]. The parameter $\boldsymbol{\mu}_g$ could be consistently estimated if no information at all were available on secondary longitudinal outcomes or patient characteristics. If the class membership is cer-

tain, it follows from graphical models theory [23] that the first stage maximum likelihood estimate does not lose efficiency, since the information from upper and lower part is independent given the latent class. For uncertain class membership the first stage estimate may not be fully efficient, but it is nevertheless consistent. For the second stage, estimates will be consistent for the same reasons. Plugging in the consistent estimates from stage 1 again will not destroy consistency but may result in further loss of efficiency [24,25].

There are two reasons for using a two-stage approach. The first reason is computational; especially without further assumptions such as conditional independence of $(\tilde{\mathbf{y}}_i^1, \dots, \tilde{\mathbf{y}}_i^H)$, given the latent classes, direct estimation of all the parameters in the model using full likelihood is not feasible. It is possible to propose separate latent class joint models for each pair of longitudinal outcomes of denial and one physical/emotional functioning scale. Since parameter estimation in these latent class growth curve models is typically based on an EM-algorithm, this would require a complete EM-algorithm to run and converge for each pair of outcomes (of which there are many), which can be quite slow and time-consuming. Also, model choices would perhaps have to be made in the process (such as choosing the number of latent classes), requiring several such models to be fit for model choice, for a single pair of outcomes. In our approach, the EM-algorithm has to be applied only at one stage, namely in identifying latent classes of denial, but not when relating these classes to the other outcomes. The second reason for using a two-stage approach is interpretational. First of all, we were interested in distinguishing patterns of denial over time. This interest was specifically stated as an objective in the research proposal. Moreover, using these latent classes it is straightforward to show the evolvement over time of the other longitudinal health measure for each of the different latent denial classes, thus allowing easy visual assessment of association of denial and physical/emotional functioning.

4 FIRST STAGE: LATENT CLASSES OF DENIAL

Recall that $\mathbf{y}_i$ denotes the vector of observations of DCI measurements at $T_1, \dots, T_4$ for subject number i , and that G_i denotes the group or class g to which subject i belongs, for $g = 1, \dots, L$. In our application we assume a mixed effects model within each class, given by

$$y_{ij} = \mu_j + b_i + e_{ij} \quad (7)$$

where μ_j is the mean DCI at T_j , b_i is a random person effect, distributed $N(0, \tau^2)$, and e_{ij} is independent random error, distributed $N(0, \sigma^2)$. This corresponds to (1) and (2) with $\eta_{ij} = \mu_j + b_i$, $\mathbf{D}_g = \tau^2$, and $\mathbf{R}_i = \mathbf{I}_m$, where $\mathbf{I}_m$ denotes the $m \times m$ identity matrix throughout this paper, and $m = 4$. Although in principle finite mixtures of multivariate normals are identifiable even with variable mean and covariance matrices [26], in order to ensure reliable estimation, the vectors $\boldsymbol{\mu} = (\mu_1, \dots, \mu_m)$ are allowed to differ between

classes, whereas σ^2 and τ^2 are restricted to be identical for all classes. The parameters to be estimated in the first stage are gathered into the vector $\boldsymbol{\theta} = (\pi_1, \dots, \pi_L, \boldsymbol{\mu}_1, \dots, \boldsymbol{\mu}_L, \sigma^2, \tau^2)$, with $\boldsymbol{\mu}_g$ the mean vector for class g and π_g the probability of a random individual to belong to class g . Let $f_g(\mathbf{y} \mid \boldsymbol{\mu}_g, \sigma^2, \tau^2)$ denote the density of $\mathbf{y}$ within class g . Then the log-likelihood is given by

$$\ell(\boldsymbol{\theta}) = \sum_{i=1}^n \log \left(\sum_{g=1}^L \pi_g f_g(\mathbf{y}_i \mid \boldsymbol{\mu}_g, \sigma^2, \tau^2) \right). \quad (8)$$

We implemented an EM-algorithm [27] to obtain maximum likelihood estimates (MLEs) of the parameters of the model. The EM-algorithm we employed is detailed in the appendix, where a more general setup is used to describe it. It is a hybrid algorithm combining what are probably the two best-known applications of the EM-algorithm, the first being for random effects models [28–30], the second being for mixtures of normals [31]. For a given class size, the EM-algorithm was run five times with different, random, starting values, in order to judge the sensitivity of the convergence to starting values. Convergence was rather slow, especially for larger class size (on average, 75, 87, 100, and 320 iterations were needed to achieve convergence for 2, 3, 4, and 5 classes, respectively), but robust to starting values; for all choices of number of classes that we considered, each choice of starting values resulted in the same maximum likelihood estimates. Important to mention at this point is the fact that upon convergence not only the MLEs are obtained but also the posterior class membership probabilities, i.e. for each individual the probabilities to belong to each class, given the data and the estimated parameters. These are simply obtained by Bayes' rule,

$$p_{ig} = P(G_i = g \mid \mathbf{y}_i, \boldsymbol{\theta}) = \frac{\pi_g f_g(\mathbf{y}_i \mid \boldsymbol{\mu}_g, \sigma^2, \tau^2)}{\sum_{l=1}^L \pi_l f_l(\mathbf{y}_i \mid \boldsymbol{\mu}_l, \sigma^2, \tau^2)},$$

where $f_g(\mathbf{y} \mid \boldsymbol{\mu}_g, \sigma^2, \tau^2)$ denotes the density within class g , and they are estimated by plugging in the MLEs for π_g , $\boldsymbol{\mu}_g$, σ^2 and τ^2 , yielding

$$\hat{p}_{ig} = \frac{\hat{\pi}_g f_g(\mathbf{y}_i \mid \hat{\boldsymbol{\mu}}_g, \hat{\sigma}^2, \hat{\tau}^2)}{\sum_{l=1}^L \hat{\pi}_l f_l(\mathbf{y}_i \mid \hat{\boldsymbol{\mu}}_l, \hat{\sigma}^2, \hat{\tau}^2)}. \quad (9)$$

Table II shows an analysis of variance table, containing the degrees of freedom, log-likelihood, and two of the most common criteria for comparing models, AIC and BIC, of the models with 2, 3, 4, and 5 classes.

Table II. *Analysis of variance table for the models with 2, 3, and 4 classes.*

No of classes	Df	Log-likelihood	AIC	BIC
2	11	−1260.014	2542.028	2578.031
3	16	−1246.779	2525.557	2577.925
4	21	−1237.891	2517.783	2586.516
5	26	−1233.078	2518.155	2615.253

Depending on which criterion to use, a model with 3 or 4 classes appears to be the model of choice; based on the AIC one would choose a model with 4 classes, based on BIC a model with 3 classes. Figure 2 shows in bold estimated means and 95% confidence intervals for the models with three and four classes.

Figure 2 Estimated means (bold) and individual patient trajectories for all classes. Models shown here are those with 3 and 4 classes.

For the model with three classes, a clear pattern emerges. The largest class, with solid lines, represents a large group, containing 69% of all individuals, with what could be termed ‘low deniers’. The second largest class, long-dashed, containing 19% of all individuals could be termed ‘moderate deniers’, in correspondence with [6]. The smallest class, short-dashed, containing the remaining 13%, is a group that is like the low deniers in the beginning and increases to a level comparable to the high deniers at the end. We will refer to this group as the ‘increasing deniers’. The individual patient trajectories are also shown. The model with four classes shows a pattern that is harder to interpret. In a review of the performance of AIC and BIC, McLachlan & Peel [22] showed that the AIC tends to overestimate and the BIC to underestimate the number of classes. Since the two information criteria indicated different models, interpretability was the decisive argument here to select the model with three classes. For the remaining part of the paper, we will therefore use the three-class model.

5 SECOND STAGE: RELATING LATENT CLASSES TO PATIENT CHARACTERISTICS AND HEALTH MEASURES

The next objective is to study how patients in different classes differ with respect to patient characteristics and with respect to other, secondary, outcomes, like quality of life, emotional functioning and physical functioning. A quick and dirty way to proceed would be to ignore the uncertainty of class membership, and assign the most likely class to each individual. In principle, this procedure would not give too much bias, although classes ‘in the middle’ would tend to be under-represented. The main problem with this approach is that in case of moderate to substantial uncertainty, ignoring the uncertainty is likely to yield overly optimistic standard errors and hence overly liberal testing procedures.

The degree of uncertainty is shown in Figure 3 which shows a barycentric representation of the posterior class membership probabilities. In this representation, probabilities (π_1, π_2, π_3) with $0 \leq \pi_i \leq 1$ and $\pi_1 + \pi_2 + \pi_3 = 1$ are mapped to an equilateral triangle. Each corner corresponds to a class; when an individual is certain to belong to a particular class, its barycentric representation maps it to the corresponding corner in the triangle. Points further away from a corner indicate increasing uncertainty with respect to the class membership. For a given point in the triangle (standardized so as to have unit height), π_i is given by the orthogonal distance to the side of the triangle facing cluster i , for $i = 1, 2, 3$. Figure 3 shows that many points are close to the corner corresponding to class 1, but there is also a considerable number of patients, not to be ignored, that cannot be assigned to a class with certainty. In particular, it is sometimes difficult to choose between classes 1 and 3 and between classes 2 and 3. Referring to Figure 3, assigning the most likely class to each individual would mean assigning each individual to the class corresponding to the closest corner in the triangle. Each area in the triangle corresponds to a probability

Figure 3 *Barycentric representation of the posterior class membership probabilities obtained by the EM-algorithm with 3 classes.*

configuration resulting in different most likely classes; the corresponding class names are indicated as well.

We shall use two distinct approaches of dealing with class membership uncertainty. This choice is deliberate. At the most fundamental level, the difference between the problems of relating latent denial classes to patient characteristics and other longitudinal outcomes is in the direction of this relation. For the association of latent denial classes and patient characteristics, the patient characteristics are modeled as predictors of class membership. For the longitudinal health measures, the latent classes are assumed to affect the mean structure of the longitudinal health outcomes. In the graphical model of Figure 1, the direction of the arrows reflects this difference; they point into the latent classes from the patient characteristics and out from the latent classes into the longitudinal outcomes. For the problem of relating class membership to patient characteristics we use Pearson's chi-square statistic for contingency tables, with an adjusted estimate of the variance of the test statistic. The problem of relating class membership and longitudinal health measures is predominantly an estimation and modeling problem, where we want to estimate the development over time of the health measures for the different classes and where we may want to consider and compare different longitudinal models. This problem asks for a more flexible approach of dealing with class membership uncertainty, and multiple imputation is very well suited for this purpose.

Below we describe the two approaches of dealing with class membership uncertainty in more detail.

5.1 Latent classes and patient characteristics

For the problem of relating patient characteristics to classes, two approaches are possible. First, patient characteristics can be incorporated into the latent class estimation procedure, for instance assuming their effects are the same for all classes. Here we take a different approach since we are interested in predicting the probability that an individual belongs to a particular class.

Recall from Section 3.2 that estimation of $\boldsymbol{\beta}$ is based on Equation (3). Then the contribution to the score for $\boldsymbol{\beta}$ of individual i is given by

$$\begin{aligned}\dot{\ell}_{\boldsymbol{\beta}i} &= \frac{\partial}{\partial \boldsymbol{\beta}} \log \left(\sum_g f(\mathbf{y}_i | G_i = g; \boldsymbol{\mu}) \cdot P(G_i = g | Z_i; \boldsymbol{\beta}) \right) \\ &= \frac{\sum_g f(\mathbf{y}_i | G_i = g; \boldsymbol{\mu}) \cdot P(G_i = g | Z_i; \boldsymbol{\beta}) \frac{\partial}{\partial \boldsymbol{\beta}} \log P(G_i = g | Z_i; \boldsymbol{\beta})}{\sum_l f(\mathbf{y}_i | G_i = l; \boldsymbol{\mu}) \cdot P(G_i = l | Z_i; \boldsymbol{\beta})} .\end{aligned}\quad (10)$$

Evaluating (10) at the null-hypothesis of no association between Z_i and G_i implies that $P(G_i = g | Z_i; \boldsymbol{\beta})$ may be replaced by $\hat{\pi}_g$ and $f(\mathbf{y}_i | G_i = g; \boldsymbol{\mu})$ by $f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_g)$, so (10) becomes a weighted mean of

$$\dot{\ell}_{\boldsymbol{\beta}i}^G(g) = \frac{\partial}{\partial \boldsymbol{\beta}} \log P(G_i = g | Z_i; \boldsymbol{\beta}) \quad (11)$$

given by

$$\dot{\ell}_{\boldsymbol{\beta}i} = \sum_g \hat{p}_{ig} \dot{\ell}_{\boldsymbol{\beta}i}^G(g) , \quad (12)$$

where $\hat{p}_{ig}$ is the posterior probability of individual i belonging to class g (cf. (9)), and $\dot{\ell}_{\boldsymbol{\beta}i}^G$ is the score contribution of individual i corresponding to the conditional distribution of G given Z .

The second derivative of (3), evaluated at the null-hypothesis, is given by

$$\begin{aligned}\ddot{\ell}_{\boldsymbol{\beta}i} &= \frac{\sum_g f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_g) \hat{\pi}_g \left[\dot{\ell}_{\boldsymbol{\beta}i}^G(g) \dot{\ell}_{\boldsymbol{\beta}i}^{G^T}(g) + \ddot{\ell}_{\boldsymbol{\beta}i}^G(g) \right]}{\sum_l f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_l) \hat{\pi}_l} \\ &\quad - \left(\frac{\sum_g f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_g) \hat{\pi}_g \dot{\ell}_{\boldsymbol{\beta}i}^G(g)}{\sum_g f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_g) \hat{\pi}_g} \right) \left(\frac{\sum_g f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_g) \hat{\pi}_g \dot{\ell}_{\boldsymbol{\beta}i}^G(g)}{\sum_g f(\mathbf{y}_i | \hat{\boldsymbol{\mu}}_g) \hat{\pi}_g} \right)^T \\ &= \sum_g \hat{p}_{ig} \ddot{\ell}_{\boldsymbol{\beta}i}^G(g) + \sum_g \hat{p}_{ig} \dot{\ell}_{\boldsymbol{\beta}i}^G(g) \dot{\ell}_{\boldsymbol{\beta}i}^{G^T}(g) - \left(\sum_g \hat{p}_{ig} \dot{\ell}_{\boldsymbol{\beta}i}^G(g) \right) \left(\sum_g \hat{p}_{ig} \dot{\ell}_{\boldsymbol{\beta}i}^G(g) \right)^T ,\end{aligned}$$

so with $\mathcal{J}_{\boldsymbol{\beta}i} = -\ddot{\ell}_{\boldsymbol{\beta}i}$, $\mathcal{J}_{\boldsymbol{\beta}i}^G(g) = -\ddot{\ell}_{\boldsymbol{\beta}i}^G(g)$, we have

$$\begin{aligned} \mathcal{J}_{\beta i} &= \sum_g \hat{p}_{ig} \mathcal{J}_{\beta i}^G(g) \\ &- \left(\sum_g \hat{p}_{ig} \dot{\ell}_{\beta i}^G(g) \dot{\ell}_{\beta i}^{G^T}(g) - \left(\sum_g \hat{p}_{ig} \dot{\ell}_{\beta i}^G(g) \right) \left(\sum_g \hat{p}_{ig} \dot{\ell}_{\beta i}^G(g) \right)^T \right). \end{aligned} \quad (13)$$

Recognizing that $\hat{p}_{ig} = P(G_i = g | \mathbf{y}_i; \hat{\boldsymbol{\theta}})$, we can rewrite (12) and (13) as

$$\dot{\ell}_{\beta i} = E \dot{\ell}_{\beta i}^G, \quad \mathcal{J}_{\beta i} = E \mathcal{J}_{\beta i}^G - \text{var } \dot{\ell}_{\beta i}^G, \quad (14)$$

where expectation and variance are taken with respect to the conditional distribution of G_i given $\mathbf{y}_i$ evaluated at $\hat{\boldsymbol{\theta}}$. In other words we may think of eq:scoreinfoG as arising as the formulas of Louis [32] for the score and Fisher information for β in the direct model for $P(G_i = g | Z_i; \beta)$ where the uncertain class membership constitutes the missing information and where the last term in large brackets in eq:fisherbeta, $\text{var } \dot{\ell}_{\beta i}^G$, expresses the loss of information due to uncertain class membership.

Although the score $\dot{\ell}_{\beta i}^G$ and Fisher information $\mathcal{J}_{\beta i}^G$ could in principle be derived from any model of $P(G_i = g | Z_i; \beta)$, we will now specialize to categorical patient characteristics Z_i , taking K possible values $k = 1, \dots, K$, say. We assume a multinomial logistic model, given by $P(G_i = g | Z_i; \beta) = e^{\lambda_{ig}} / \sum_{h=1}^L e^{\lambda_{ih}}$, with $\lambda_{ig} = \beta_{g1} + \sum_{k=2}^K \beta_{gk} \mathbf{1}\{Z_i = k\}$. We are interested in testing the null hypothesis $H_0 : \boldsymbol{\delta} = \mathbf{0}$, with $\boldsymbol{\delta} = (\beta_{12}, \dots, \beta_{1K}, \dots, \beta_{L2}, \dots, \beta_{LK})^T$. The vector $\boldsymbol{\gamma} = (\boldsymbol{\eta}_{11}, \dots, \boldsymbol{\eta}_{L1})$ consists of nuisance parameters, describing $P(G_i = g)$ in the absence of covariates under the null hypothesis. In the appendix we derive the score test based on eq:scoreinfoG for testing $H_0 : \boldsymbol{\delta} = \mathbf{0}$ in the presence of the nuisance parameters $\boldsymbol{\gamma}$.

Table III shows the results of this analysis for the patient characteristics in Table I. The numbers shown for a particular patient characteristic level are the sums of the posterior class membership probabilities over all patients with that level. P -values reported are obtained from the score test accounting for class membership uncertainty.

5.2 Latent classes and longitudinal health measures

In this subsection we consider a generic longitudinal health measure, and we again suppress the superscript h in $\tilde{\mathbf{y}}_i^h$ throughout. The relation between $\mathbf{y}_i$ and $\tilde{\mathbf{y}}_i$ will be assessed using (6). An EM-algorithm could be used to estimate $\boldsymbol{\eta}$ in (6), but we will use multiple imputation. Multiple imputation is described in general by Little & Rubin [33], but for completeness we briefly describe the implementation in our situation below. We construct a complete dataset by randomly drawing class memberships, for each individual corresponding to his or her posterior class membership probabilities $\hat{p}_{ig} = P(G_i = g | \mathbf{y}_i, \hat{\boldsymbol{\theta}})$, given by equation (9). A complete dataset, denoted by $(\tilde{\mathbf{y}}, \mathbf{g})$, consists of $\tilde{\mathbf{y}}$, with $\tilde{y}_{ij}$ denoting the quality of life, emotional functioning or physical functioning out-

Table III. Class membership predicted by patient characteristics

Characteristic	Low	Increasing deniers	Moderate deniers	χ^2	P
Gender					
Male	70 (61%)	16 (14%)	29 (25%)	11.93	0.0026
Female	64 (80%)	9 (11%)	7 (9%)		
Age					
≤ 60	54 (78%)	7 (10%)	8 (12%)	7.53	0.11
60 – 70	34 (63%)	9 (17%)	11 (20%)		
> 70	45 (63%)	9 (13%)	17 (24%)		
Partner					
No	41 (71%)	6 (10%)	11 (19%)	1.09	0.58
Yes	92 (68%)	19 (14%)	25 (18%)		
Children					
No	24 (69%)	5 (14%)	6 (17%)	0.20	0.91
Yes	110 (69%)	20 (13%)	29 (18%)		
Education level					
Primary	44 (63%)	7 (10%)	19 (27%)	8.98	0.06
Secondary	38 (70%)	9 (17%)	7 (13%)		
College/University	49 (73%)	7 (12%)	10 (15%)		
Religion					
No	63 (64%)	11 (11%)	24 (25%)	6.44	0.04
Yes	70 (73%)	14 (15%)	12 (12%)		
Type of tumor					
NSCLC	95 (68%)	19 (14%)	25 (18%)	4.09	0.39
SCLC	22 (63%)	4 (11%)	9 (26%)		
Other/unknown	17 (81%)	2 (10%)	2 (10%)		
Current treatment					
Surgery	24 (67%)	4 (11%)	8 (22%)	2.10	0.91
Chemotherapy	51 (71%)	9 (12%)	12 (17%)		
Radiotherapy	33 (69%)	7 (15%)	8 (17%)		
No treatment	22 (63%)	5 (14%)	8 (23%)		
UICC grade					
0	39 (65%)	8 (13%)	13 (22%)	0.75	0.94
I	66 (69%)	13 (13%)	17 (18%)		
II-IV	28 (70%)	5 (13%)	7 (18%)		

come of individual i at time j , $j = 1, \dots, 4$, and g_i the (randomly assigned) class membership of individual i .

Within a complete dataset $(\tilde{\mathbf{y}}, \mathbf{g})$ we specify the following mixed effects model:

$$\tilde{y}_{ij} = \nu_{g_i, j} + \tilde{b}_i + \tilde{e}_{ij}, \quad i = 1, \dots, n, j = 1, \dots, m,$$

mimicking the model (7) we used in Section 4 for the primary outcome, DCI, with different mean vectors $\mathbf{v}_g = (\nu_{g1}, \dots, \nu_{gm})$ for different classes, $g = 1, \dots, L$, random person effects $\tilde{b}_i$ with a $N(0, \tilde{\tau}^2)$ distribution and independent random error $\tilde{e}_{ij}$ with a $N(0, \tilde{\sigma}^2)$ distribution. This corresponds to (4) and (5) with $\tilde{\xi}_{ij} = \nu_j + \tilde{b}_i$, $\tilde{\mathbf{D}}_g = \tilde{\tau}^2$ and $\tilde{\mathbf{R}}_i = \mathbf{I}_m$. The fixed effects are gathered

in the mL -vector $\mathbf{v} = (\mathbf{v}_1^T, \dots, \mathbf{v}_L^T)^T$. In our specific application we have $m = 4$ and $L = 3$, but we prefer to keep the notation more general here.

The procedure of constructing complete datasets is repeated $M = 10$ times and standard procedures of combining estimates and within- and between imputation variances [33] yield estimates of $\mathbf{v}$ and its covariance matrix $\Sigma_{\mathbf{v}}$.

We are interested in assessing differences in level and in development over time between the classes. To be able to distinguish between these we write the mean ν_{gj} of y_j within class g as

$$\nu_{gj} = \alpha_g + \psi_{gj}, \quad \alpha_g = \frac{1}{m} \sum_{j=1}^m \nu_{gj},$$

with α_g denoting the overall mean of class g over time, and ψ_{gj} the deviation of ν_{gj} with respect to this overall class mean. In order to quantify differences in level and development over time between the classes, we define the contrast vectors

$$\begin{aligned} \delta_{\text{level}} &= (\alpha_2 - \alpha_1, \dots, \alpha_L - \alpha_1)^T, \quad \delta_{\text{time}} = (\Psi_2^T - \Psi_1^T, \dots, \Psi_L^T - \Psi_1^T)^T, \\ \delta_{\text{overall}} &= (\mathbf{v}_2^T - \mathbf{v}_1^T, \dots, \mathbf{v}_L^T - \mathbf{v}_1^T)^T. \end{aligned}$$

The vector δ_{level} has length $L - 1$, δ_{time} and δ_{overall} both have length $m(L - 1)$, but δ_{time} is overparametrized. In terms of main effects and interactions, the contrast vector δ_{level} describes class main effects, δ_{time} describes time by class interactions, and δ_{overall} class main effects plus time by class interactions. Time main effects are not assessed, since they are not of prime interest here. We test the hypotheses $\delta_{\text{contr}} \equiv 0$ with Wald-type statistics (with contr being either level, time, or overall)

$$W_{\text{contr}} = \hat{\delta}_{\text{contr}}^T \hat{\Sigma}_{\text{contr}}^{-1} \hat{\delta}_{\text{contr}},$$

with

$$\Sigma_{\text{contr}} = \left(\frac{\partial \delta_{\text{contr}}}{\partial \mathbf{v}} \right)^T \Sigma_{\mathbf{v}} \left(\frac{\partial \delta_{\text{contr}}}{\partial \mathbf{v}} \right),$$

and where in $\hat{\delta}_{\text{contr}}$ and $\hat{\Sigma}_{\text{contr}}$, $\mathbf{v}$ is replaced throughout by its estimate $\hat{\mathbf{v}}$. It is not hard to see that

$$\begin{aligned} \frac{\partial \delta_{\text{level}}}{\partial \mathbf{v}} &= \mathbf{H} \otimes \frac{1}{m} \mathbf{1}_m, \quad \frac{\partial \delta_{\text{time}}}{\partial \mathbf{v}} = \mathbf{H} \otimes \left(\mathbf{I}_m - \frac{1}{m} \mathbf{J}_m \right), \\ \frac{\partial \delta_{\text{overall}}}{\partial \mathbf{v}} &= \mathbf{H} \otimes \mathbf{I}_m, \quad \mathbf{H} = \begin{pmatrix} -1 & \dots & -1 \\ & & \mathbf{I}_{L-1} \end{pmatrix} \end{aligned}$$

where $\mathbf{I}_m$ again denotes the $m \times m$ identity matrix and $\mathbf{1}_m$ and $\mathbf{J}_m$ denote the m -vector and $m \times m$ matrix, respectively, filled with 1's throughout.

Under the appropriate null hypotheses of $\delta_{\text{contr}} \equiv 0$, W_{level} , W_{time} , and W_{overall} follow, asymptotically, χ^2 distributions with degrees of freedom equal to $L - 1$, $(m - 1)(L - 1)$, and $m(L - 1)$, respectively (the inverse of $\hat{\Sigma}_{\text{time}}$ needs to be replaced by a Moore-Penrose generalized inverse because the Ψ_g 's are over-determined).

Figure 4 shows the estimated mean 'subjective health' and 'objective health' measures and associated 95% confidence intervals for each of the three classes.

Figure 4 Estimated mean and 95% confidence intervals of 'subjective health' (left) and 'objective health' (right), for each of the three classes.

The left plot of Figure 4 shows that the class representing the low deniers have lowest 'subjective health', while the class representing the moderate deniers have highest 'subjective health'. The class representing increasing deniers follow the same pattern with respect to 'subjective health' as the corresponding DCI scores, i.e., comparable to the low deniers in the beginning and increasing to the same level as the moderate deniers towards the end. The Wald-statistics for the hypotheses $\delta_{\text{level}} \equiv 0$, $\delta_{\text{time}} \equiv 0$, and $\delta_{\text{overall}} \equiv 0$ have values of 19.5, 7.3, and 29.7, respectively, with 2, 6, and 8 degrees of freedom respectively. This leads to P -values of 5.7×10^{-5} , 0.29, and 2.4×10^{-4} , for level, time and overall, respectively. The observed pattern for 'subjective health' is typical for the other subjective physical and emotional functioning scales. These will be reported in detail elsewhere. The question then remains whether the patients with higher levels of denial are really in better health or whether the observed differences in 'subjective health' are only experienced this way by the patient. The right plot of Figure 4 shows quite a different picture from that of the 'subjective health' measure. The Wald-statistics for *level*, *time*, and *overall* equal 3.20, 4.57, and 7.80, respectively, with the same degrees of freedom as above, correspond-

ing to P -values of 0.20, 0.60, and 0.45, respectively. Although the low deniers appear to have somewhat lower 'objective health', we can reasonably discard the possibility of true differences in health between low, moderate and increasing deniers, and ascribe the observed differences in 'subjective health' between classes to patient perception.

6 DISCUSSION

Joint mixed effect models are not straightforward to fit and interpret. Fieuwis & Verbeke [7] demonstrated that assumptions on certain components in the joint model can have profound effects on seemingly unrelated aspects of the model. Specifically, they showed that the assumption of independence between the errors in the two longitudinal outcomes greatly influences the implied evolution of the correlation between the two outcomes over time. This may seem surprising given the fact that the parameter describing the dependence between the two error terms does not even enter into the formula of the evolution of the association. This example shows that unexpected things can happen and that one should be careful in applying and interpreting these models.

Latent class growth curve models very similar to ours have been proposed earlier in a variety of contexts [13,18,34–36]. The advantage of this type of models is that by bringing in some structure into the model the number of parameters to be estimated is reduced. Of course this comes at the price of quite specific model assumptions and the danger of endogeneity, since it implicitly correlates all longitudinal outcomes at all time points. Endogeneity is a result of the wish to reduce the dimensionality of the problem; in some sense all reasonable random effect joint models are subject to endogeneity since correlation of the random effects of the different outcomes will induce correlation of all observations at different time points. It is appropriate to mention another limitation of latent class modeling that applies here as well. It cannot be excluded that the latent classes only serve to explain lack of normality in a population that is in fact perfectly homogenous, as made clear in for instance [37].

The majority of the papers above jointly fit all parts of the model directly. In contrast, our method is a two-stage approach in which we first identify the latent classes for the first longitudinal outcome and in a second stage relate these classes to the second longitudinal outcome. The joint estimation approach is to be preferred if interest is in relating a single pair of longitudinal measurements, since it avoids the need of adjusting for the uncertainty of classifying subjects. For our particular problem we prefer a two-stage approach for two reasons. First, there is real interest in a substantive interpretation of these latent classes (in fact formulated as a formal research question in the study proposal). Moreover, by first identifying latent denial classes, it is straightforward to visualize differences in the development over time of physical and emotional functioning scales, as we illustrated in Figure 4. Second, although

we showed only two representative outcomes, ‘subjective health’ and ‘objective health’, we are in fact interested in the relation between denial on the one hand and a large number of physical and emotional functioning scales on the other hand. As mentioned before, in a joint estimation approach, the joint model would have to be completely refit for each pair of longitudinal measurements, typically involving application of an EM-algorithm, which can become very time-consuming. In our approach, the EM-algorithm has to be applied only at one stage, namely in identifying latent classes of denial, but not when relating these classes to the other outcomes. So in case of multiple longitudinal outcomes, our approach is easier to carry out, interpret, and report.

For a given number of latent classes, L , standard results on composite likelihood [38] imply that the maximum likelihood estimates of the μ_g ’s and π_g ’s based on the upper part of Figure 1, the relation between G_i and $\mathbf{y}_i$ through ξ_i , so ignoring the patient characteristics and the other longitudinal health measures, is consistent. Since the estimates of μ_g and π_g are consistent, also the second stage estimates of β_g and $\mathbf{v}_g$ will be consistent. In principle, after estimating the effect of patient characteristics or the effect of the latent classes on the health measures, the estimates of the DCI means μ_g and the class probabilities π_g could be updated, which should increase the efficiency of the estimates of μ_g . For example, for an individual with low ‘subjective health’, the posterior probability of belonging to the low deniers will increase, because overall low deniers tend to have lower ‘subjective health’. More formally, with G_i denoting the class to which subject i belongs, $\mathbf{y}_i$ and $\tilde{\mathbf{y}}_i$ denoting the longitudinal outcomes of DCI and for instance ‘subjective health’ of subject i , and $p_{ig} = P(G_i = g | \mathbf{y}_i)$, ignoring unknown parameters, Bayes’ rule can be used to obtain

$$P(G_i = g | \mathbf{y}_i, \tilde{\mathbf{y}}_i) = \frac{f(\tilde{\mathbf{y}}_i | G_i = g, \mathbf{y}_i)P(G_i = g | \mathbf{y}_i)}{\sum_l f(\tilde{\mathbf{y}}_i | G_i = l, \mathbf{y}_i)P(G_i = l | \mathbf{y}_i)} = \frac{p_{ig}f(\tilde{\mathbf{y}}_i | G_i = g)}{\sum_l p_{il}f(\tilde{\mathbf{y}}_i | G_i = l)}.$$

The mean parameters μ_g could be updated in a similar way. In fact, in turn updating the different parameters in this way is quite similar to Gibbs sampling. We have not pursued this, since our primary interest is consistency, not efficiency.

In Appendix B it was shown that without taking into account the adjustment term of $\text{var } \hat{\ell}_\beta$, the resulting score test for $\delta = 0$ would correspond to a weighted χ^2 -test, where each individual is represented by L lines in a dataset and each resulting case is weighted by the posterior probability $\hat{p}_{ig}$ of belonging to case g . Compared to this weighted χ^2 -test, which does not account for class membership uncertainty, the P -values were smaller when accounting for class membership uncertainty. This may seem unexpected, but it can be explained in two ways. From a mathematical point of view, it can be seen from equation (14) that the numerator of the score test with and without accounting for class membership uncertainty are identical, while the denominator (the variance of the score) becomes smaller when accounting for class membership uncertainty, because information is lost. As a result, the score test statistic is

larger when accounting for class membership uncertainty. From a heuristic point of view, what happens is that uncertainty of class membership makes the different classes more similar. Large differences between different classes will therefore be less likely. If a large difference is nevertheless observed, this will make the observed difference more significant. A similar phenomenon has been observed when accounting for haplotype uncertainty in association testing; in fact, the score test derived here is very similar to that of Schaid et al. [39] in the context of generalized linear models.

Although the approach we took was motivated by the particular application, we do feel that it has promise of wider application, for instance in the joint modeling of CD4-counts and HIV-RNA in AIDS studies. In this context, it would be of interest to find latent classes with respect to the longitudinal development of HIV-RNA viral load, and then relating these latent classes to longitudinal development of CD4+ and/or CD8+ T-cell counts, or their ratio, all considered to be important prognostic markers for AIDS progression in HIV-infected individuals. Another application would be in joint modeling of longitudinal outcome(s) and survival, in which latent normal random variables or processes are used essentially to account for measurement error in the longitudinal outcome [40,41], see also for a review and for a recent relevant paper. The use of latent classes in this context has been pioneered by Lin et al. [42], and is potentially useful as well.

APPENDIX

A.1. EM-algorithm

In the general notation of the Laird & Ware [28] mixed effects model, within a class we have, for individual $i = 1, \dots, n$,

$$\mathbf{y}_i = \mathbf{X}_i \boldsymbol{\mu} + \mathbf{Z}_i \mathbf{b}_i + \mathbf{e}_i ,$$

where $\mathbf{y}_i$ is an n_i -vector of outcomes for individual i , $\mathbf{X}_i$ is an $n_i \times p$ fixed effects design matrix, $\boldsymbol{\mu}$ is a p -vector of fixed effects, $\mathbf{Z}_i$ is an $n_i \times q$ random effects design matrix, $\mathbf{b}_i$ is a q -vector of random effects with a $N(0, \mathbf{D})$ distribution with unknown $q \times q$ covariance matrix $\mathbf{D}$, and $\mathbf{e}_i$ is random noise with a $N(0, \sigma^2 \mathbf{R}_i)$ distribution, where $\mathbf{R}_i$ is known and σ^2 unknown. Note that in our case all $\mathbf{y}_i$ have the same length in principle, but $\mathbf{y}_i$ may have missing values, in which case $\mathbf{X}_i$, $\mathbf{Z}_i$, $\mathbf{R}_i$ are the appropriate sub-matrices of common matrices $\mathbf{X}$, $\mathbf{Z}$, $\mathbf{R}$.

The EM-algorithm iterates between the E-step and M-step described below.

A.1.1. E-step

Given the present value $\boldsymbol{\theta}^* = (\pi_1^*, \dots, \pi_L^*, \boldsymbol{\mu}_1^*, \dots, \boldsymbol{\mu}_L^*, \sigma^{*2}, \mathbf{D}^*)$ of the parameter vector $\boldsymbol{\theta}$, calculate, for individual $i = 1, \dots, n$, and class $g = 1, \dots, L$:

$$\begin{aligned}
\boldsymbol{\Sigma}_i &= \sigma^{2*} \mathbf{R}_i + \mathbf{Z}_i \mathbf{D}^* \mathbf{Z}_i^T, \\
\mathbf{r}_{ig} &= \mathbf{y}_i - \mathbf{X}_i \boldsymbol{\mu}_g^*, \\
\mathbf{b}_{ig} &= \mathbf{D}^* \mathbf{Z}_i^T \boldsymbol{\Sigma}_i^{-1} \mathbf{r}_{ig}, \\
p_{ig} &= P(G_i = g \mid \mathbf{y}_i, \boldsymbol{\theta}^*) = \frac{\pi_g^* f_g(\mathbf{y}_i \mid \boldsymbol{\mu}_g^*, \sigma^{2*}, \mathbf{D}^*)}{\sum_{k=1}^L \pi_k^* f_k(\mathbf{y}_i \mid \boldsymbol{\mu}_k^*, \sigma^{2*}, \mathbf{D}^*)}.
\end{aligned}$$

A.1.2. M-step

New values of π_g , $\boldsymbol{\mu}_g$, σ^2 and $\mathbf{D}$ are given by:

$$\begin{aligned}
\pi_g &= \frac{1}{n} \sum_{i=1}^n p_{ig}, \\
\boldsymbol{\mu}_g &= \left(\sum_{i=1}^n \mathbf{X}_i^T \boldsymbol{\Sigma}_i^{-1} \mathbf{X}_i p_{ig} \right)^{-1} \sum_{i=1}^n \mathbf{X}_i^T \boldsymbol{\Sigma}_i^{-1} \mathbf{y}_i p_{ig}, \\
\sigma^2 &= \frac{\sum_{g=1}^L \sum_{i=1}^n p_{ig} \left\{ (\mathbf{r}_{ig} - \mathbf{Z}_i \mathbf{b}_{ig})^T (\mathbf{r}_{ig} - \mathbf{Z}_i \mathbf{b}_{ig}) + \sigma^{2*} \text{tr}(\mathbf{I} - \sigma^{2*} \mathbf{W}_i \mathbf{R}_i) \right\}}{\sum_{g=1}^L \sum_{i=1}^n n_i p_{ig}}, \\
\mathbf{D} &= \frac{\sum_{g=1}^L \sum_{i=1}^n p_{ig} \left\{ \mathbf{b}_{ig} \mathbf{b}_{ig}^T + \mathbf{D}^* (\mathbf{I} - \mathbf{Z}_i^T \mathbf{W}_i \mathbf{Z}_i \mathbf{D}^*) \right\}}{\sum_{g=1}^L \sum_{i=1}^n p_{ig}}. \tag{A1}
\end{aligned}$$

Convergence is obtained when the log-likelihood given by (8) changes no more than a pre-specified small number ε (in our application we have taken $\varepsilon = 10^{-5}$). The MLEs are the values of π_g , $\boldsymbol{\mu}_g$, σ^2 and $\mathbf{D}$ at convergence. At convergence we also have the estimated covariance matrix of $\hat{\boldsymbol{\mu}}_g$, conditional on the other estimated parameters,

$$\widehat{\text{var}}(\hat{\boldsymbol{\mu}}_g) = \left(\sum_{i=1}^n \mathbf{X}_i^T \boldsymbol{\Sigma}_i^{-1} \mathbf{X}_i \hat{p}_{ig} \right)^{-1}, \tag{A2}$$

with $\hat{p}_{ig}$ the estimated posterior class membership probabilities, obtained in the E-step above, but with $\boldsymbol{\theta}^*$ replaced by $\hat{\boldsymbol{\theta}}$ obtained at convergence.

A.2. Multinomial test accounted for class membership uncertainty

In Section 5, in ‘Latent Classes and patient characteristics’ we saw that the contributions to the score $\dot{\ell}_{\boldsymbol{\beta}i}$ and Fisher information $\mathcal{J}_{\boldsymbol{\beta}i}$ of individual i of $f(\mathbf{y}_i \mid Z_i; \boldsymbol{\mu}, \boldsymbol{\beta})$, evaluated at the null-hypothesis of no association between Z_i and $\mathbf{y}_i$ through the latent classes, could be expressed as conditional expectations and/or variances of the score $\dot{\ell}_{\boldsymbol{\beta}i}^G$ and Fisher information $\mathcal{J}_{\boldsymbol{\beta}i}^G$ in the direct model for $P(G_i = g \mid Z_i; \boldsymbol{\beta})$, see Equation (14). It was also mentioned that these expressions are equivalent to the formulas of Louis [32] for $\dot{\ell}_{\boldsymbol{\beta}i}^G$ and $\mathcal{J}_{\boldsymbol{\beta}i}^G$ in the model for $P(G_i = g \mid Z_i; \boldsymbol{\beta})$, accounting for the class membership uncertainty.

We will therefore first derive expressions for $\dot{\ell}_{\beta}^G$ and $\mathcal{J}_{\beta}^G$ and their sum over all individuals $\dot{\ell}_{\beta}^G = \sum_{i=1}^n \dot{\ell}_{\beta i}^G$ and $\mathcal{J}_{\beta}^G = \sum_{i=1}^n \mathcal{J}_{\beta i}^G$, and subsequently apply Louis's formula.

Let Z be a patient characteristic with K levels, and assume $P(G_i = g | Z_i; \beta) = \omega_{ig} = e^{\lambda_{ig}} / \sum_{l=1}^L e^{\lambda_{il}}$, with $\lambda_{ig} = \beta_{g1} + \sum_{k=2}^K \beta_{gk} \mathbf{1}\{Z_i = k\}$. We follow [43] in writing $y_{ig} = \mathbf{1}\{G_i = g\}$, ω_{ig} , λ_{ig} in long vectors of length nL , for instance $\mathbf{y} = (y_{11}, \dots, y_{n1}, \dots, y_{1L}, \dots, y_{nL})^T$, and similarly for $\boldsymbol{\omega}$ and $\boldsymbol{\lambda}$. In long vector form, the linear predictors $\boldsymbol{\lambda}$ are related to the latent classes through $\boldsymbol{\lambda} = \mathbf{X}\boldsymbol{\beta}$, with $\mathbf{X} = \mathbf{I}_L \otimes X$, X an $n \times K$ matrix with $X_{i1} = 1$, $X_{ik} = \mathbf{1}\{Z_i = k\}$, for $2 \leq k \leq K$, and finally $\otimes$ denoting Kronecker product. The score function and Fisher information matrix for $P(G_i = g | Z_i; \beta)$ are given by

$$\begin{aligned}\dot{\ell}_{\beta}^G &= \mathbf{X}^T(\mathbf{y} - \boldsymbol{\omega}) , \\ \mathcal{J}_{\beta}^G &= \mathbf{X}^T \mathbf{W} \mathbf{X} ,\end{aligned}$$

where the $np \times np$ matrix $\mathbf{W}$ is given by

$$\mathbf{W} = \begin{pmatrix} W^{11} & W^{12} & \dots & W^{1L} \\ W^{21} & W^{22} & & \vdots \\ \vdots & & \ddots & \\ W^{L1} & \dots & & W^{LL} \end{pmatrix} ,$$

with each W^{gh} an $n \times n$ diagonal matrix with i^{th} diagonal element $W_{ii}^{gh} = -\omega_{ig}\omega_{ih} + \mathbf{1}\{g = h\}$. Note that, due to the overparametrization of the model, $\mathcal{J}_{\beta}$ is of rank $K(L-1)$. In our application we are interested in testing the null hypothesis $H_0: \boldsymbol{\delta} = 0$, with $\boldsymbol{\delta} = (\beta_{12}, \dots, \beta_{1K}, \dots, \beta_{L2}, \dots, \beta_{LK})^T$. The vector $\boldsymbol{\gamma} = (\beta_{11}, \dots, \beta_{L1})$ consists of nuisance parameters, describing $P(G_i = g)$ in the absence of covariates under the null hypothesis. Under H_0 , $\boldsymbol{\gamma}$ is estimated by the maximum likelihood estimator $\hat{\boldsymbol{\gamma}} = \log(\boldsymbol{\pi})$, with $\pi_g = n^{-1} \sum_{i=1}^n \mathbf{1}\{G_i = g\}$, the estimated class probabilities. After changing the order of the parameters, the vector $\boldsymbol{\beta}$ can be written as $\boldsymbol{\beta} = (\boldsymbol{\delta}, \boldsymbol{\gamma})^T$. The score function and Fisher information can be structured accordingly, and we define $\dot{\ell}_{\delta}^G$, $\dot{\ell}_{\gamma}^G$, $\mathcal{J}_{\delta\delta}^G$, $\mathcal{J}_{\delta\gamma}^G$, $\mathcal{J}_{\gamma\delta}^G$, and $\mathcal{J}_{\gamma\gamma}^G$ as the appropriate sub-vectors and sub-matrices of $\dot{\ell}_{\beta}^G$ and $\mathcal{J}_{\beta}^G$. The score function $\dot{\ell}_{\delta}^G$ is given by

$$\dot{\ell}_{\delta}^G = \begin{pmatrix} \dot{\ell}_{\delta}^{G^1} \\ \vdots \\ \dot{\ell}_{\delta}^{G^L} \end{pmatrix} ,$$

with $\dot{\ell}_{\delta,k}^{G^g} = \sum_{i=1}^n (y_{ig} - \omega_{ig}) \mathbf{1}\{Z_i = k\}$, for $k \geq 2$. The score function $\dot{\ell}_{\gamma}^G$ is identically zero at $\boldsymbol{\gamma} = \hat{\boldsymbol{\gamma}}$. Define $\zeta_k = n^{-1} \sum_{i=1}^n \mathbf{1}\{Z_i = k\}$, and $\boldsymbol{\zeta} = (\zeta_2, \dots, \zeta_K)^T$, the vector of sample proportions for all levels of the covariate except the first. Under H_0 it can be shown that $\dot{\ell}_{\delta,k}^{G^g}$ has the symmetric form $\dot{\ell}_{\delta,k}^{G^g} = \sum_{i=1}^n (\mathbf{1}\{G_i = g\} - \pi_g)(\mathbf{1}\{Z_i = k\} - \zeta_k)$, and that $\mathcal{J}_{\delta\delta}^G = n\boldsymbol{\Omega} \otimes \text{diag}(\boldsymbol{\zeta})$,

$\mathcal{J}_{\delta\gamma}^G = n\mathbf{\Omega} \otimes \zeta^T$, $\mathcal{J}_{\gamma\delta}^G = n\mathbf{\Omega} \otimes \zeta$, and $\mathcal{J}_{\gamma\gamma}^G = n\mathbf{\Omega}$, with $\mathbf{\Omega} = \text{diag}(\boldsymbol{\pi}) - \boldsymbol{\pi}\boldsymbol{\pi}^T$. The matrix $\mathbf{\Omega}$ has rank $L - 1$. The efficient score and information matrix are given by

$$\begin{aligned}\dot{\ell}_{\delta}^{G*} &= \dot{\ell}_{\delta}^G - \mathcal{J}_{\delta\gamma}^G \mathcal{J}_{\gamma\gamma}^{G^{-1}} \dot{\ell}_{\gamma}^G, \\ \mathcal{J}_{\delta}^{G*} &= \mathcal{J}_{\delta\delta}^G - \mathcal{J}_{\delta\gamma}^G \mathcal{J}_{\gamma\gamma}^{G^{-1}} \mathcal{J}_{\gamma\delta}^G.\end{aligned}\quad (\text{A3})$$

Straightforward calculations show that $\dot{\ell}_{\delta}^{G*} = \dot{\ell}_{\delta}^G$, and $\mathcal{J}_{\delta}^{G*} = n\mathbf{\Omega} \otimes (\text{diag}(\zeta) - \zeta\zeta^T)$. The score test for $H_0 : \delta = 0$ with complete data is given by $\dot{\ell}_{\delta}^{G*T} \mathcal{J}_{\delta}^{G*^{-1}} \dot{\ell}_{\delta}^{G*}$, with $\dot{\ell}_{\delta}^G$ and $\mathcal{J}_{\delta}^G$ evaluated at $\delta = 0$, which has, under H_0 , a χ^2 -distribution with $(K - 1)(L - 1)$ degrees of freedom. In the case of complete data, this test corresponds to the familiar Pearson's χ^2 -test for contingency tables.

Turning to the score test for $\delta = 0$ in $f(\mathbf{y}_i | Z_i; \boldsymbol{\theta}, \boldsymbol{\beta})$, recall Equation (14). It is not hard to see that $\dot{\ell}_{\beta}$ is as $\dot{\ell}_{\beta}^G$ above, and $E\mathcal{J}_{\beta}$ as $\mathcal{J}_{\beta}$ above, but with $\pi_g = n^{-1} \sum_{i=1}^n \mathbf{1}\{G_i = g\}$ replaced by $\hat{\pi}_g = n^{-1} \sum_{i=1}^n \hat{p}_{ig}$, with $\hat{p}_{ig}$ the (estimated) posterior class membership probabilities. Without taking into account the adjustment term of $\text{var } \dot{\ell}_{\beta}$ in (14), the resulting score test for $\delta = 0$ would correspond to a weighted χ^2 -test, where each individual is represented by L lines in a dataset and each resulting case is weighted by the posterior probability $\hat{p}_{ig}$ of belonging to case g . The term $\text{var } \dot{\ell}_{\beta}^G$ gives a matrix $\mathbf{B}$ with submatrices $\mathbf{B}_{\delta\gamma}$, $\mathbf{B}_{\gamma\delta}$, $\mathbf{B}_{\gamma\gamma}$ all equal to zero, and

$$\mathbf{B}_{\delta\delta} = \begin{pmatrix} B^{11} & \dots & B^{K1} \\ \vdots & \ddots & \vdots \\ B^{1K} & \dots & B^{KK} \end{pmatrix},$$

with

$$B_{gh}^{kl} = \begin{cases} -\sum_{i=1}^n (\mathbf{1}\{Z_i = k\} - \zeta_k)(\mathbf{1}\{Z_i = l\} - \zeta_l) \hat{p}_{ig} \hat{p}_{ih}, & \text{if } g \neq h; \\ \sum_{i=1}^n (\mathbf{1}\{Z_i = k\} - \zeta_k)(\mathbf{1}\{Z_i = l\} - \zeta_l) \hat{p}_{ig} (1 - \hat{p}_{ig}), & \text{if } g = h. \end{cases}$$

The efficient score and information matrix follow from equations (A3) and (14), and the score statistic by $\dot{\ell}_{\delta}^{*T} \mathcal{J}_{\delta}^{*-1} \dot{\ell}_{\delta}^*$, which again has, under H_0 , a χ^2 -distribution with $(K - 1)(L - 1)$ degrees of freedom.

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Samenvatting

HOOFDSTUK 1

In dit proefschrift wordt de relatie tussen ontkenning en kwaliteit van leven bij patiënten met longkanker beschreven.

In Nederland krijgen per jaar ongeveer 9000 mensen longkanker. Voor de meeste mensen die te horen krijgen longkanker te hebben, verandert het toekomstperspectief ingrijpend. Er moeten beslissingen genomen worden over mogelijke behandelingen en het dagelijks leven moet worden aangepast aan de bezoeken aan het ziekenhuis. Gezien de bekende slechte prognose van longkanker is de levensverwachting onzeker, de 5-jaarsoverleving van longkanker is ongeveer 15%. Sommigen beleven de diagnose als een doodvonnis. Hoe reageren longkankerpatiënten op deze ingrijpende veranderingen in het leven? Proberen ze te ontkomen aan de werkelijkheid en de gevoelens van bedreiging? Dat heb ik willen onderzoeken.

Met de invoering van de WGBO in 1995 is iedere arts verplicht de diagnose en de behandelmogelijkheden met de patiënt te bespreken. Maar betekent dit dan ook dat de patiënt na dit gesprek 'weet' dat hij of zij lijdt aan longkanker? En als de patiënt dit niet wil weten, is dat dan een probleem?

Onze keuze om ontkenning bij patiënten met longkanker te onderzoeken is gebaseerd op een aantal overwegingen.

Ten eerste is er tot op heden weinig onderzoek gedaan naar de kwaliteit van leven bij longkankerpatiënten vergeleken met psychosociale studies bij patiënten met borstkanker, terwijl er per jaar meer mensen overlijden aan longkanker dan aan borstkanker. Dit kan te maken hebben met de slechte prognose, maar ook met het taboe rondom longkanker, vanwege de mogelijke eigen verantwoordelijkheid bij het ontstaan ervan door roken. Om longkankerpatiënten betere zorg te kunnen bieden gedurende hun ziekteproces, hebben we meer inzicht nodig in hun beleavingswereld.

Ten tweede veronderstelden we dat longkanker patiënten mogelijk meer redenen hebben om hun ziekte te ontkennen dan andere kankerpatiënten, omdat: 1] de slechte prognose hen weinig tijd biedt tot aanpassing en verwerking, 2] deze patiënten vaak last hebben van kortademigheid, hetgeen zeer beangstigend kan zijn; ontkenning zou een manier kunnen zijn om te ontkomen aan deze angst, en 3] schaamte en stigma tot de behoefte kunnen leiden om de pijnlijke realiteit te verbergen.

Op grond van bovenstaande overwegingen is het doel van de onderhavige studie om onderzoek te doen naar:

1. de prevalentie van ontkenning bij longkankerpatiënten

2. de invloed van achtergrondkarakteristieken, zoals bijvoorbeeld leeftijd en geslacht, op de prevalentie van ontkenning
3. patronen van ontkenning in het verloop van de ziekte bij deze patiëntengroep
4. de relatie tussen de gevonden patronen van ontkenning en de kwaliteit van leven in longkankerpatiënten.

HOOFDSTUK 2

In de pilot-fase van de studie werden tien patiënten met longkanker geïnterviewd om hun gedachten en gevoelens te exploreren en om te kijken of ze bereid zouden zijn mee te werken aan het onderzoek. Drie van deze patiënten worden in dit hoofdstuk beschreven.

Een man van 68 jaar oud, die zich gezond en fit voelde, werd overvallen door de mededeling dat hij longkanker bleek te hebben. Aanvankelijk wilde hij hier niets van weten. Na enkele weken besloot hij toch zich te laten opereren. De functie van zijn ontkenning leek bescherming tegen de plotselinge bedreigende informatie.

Aan een vrouw van 69 jaar oud was verteld dat ze longkanker had, met waarschijnlijk uitzaaiingen naar de lever. Er was een biopsie uit haar lever genomen. Ze kwam voor de uitslag bij de longarts, die vertelde dat er geen kwaadaardige cellen in het biopsie waren aangetroffen. “Zie je wel, ik ben niet ziek, het was gewoon een griepje, ik had helemaal niet naar de dokter hoeven gaan” zei patiënte in het interview. Ze onttrok zich aan behandeling. Bij deze patiënte was sprake van persisterende ontkenning van ziekte.

Een zakenman van 52 jaar oud werd behandeld met chemotherapie in verband met een kleincellig bronchuscarcinoom. Hij vertelde aan iedereen dat hij zeker zou genezen en binnen een jaar de marathon in New York zou lopen. Als bewijs voerde hij aan dat een astroloog bij zijn geboorte had gezegd dat hij 100 jaar oud zou worden. Bij deze man zagen we ontkenning in de vorm van irrationeel optimisme.

Met de beschrijving van deze drie vormen van ontkenning willen we laten zien, dat de term ontkenning een verzamelbegrip is, dat verschillende manieren van afweer om te ontkomen aan ondraaglijke gebeurtenissen of gevoelens omvat.

HOOFDSTUK 3

Ontkenning bij patiënten met kanker is een klinisch relevant begrip, waar veel publicaties over verschenen zijn. Historisch gezien is de definitie van ontkenning onderhevig geweest aan verschillende theoretische stromingen.

Vanuit psychoanalytische invalshoek is ontkenning een pathologisch en infectief afweermechanisme, maar volgens de stress- en copingtheorie kan ont-

kenning juist gezien worden als een adaptieve strategie ter bescherming tegen overweldigende gebeurtenissen en gevoelens.

In dit hoofdstuk wordt een literatuuroverzicht gegeven van de verschillende concepten van ontkenning bij kankerpatiënten. Ook worden de studies naar de relatie tussen ontkenning en achtergrondkarakteristieken, zoals b.v. leeftijd en geslacht en de invloed van ontkenning op de kwaliteit van leven beschreven.

De prevalentie van 'ontkenning van de diagnose' varieerde van 4-47%. 'Ontkenning van de impact kwam bij 8-70% van de patiënten voor en 'ontkenning van affect' bij 18-42%. Oudere patiënten ontkenden vaker dan jongere. Culturele achtergrond leek ook van invloed op de prevalentie van ontkenning. Er werd geen verband gevonden tussen ontkenning en het type kanker en ook niet tussen ontkenning en sexe. Hooguit leken mannen vaker dan vrouwen te ontkennen in de terminale fase van de ziekte. In enkele longitudinale studies leek de mate van ontkenning enigszins af te nemen in het verloop van de ziekte.

Over het effect van ontkenning op lichamelijk en sociaal functioneren konden op basis van de literatuur geen conclusies getrokken worden. Het effect van ontkenning op psychologisch functioneren bleek samen te hangen met het concept van ontkenning dat door de onderzoekers gekozen was. Ontkenning in de vorm van actieve strategieën gericht op het zoeken van afleiding bleken gerelateerd aan stressvermindering, terwijl passieve mechanismen, zoals vluchten in te veel drank, een nadelig effect hadden op het psychologisch welzijn.

Op grond van dit literatuuroverzicht concludeerden wij, dat meer onderzoek nodig is naar de prevalentie en de functie van ontkenning bij patiënten met kanker. Dit onderzoek dient gebaseerd te zijn op een helder begrip van ontkenning. Metingen op meerdere tijdstippen in het verloop van de ziekte en

het nauwkeurig vastleggen van de patiëntgegevens zijn nodig om meer inzicht te krijgen in het verschijnsel ontkenning.

HOOFDSTUK 4

Uitgaande van de definitie van ontkenning van Weismann and Hackett ('de bewuste of onbewuste afwijzing van een deel of de gehele betekenis van een gebeurtenis om angst, vrees of andere onaangename gevoelens te verlichten') werd een semi-gestructureerd interview ontwikkeld om ontkenning bij patiënten met kanker te meten. Het 'Denial of Cancer Interview' (DCI) omvat zowel de informatie van de patiënt over diens ziektebeleving als de klinische indruk van het type en de mate van ontkenning van de interviewer.

In dit hoofdstuk worden de ontwikkeling en de eerste psychometrische analyse van het meetinstrument beschreven.

De ontwikkeling van de DCI is gebaseerd op klinische observaties, op het oordeel van acht psychiaters met ervaring in de psycho-oncologie en op drie pilotstudy's om te onderzoeken of het afnemen van het instrument uitvoerbaar was.

De DCI bestaat uit twee delen: een semi-gestructureerd interview, bestaande uit negen vragen die door de patiënt beantwoord moeten worden (Patient Assessment Scale, PAS) en twee items die de klinische indruk van de interviewer over het type en de mate van ontkenning weergeven (Clinical Impression of Type, CIT en Clinical Impression of Level, CIL).

Vier interviews met iedere patiënt werden gepland. De eerste binnen 8 weken nadat de diagnose was gesteld en de vervolginterviews 8, 16 en 32 weken later.

Om te beoordelen of de interviewers de antwoorden van de patiënten op dezelfde manier scoorden, werden de interviews opgenomen en onafhankelijk gescoord door de interviewer en één van de onderzoekers. Honderdvijfennegentig opeenvolgende nieuwe longkankerpatiënten werden geïnterviewd. De interne consistentie van de DCI, Cronbach's α , was 0.84 voor de eerste meting en respectievelijk 0.85, 0.82 en 0.83 voor de vervolgmetingen. De overeenkomst in beoordeling tussen de interviewers was goed voor de gehele DCI ($\kappa = 0.81$) en de PAS ($\kappa = 0.89$) en redelijk voor de scores van de CIT ($\kappa = 0.61$) en de CIL ($\kappa = 0.68$). De inhoudsvaliditeit werd gesteund door klinische observatie, diepte-interviews en het oordeel van deskundigen.

De DCI bleek een geschikt en betrouwbaar instrument te zijn om ontkenning bij longkankerpatiënten te meten. Of de DCI bruikbaar is voor patiënten met een andere vorm van kanker moet eerst getest te worden.

HOOFDSTUK 5

Hoewel ontkenning bij patiënten met kanker een klinisch relevant begrip is, zijn er weinig studies naar de prevalentie en het verloop van ontkenning gedurende het ziekteproces.

In dit hoofdstuk wordt het onderzoek naar de mate van ontkenning bij patiënten met longkanker in het verloop van het ziekteproces beschreven. Ook werd de invloed van achtergrondkarakteristieken en ziektegerelateerde variabelen op ontkenning in deze patiëntengroep onderzocht.

De mate van ontkenning werd vier maal in de loop van acht maanden gemeten met de DCI bij dezelfde 195 nieuwe longkankerpatiënten als beschreven in hoofdstuk 4. Gegevens over de patiënt, zoals bijvoorbeeld leeftijd, geslacht, burgerlijke staat en opleidingsniveau, werden gedurende de interviews verzameld. Medische gegevens werden verstrekt door de longartsen.

De meeste patiënten (86.6 %) toonden een laag tot matig niveau van ontkenning bij de eerste meting en een klein aantal (3%) een hoog niveau. Het gemiddelde niveau van ontkenning in de onderzoeksgroep was het laagste bij de eerste meting en nam toe in de loop van de maanden.

Mannen met longkanker ontkenen sterker dan vrouwen en jongere patiënten ontkenen minder dan de ouderen. Vlak na de diagnose bleken patiënten met een lagere opleiding sterker te ontkennen dan de hoger opgeleiden, maar enkele maanden later was dit verschil verdwenen.

Op grond van deze resultaten kan de conclusie getrokken worden dat een zekere mate van ontkenning bij patiënten met longkanker normaal is en gezien kan worden als een onderdeel van hun ziekteproces.

HOOFDSTUK 6

Hoewel ontkenning bij patiënten met kanker veel voorkomt, is er nauwelijks onderzoek verricht naar de relatie tussen ontkenning en lichamelijke klachten bij deze patiëntengroep.

In dit hoofdstuk worden patronen van ontkenning in het verloop van de ziekte en de relatie tussen deze patronen en de gerapporteerde lichamelijke klachten van longkankerpatiënten beschreven. De onderzochte patiëntengroep is dezelfde als beschreven in hoofdstuk 4 en 5. Lichamelijke klachten werden gemeten met een algemene en ziektespecifieke kwaliteit van leven vragenlijst (EORTC-QLQ + longmodule).

We vonden drie patronen van ontkenning over een periode van acht maanden: een stabiel laag niveau van ontkenning, een stabiel matig niveau van ontkenning en een patroon met toenemende ontkenning in de loop van de tijd. Mannelijke longkankerpatiënten bleken vaker op een matig niveau te ontkennen en vrouwen vaker op een laag niveau. De patiënten die stabiel matig of in toenemende mate ontkenden, rapporteerden minder lichamelijke klachten, ze waren minder moe, hadden minder last van misselijkheid, braken, eetlustverlies, slikklachten en pijn in arm en schouder. Over het geheel genomen voelden ze zich gezonder en functioneerden lichamelijk beter dan de patiënten bij wie een stabiel laag niveau van ontkenning was gemeten.

Ontkenning bij patiënten met longkanker lijkt dus een gunstig effect te hebben en dient daarom gerespecteerd te worden.

HOOFDSTUK 7

Ook al is ontkenning een bekend fenomeen in de klinisch oncologische praktijk, is niet duidelijk of het effect op sociaal en emotioneel functioneren gunstig of schadelijk is.

In dit hoofdstuk worden de resultaten van de studie naar de relatie tussen ontkenning en sociale en emotionele gevolgen beschreven. De onderzoeksgroep is dezelfde als beschreven in de hoofdstukken 4, 5 en 6.

Sociaal en emotioneel functioneren werden gemeten met de EORTC-QLQ-30 en de Hospital Anxiety and Depression Scale (HADS).

Patiënten met een patroon van stabiele matig niveau van ontkenning of met een toenemende ontkenning in de loop van het ziekteproces rapporteerden betere uitkomsten op sociaal gebied en minder angst en depressie dan patiënten met een stabiel laag niveau van ontkenning.

De kwaliteit van leven onder longkankerpatiënten met matige of toenemende ontkenning was beter in vergelijking met de kwaliteit van leven bij patiënten met een laag niveau van ontkenning.

Een bepaalde mate van ontkenning kan dus een gunstig effect hebben op sociaal en emotioneel functioneren bij patiënten met longkanker.

HOOFDSTUK 8

In dit hoofdstuk wordt op een aantal thema's uit het onderzoek dieper ingegaan: de complexiteit van het begrip ontkenning en het meten hiervan, enkele methodologische kwesties, de patronen van ontkenning in de loop van het ziekteproces, de relatie tussen ontkenning en lichamelijk, sociaal en emotioneel functioneren en het verschil in de mate van ontkenning tussen mannen en vrouwen.

Tot slot wordt ingegaan op de klinische implicaties van dit onderzoek. Hoewel deze studie primair beschrijvend is, zijn op grond van de resultaten enkele overwegingen ten behoeve van de klinische praktijk gerechtvaardigd.

Daar een zekere mate van ontkenning een beschermend effect blijkt te hebben voor patiënten met longkanker, dienen artsen hier rekening mee houden wanneer ze informatie over diagnose, behandeling en prognose geven. Ook is het van belang dat artsen aandacht besteden aan de rol van de familie, maar ook aan de houding van de arts zelf ten opzichte van de ontkenning van de patiënt.

In onze tijd van zelfonthulling en nagenoeg grenzeloze openhartigheid moeten we beseffen dat sommige patiënten behoefte hebben aan bescherming tegen ondraaglijke feiten en gevoelens. Een zekere mate van ontkenning kan in deze behoefte voorzien. Artsen kunnen deze patiënten steunen door onderkenning van en respect voor ontkenning.

Dankwoord

Eind 1995 besloot ik onderzoek te gaan doen. Ik had behoefte aan verdieping in mijn vak, doorgronden wat ik nog niet voldoende begreep. Ik wilde meer weten over de creatieve bochten waarin de geest zich kan manoeuvreren wanneer het leven een ongewenste wending neemt.

Deze behoefte werd concreet toen ik op een zondagmiddag het artikel las van Greer, Morris en Pettingale: "Psychological Response to Breast Cancer: Effect on Outcome" (Lancet 1979, October 13, 785-787). De conclusie luidde: "A favourable outcome was more frequent in patients whose responses were categorised as denial or fighting spirit...."

Veertien jaar later is mijn proefschrift over ontkenning af.

Bij het schrijven van dit dankwoord komt het mij onbegrijpelijk voor, dat ik periodes heb gekend waarin ik onderzoek doen en het schrijven van een proefschrift een solitaire aangelegenheid vond. Zo velen hebben hun bijdrage geleverd aan de totstandkoming van dit proefschrift. Niet alleen een groot aantal maar ook een grote verscheidenheid aan mensen heeft me geholpen. Aan allen wil ik dank zeggen.

DE PARTICIPANTEN

Allereerst wil ik mijn grote waardering en erkentelijkheid uitspreken aan de patiënten en hun familieleden die meegewerkt hebben aan dit onderzoek. De interviews, waarin de patiënten ons hun beleavingswereld toevertrouwden, waren altijd boeiend en betekenisvol. Meestal voelde ik me welkom, zelfs met videocamera, waar ik soms meer moeite mee had dan de geïnterviewde. De uitspraak van één van de geïnterviewden: "dokter, ik ben lid van de struisvogel-partij" is tot op de dag van vandaag mijn hartversterker gebleven. De beelden van ernstig zieke mensen, thuis of in het ziekenhuis, die toch antwoordden op mijn vragen en bereid waren vragenlijsten in te vullen, blijven me bij en hebben veel indruk gemaakt.

MIJN H-TEAM

Hanneke de Haes, Hans van Houwelingen, Hein Putter, Harry Rooijmans en Harriet van Heusden. Het aantal woorden om uit te leggen wat jullie in de afgelopen veertien jaar voor me betekend hebben, overstijgt de woordlimiet van een peer-reviewed artikel. Kort samengevat: zonder jullie was dit proefschrift er nooit gekomen.

Hanneke: jij komt straks nog apart aan bod.

Hans: dank zij jouw rijke brein heeft ons onderzoek een prachtig biostatistisch skelet. Als je uitlegde hoe het zat, begreep ik het echt. Dat ik het niet allemaal heb onthouden komt omdat ik psychiater ben en mijn brein vaak de andere kant op staat.

Hein: In soorten en maten heb ik minstens 80 bestanden met de naam `tablesandfigures.hein`. Wat kan jij prachtige kleurenplaatjes maken van al die cijfertjes en lettertjes. Je wou het liefst dat ik vragen stelde, die jij kon beantwoorden. Voor alle antwoorden waar we geen vraag bij konden vinden, had jij altijd koffie of kwam je op de fiets naar Bronovo.

Harry: jij was er de eerste jaren en bracht grote lijnen aan. De weerbarstigste materie van het meten van ontkenning plaatste jij in een aangenaam relativerend perspectief met je uitspraak: “iedereen weet wat liefde is, maar hoe moet je het meten? Één kus per dag? Of twee?”.

Harriet: vijf jaar lang zat je in een uithoekje bij de directie en de dominees nauwgezet en geduldig al onze data in te voeren, ons op tijd op pad te sturen en heb je duizenden papieren geordend. Ik prijs mij gelukkig dat jij aan mijn zijde hebt gestaan tijdens mijn onderzoek.

DE VELDWERKERS

Amber Leurs en Caro van der Wijk. Met ons drieën hebben we gedurende 2 jaar en 10 maanden de patiënten geïnterviewd en elkaars videobanden beoordeeld. Onze consensusbesprekingen (met kaas en wijn) waren altijd nuttig en aangenaam. Dank voor jullie inzet!

Amber, jij wist de artsen en de patiënten in het Medisch Centrum Haaglanden te motiveren om mee te doen. Soms had je creatieve kaartjes nodig om de dokters te bereiken, maar het lukte je. Je heldere commentaren tijdens onze onderzoeksbesprekingen heb ik zeer gewaardeerd.

DE EXPERTS

Marjolein Bannink, Arthur van Gool, Leo Gualtherie van Weezel, Michiel Hengeveld, Wybrand OpdenVelde, Liesbeth de Regt, Harry Rooijmans en Jolien Tuyl. In een heel vroeg stadium van mijn onderzoek leverden jullie commentaar op de eerste versie van wat later het Denial of Cancer Interview werd. Dank zij jullie bleken we over content validity te beschikken. Daar ben ik heel blij mee.

DE GEVERS VAN TIJD EN GELD

De Raden van Bestuur van Bronovo wil ik danken voor hun vertrouwen in mij. Het resultaat van de onderhandelingen met Roel van Neerbos in 1998 was, dat

ik tijd kreeg om mijn proefschrift te schrijven op voorwaarde dat mijn klinische werk er niet onder zou lijden. Henk Knook, Huybert van Eck en Joop Hendriks hebben die lijn vastgehouden en mij de tijd gegund.

In 1999 besloot het Koningin Wilhelmina Fonds subsidie te verstrekken aan ons onderzoek. Daarmee werd het echt en konden we een onderzoeksgroep samenstellen. Wat was dat een vreugde! Ik heb deze subsidie ervaren als een grote steun en erkenning en tegelijk voelde ik daarmee ook de verantwoordelijkheid om het onderzoek tot een goed einde te brengen.

Toen het geld van het KWF op was, maar het onderzoek nog niet af, besloot het Research Fonds subsidie te geven om Harriet van Heusden nog een jaar door te laten werken en bij te dragen in de kosten van de publicaties. Hierdoor kon het onderzoek voltooid worden en gloorde de aula van de UvA aan de horizon.

DE VERWIJZERS

Ik had de medewerking van collega's nodig om patiënten te vragen mee te doen aan mijn onderzoek.

Allereerst wil ik Joost Biesta, radiotherapeut, bedanken. Jij adviseerde mij om longkankerpatiënten te kiezen voor mijn onderzoek, omdat er te weinig aandacht besteed wordt aan de psychosociale gevolgen van de ziekte bij deze groep. In de fase van de interviews was jij een uitstekend vangnet. Je checkte regelmatig of de patiënten die bij jou kwamen wel meededen aan mijn onderzoek, omdat je het belangrijk vond. Ik waardeer jouw inbreng bijzonder.

In het Medisch Centrum Haaglanden onderhield Amber Leurs de contacten met dr. Bauer, dr. Den Hertog, dr Apap en dr. De Jong. Wij kennen elkaar nauwelijks, daarom waardeer ik het extra dat u bereid bent geweest mee te werken aan het onderzoek.

In Bronovo kreeg ik meer dan alleen medewerking van 'mijn' longartsen. Henk Berendsen, Klaas van Kralingen, Peter Oosterling, Janwillem van den Berg en Roos van de Heijde: dank zij jullie betrokkenheid, steun en oprechte belangstelling bleef mijn onderzoeksgeest vitaal. Een liefdesverklaring mijnerzijds aan jullie allen zou te ver gaan, maar mijn gevoelens van dank en vreugde over onze blijvende samenwerking komen wel in de buurt. Graag wil ik nog jaren jullie T-schijf blijven om longkankerpatiënten de zorg te bieden die ze nodig hebben.

MIJN ACHTERBAN

In de loop van de 14 jaar dat ik bezig was met mijn onderzoek heb ik enorm veel belangstelling gekregen. De eerste jaren kon ik het niet verdragen als er gevraagd werd "hoe gaat het met je proefschrift?". Ik was er helemaal niet zeker van dat er een proefschrift zou komen. Gedurende de middenfase werd de

belangstelling tanende. Dat vond ik wel prettig, mogelijk heb ik het zelf veroorzaakt door niet enthousiast meer te reageren, maar gewoon te zeggen dat ik er aan werkte. Er is één periode geweest dat ik erg in spanning heb gezeten, omdat het instrumentartikel door een aantal tijdschriften afgewezen werd. Maar toen dat toch geaccepteerd werd, groeide mijn vertrouwen. De brug naar de andere artikelen was nu gepubliceerd. Twee jaar lang heb ik verteld dat het nog twee jaar zou duren.

Familie, vrienden, collega's en kennissen: dank voor al die belangstelling, het medeleven en de opbeurende woorden gedurende al die jaren.

Een aantal groepen in mijn achterban wil ik speciaal noemen.

Onze oncoclub, met Marjolein Bannink, Arthur van Gool, Rolf Lanting, Leo van Gualthérie Weezel en sinds kort Paul Bouvy: op de agenda van onze bijeenkomsten stond vaak het punt 'onderzoek Tineke', dat hoeft nu niet meer! Onze uitwisseling van ontwikkelingen en opvattingen betekent veel voor mij. Mede door deze groep weet ik mij erkend als 'oncopsychiater' en dat stemt mij tot grote tevredenheid.

Onze ouwe trouwe intervisiegroep, met Marc Blom, Ariette van Reekum, Jan Spijker en Helen Winkel. We bestaan al sinds 1992 en al is de frequentie niet altijd stabiel, het weten dat er collega's zijn die je in vertrouwen kunt nemen of een moeilijke casus voorleggen is goud waard. Ik hoop dat we tot ons pensioen doorgaan.

De afdeling psychiatrie in ziekenhuis Bronovo: Anja Ruis, Roeland Walburgh Schmidt, Marit van der Zwan, Petra Zwarts en tot 2008 Liesbeth de Regt. Mijn onderzoek was een megaproject dat zich voor een deel buiten ons dagelijks werk afspeelde. Vaak was ik met verschillende dingen tegelijk bezig, waardoor mijn aandacht niet gericht was op pasjes, sleutels en brillen. Dank Anja, dat je altijd weer mijn eigendommen wist terug te vinden. Met vasthoudendheid belde je desnoods alle afdelingen en de portier, maar je kreeg het voor elkaar.

Marit, jij bent er altijd. Je vanzelfsprekende bereidheid om te luisteren, oplossingen te bedenken (je hebt zelfs op een vrijdagavond je echtgenoot ingeschakeld om Latex naar Word te converteren!) en je werktijden aan te passen om anderen te helpen, waardeer ik enorm.

Roeland, wij samen zijn er goed in om de weg vinden in de V.S. met een auto vol rusteloze collega's, maar wat we vooral goed kunnen is ons gezamenlijk buigen over patiënten met complexe problemen. Ik ben blij met je als maat in het werk en op de golfbaan.

Petra, jij en ik zijn complementair. Doordat jij jouw aandachtsgebieden sterk hebt ontwikkeld, is het palet van onze ziekenhuispsychiatrische deskundigheid breed geworden en dat is een groot goed. Jij bent de sociaal bindende factor in onze afdeling, want je denkt aan cadeautjes en bloemetjes voor iedereen die jarig is of afscheid neemt. Na 28 oktober is mijn onderzoeksvrijdag over, dat biedt kansen om samen nieuwe plannen te maken.

Liesbeth, rust en concentratie bood het mij, toen je kwam invallen in de periode dat ik echt moest schrijven. Dank zij de zekerheid dat de patiëntenzorg in jouw goede handen lag, kon de telefoon er bij mij uit.

MIJN ENGELN

Bij de gang naar de aula van de UvA weet ik mij omringd door drie engelen: Mary Köhne en Catie Oberman en Henk Berendsen.

Alle drie hebben ze hun specialiteit.

Mary, mijn trouwe vriendin in werk en privé. Een ster in organiseren, regelen en adviseren. Op iedere valreep en op ieder stressmoment denk je rustig mee, weet je de juiste personen te vinden, vallen de oplossingen je in of overtuig je me op relativerende toon dat het niet erg is dat het niet opgelost wordt. Het samen met jou de voorbereidingen treffen voor het promotiediner is al een feest. Je verrast me steeds weer met wie je bent en hoe je er voor mij bent.

Catie, mijn vriendin uit Amsterdam.

Jij en ik kunnen gesprekken voeren over onderwerpen die de ontkenning gepasseerd hebben. Na de bezoeken aan jou, op de terugreis naar Den Haag, zit ik veelal ruimer in mijn gedachten. Jij hebt verstand van kunst, daarom is de omslag met de twee figuren van Malevich zo mooi geworden. Dankzij je kritische commentaar is de Nederlandse samenvatting van dit proefschrift ontdaan van onuitsprekbare woorden en voor iedereen leesbaar. Je hebt laten weten dat je de kern van mijn verhaal begrijpt. Wat ben ik blij dat jij naast mij staat als ik mijn proefschrift moet verdedigen.

Henk, mijn goede vriend en collega.

Op de dag dat bekend werd dat het KWF ons onderzoek financieel zou ondersteunen, liet jij in sociëteit de Witte in het geheim door de kok een grand dessert maken met in chocolade de tekst: 'Erkenning voor Ontkenning'. Verreweg de meest longkankerpatiënten in het onderzoek zijn door jou ingebracht. Jij stelde mij gerust als ik twijfelde of er wel een proefschrift zou komen, door te zeggen dat alleen al de interviews met de patiënten van grote waarde waren en dat met mijn onderzoek de psycho-oncologische zorg in ons ziekenhuis een ruime plaats heeft gekregen. De eerste publicatie uit het onderzoek is van ons samen. Beste Henk, het is mij een grote eer en een bijzonder genoegen dat je naast mij zult staan tijdens de verdediging van dit proefschrift.

TWEE PERSONEN

Tot slot zijn er twee personen die buiten alle categorieën vallen en daarom een eigen plaats krijgen in dit dankhoofdstuk.

Hanneke de Haes, mijn standvastige promotor

Voorjaar 1996. Met onrijpe, uitwaaierende gedachten en vijf mogelijke onderzoeksthema's kwam ik voor het eerst bij je. Ik verzamelde literatuur over ontkenning, van Freud tot heden. Vellen vol tabellen aan elkaar geplakt met definities en meetinstrumenten. Ik dacht en schreef van alles, maar wist nog niet waar ik het moest zoeken. De omslag kwam toen ik een concept onder-

zoeksvoorstel van je terug kreeg, waarop met potlood 'mooi !' stond geschreven. Gedurende veertien jaar was je altijd als observerend alter in mijn denken aanwezig. De eerste tijd was de relatie promotor-promovenda een apart proces binnen ons onderzoek. Ik noemde jou een keer schooljuf en jij vond mij koppig. Ik was een keer boos en jij nam me mee uit eten. Jij vond mijn conceptuele niveau niet goed genoeg en ik vond dat patiënten geen concepten waren. Maar het kwam altijd weer goed, want je liet blijken dat je er vertrouwen in had dat ik zou doorzetten. Je toonde begrip dat het soms een eenzame aangelegenheid was, om als externe promovenda thuis te zitten broeden op publicaties en om de teleurstelling over afwijzingen niet bij de koffie te kunnen delen met collega-onderzoekers die ook ervaring hebben met afgewezen artikelen.

Wanneer een artikel wel geaccepteerd was, was je de eerste om op hartverwarmende wijze de vreugde te delen, de mailtjes met 'great !' en 'yes !' en 'geweldig !' heb ik bewaard.

Nu is het proefschrift af. Ik zal de besprekingen met jou missen. Je ontving mij altijd hartelijk. Ik ben aan je gehecht geraakt. Als ik er teveel last van krijg dat we geen gezamenlijk doel meer hebben, ga ik alsnog beginnen aan de klinische les voor the Journal of Clinical Oncology.

Lieve Hanneke, dank voor je intensieve begeleiding. Ik heb veel van je geleerd en dat heeft mij verrijkt.

Jules Theeuwes

Wij woonden samen toen mijn behoefte aan onderzoek doen begon op te spelen. Jij hebt mij daarbij vanaf het begin krachtig gestimuleerd.

Nu zijn we een tevreden setje wandelende singles. Maar je bent er altijd. Om op mijn verbaasde vraag op vrijdagavond half tien uit te leggen hoe het kan dat de standaarddeviatie van een getal vele malen groter kan zijn dan het getal zelf. En om een rustige analyse te maken toen ik bijna flauw viel van de schrik omdat mijn computer helemaal niets meer deed. Op zondagen gingen tekstfragmenten tussen ons heen en weer, waarin jij de Engelse leesbaarheid verbeterde. Je troostte bij tegenslag en je deelde bij vreugde. Jouw bijdrage aan dit proefschrift is pure vriendschap.

EPILOOG

Veertien jaar geleden besloot ik onderzoek te doen om te doorgronden wat ik nog niet goed begreep. Nu het proefschrift af is, ben ik tot de conclusie gekomen dat ik beter begrijp hoe patiënten met kanker proberen te ontkomen aan bedreigende feiten en gevoelens. Dat komt door Ilse de Winne. Ilse is overleden. Met toestemming van haar broer Niels, haar wettelijk vertegenwoordiger, mag ik over haar schrijven. Gezien de vertrouwelijkheid doe ik dat summier.

Ilse was 25 jaar oud, net afgestudeerd als psycholoog, toen bleek dat ze longkanker met uitzaaiingen had. Ze had nooit gerookt en altijd gezond geleefd. Ze wist dat de behandelingen palliatief waren. De frequente bezoeken aan verschillende artsen, de onderzoeken en de therapieën hoorden voor haar tot het 'project' zoals ze haar ziekte noemde. Ze wilde leven, schrijven, betekenis hebben in de wereld en vrolijk zijn. "...hoe zwaarder het allemaal wordt, hoe meer je het lachen nodig hebt.." zegt ze in een televisie-uitzending[†]. Ze werd in haar verlangens belemmerd door het 'project'.

Ze maakte mij deelgenoot van haar moedige en ook creatieve manier van omgaan met de ondraaglijkheid van de naderende dood. Ze hanteerde genuanceerde vormen van ontkenning, vooral om haar gevoelens onder controle te houden. Ik begreep die ontkenning. Want hoe moet dat, sterven als je 27 jaar oud bent?

Nadat ik afscheid van haar had genomen, reed ik naar huis. Ik voelde dat ik een vriendinnetje had verloren. Ik besepte dat ik Ilse goed kon begrijpen. Misschien ook omdat ik me veertien jaar lang verdiept had in ontkenning bij patiënten zoals zij en wist hoe dat verlichting bracht. Van dat besef werd ik rustig. Ik draag dit proefschrift op aan haar.

[†] "Liefde gaat door de maag" van Heddy Honigmann, 31 januari en 19 april 2009

Curriculum vitae

Martina Sita Vos

Geboren 2 oktober 1953 te Oldebroek

- 1972: eindexamen HBS-B te Ede
- 1976: kandidaats biologie aan de Vrije Universiteit te Amsterdam (cum laude)
- 1976-1984: studie geneeskunde aan de Vrije Universiteit te Amsterdam
- 1987-1992: specialisatie psychiatrie aan het Academisch Ziekenhuis Groningen (hoofdopleider Prof dr R.J. van den Bosch), stage sociale psychiatrie bij RIAGG Den Haag (opleider V.M. Vladár Rivero) en keuzejaar biologische psychiatrie en research in Psychiatrisch Centrum Bloemendaal te Den Haag (opleider Dr. W. Nolen)
- 1992-1995: werkzaam als psychiater in het crisiscentrum en de deeltijdbehandeling bij de Stichting Schroeder van der Kolk te Den Haag, het laatste jaar ook als adjunct-directeur
- 1995-heden: werkzaam als ziekenhuispsychiater in Bronovo te Den Haag; aandachtsgebieden: psycho-oncologische zorg, palliatieve zorg, onverklaarde klachten, communicatie-onderwijs aan arts-assistenten
- 2008-heden: SCEN-arts voor de regio Den Haag

Denial in cancer patients is a well-known concept. The definition of denial, however, is not unequivocal and covers different ways of evading painful events or feelings.

This thesis studies denial and its relation to the quality of life in lung cancer patients. To assess the level of denial the 'Denial of Cancer Interview' (DCI) was developed.

Denial was measured at different time points in the course of the disease.

The key-finding from this study is that patients fare better when they express a moderate level of denial or increase their level of denial from the moment of diagnosis over time.

This study shows convincingly that denial in lung cancer patients deserves attention in clinical practice. In this era of self-disclosure it is good to realize that some patients need protection against unbearable facts and feelings. Denial can serve this need and should be respected.

Martina S. Vos is consultation-liaison psychiatrist at Bronovo Hospital in The Hague.

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