Parkinson's disease - psychological determinants of quality of life

Dubayova, Tatiana

Parkinson's disease – psychological determinants of quality of life

Tatiana Dubayova

Address for correspondence:
Tatiana Dubayova, Department of Special Education, Faculty of Education, University of Presov, ul.17. novembra 1, 08001 Presov, Slovak Republic

The project described in this thesis was supported by the Service and Technology Assistance Agency under the contract No. APVV-20-038305.

Design: Iveta Budaiova
Press: Equilibria, s.r.o.
Printed in Slovak Republic

ISBN 978 94 6070 026 2

RIJKSUNIVERSITEIT GRONINGEN

Parkinson's disease – psychological determinants of quality of life

Proefschrift

ter verkrijging van het doctoraat in de
Medische Wetenschappen
aan de Rijksuniversiteit Groningen
op gezag van de
Rector Magnificus, dr. F. Zwarts,
in het openbaar te verdedigen op
maandag 6 december 2010
om 14.45 uur

door

Tatiana Dubayová

geboren op 18 oktober 1975

te Prešov, Slowakije

Promotor:	Prof. dr. J.W. Groothoff	Rijksuniversiteit Groningen
Copromotores:	Dr. J.P. van Dijk	Rijksuniversiteit Groningen
	Dr. I. Nagyova	Šafárik University Košice, Slovakia
	Dr. Z. Gdovinová	Šafárik University Košice, Slovakia
	Dr. L.J. Middel	Rijksuniversiteit Groningen
Beoordelingscommissie:	Prof. dr. W.H. Brouwer	Rijksuniversiteit Groningen
	Prof. dr. J. Dzuka	University Presov, Slovakia
	Prof. dr. M. Hagedoorn	Rijksuniversiteit Groningen

Contents

Chapter 1 7
General introduction

Chapter 2 **21**
Neuroticism and extraversion in association with quality of life in patients with Parkinson's disease
(Quality of Life Research, 2009, 18:33-42)

Chapter 3 **37**
The association of type D personality with quality of life in patients with Parkinson's disease
(Aging and Mental Health, 2009, 13:905-912)

Chapter 4 **51**
The impact of the intensity of fear on patient's delay regarding health care seeking behavior: a systematic review
(International Journal of Public Health,2010, 55:459-468)

Chapter 5 **71**
Differences in quality of life by personality traits among delayers and non-delayers with Parkinson's disease
(submitted)

Chapter 6 **83**
Type D, depression and anxiety in association with quality of life in patients with Parkinson's disease and with multiple sclerosis
(submitted)

Chapter 7 **97**
General discussion and implications for practice and future research

Summary 107

Samenvatting 111

Zhrnutie 115

Acknowledgements 119

About the author 121

Graduate School Kosice Institute for Society and Health (KISH) and previous dissertations 123

Graduate School for Health Research (SHARE) and previous dissertations 131

Chapter 1

General introduction

People in present days in Western Europe are achieving a higher age than ever and its population is getting older. Based on recent surveys, the prevalence of neurologic diseases within aging population is increasing [1]. One of them is Parkinson's disease (PD), which affects mostly people in the age over fifty. Worsening mobility, causing problems with activities of daily living, pain and communication problems due to rigidity of facial muscles, are the main reasons of their decreasing quality of life [2]. This study is focused on the role of psychological variables, which could be associated with quality of life in PD patients. After their identification a discussion about opportunities of improvement patient's quality of life can be opened. In the first chapter a description of PD, the main aims of the thesis, theoretical models and research questions will be presented.

1.1 Parkinson's disease

In 1817 James Parkinson, a medical doctor, for the first time described the disease as *"involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured"* [3].

Prevalence/Incidence

Parkinson's disease is the second most common neurological disorder affecting disability after stroke [4,5]. The disease occurs more frequently in men than in women in every decade of life, which is explained by the neuroprotective effects of estrogens [6-8].

Prevalence and incidence of PD in European countries was estimated at approximately 108 to 257/100,000 and 11 to 19/100,000 per year, respectively, but it varied from country to country. The prevalence in Asia countries is slightly lower, all-age prevalence varied from 51.3 to 176.9/100,000 persons and the incidence from 6.7 to 8.7 per 100 000 persons per year [9]. Prevalence and incidence rates are the lowest in African countries – the crude prevalence varied from 7 to 31.4/100,000 persons and the crude incidence rate of PD was 4.5/100,000 persons per year [10]. When only older age groups (≥ 60 years) were included, rates of prevalence and incidence in Europe varied from 1280 to 1500/100,000

persons and 346/100,000 persons per year, respectively [11]. Baldareschi and colleagues estimated an average annual incidence rate of 346/100,000, but only persons aged 65–84 years were included in their study population [12].

Criteria for diagnosis

Parkinson's disease (PD) is an age-related neurodegenerative disease, characterized by relatively selective nigrostriatal dopaminergic degeneration. First symptoms of PD appear, when the remaining production of dopamine has been fallen below 20% of its original production or when 50% of the cells of the substantia nigra have been destroyed [2]. The criteria for diagnosis are including physical and mental symptoms which have an impact on quality of life (QoL) of patients with PD [14,13]. There are four main clinical symptoms of the disease: tremor, rigidity, slowness and problems with walking and posture [2]. The important physical symptoms of PD are also a blank stare (the so-called "Parkinson's mask") and troubles with manual dexterity [15]. Non-motor symptoms of the disease may include depression, sleep disorders, hallucinations and delirium, some of which may be related to treatment by dopaminergic drugs [16-18]. Table 1.1 is showing the main motor and non-motor symptoms.

Table 1.1 Motor and non-motor symptoms of Parkinson's disease

Motor	Non-motor symptoms
Tremor	Mood disorders:
	Depression, anxiety and apathy
Rigidity	Cognition:
	Bradyphrenia, dementia
	Sleep disorders:
Bradykinesia	Sleep fragmentation, REM sleep disorders, excessive daytime sleepiness,
	altered sleep–wake cycle
	Autonomic disorders:
Postural instability	Hypotension, constipation, detrusor dyssynergia, sexual dysfunction,
	seborrhea, sweating

Treatment and healthcare services

Although, over past three decades cell-based therapies, based on replacement of the lost dopamine neurons by transplantation, are developing, PD is still considered as an illness that cannot be cured [**2,**19]. There are several approaches to its treatment, from a "wait and see" policy to starting with drug treatment immediately after identifying the diagnosis, but so far neurologists did not reach consensus regarding treatment [20]. However, although curing PD is not yet possible, symptomatic treatment has improved in recent years. The most used symptomatic therapy for

PD is levodopa, introduced more than forty years ago, which efficacy is evident mostly in the beginning of the treatment [18,21]. However, after long using the levodopa the levodopa-induced side effects could appear: dyskinesias, motor fluctuations or neuropsychiatric disorders [18]. Another possibility, which has been used for treatment of PD symptoms since the 1970s, are the dopamine agonists which are associated with a lower incidence of dyskinesias, but they have less benefit on the motor function than dopamine itself, and there are increasing concerns about their side-effect profile [22]. Next possibilities are Catechol-O-Methyl-Trasnsferase (COMT) inhibitors in conjunction with levodopa for longer-lasting treatment and selective MAO-B inhibitors for adjunctive therapy and from 2006 also in monotherapy. An algorithm suggests to start with dopamine agonists in younger patients and only later to combine it with other antiparkinsonian drugs. In patients over eighty it is recommended to start with levodopa. In Slovakia patients use antiparkinsonian therapy according international guidelines [23,24].

In the examined sample of PD patients, 12% used only L-dopa, and 24% used only dopamine agonists. L-dopa in combination with Catechol-O-Methyl-Trasnsferase (COMT) inhibitors was used by 25.3% of the patients, and L-dopa with dopamine agonists was used by 20% of the patients. The combination of L-dopa, a COMT inhibitor and dopamine agonists was used by 16% of the patients from our sample [25].

Rehabilitation and physical exercises are used for slowing down the secondary damaging of motor functions [2]. However, physical therapeutists and trainers should take into account neurophysiologic aspects of motor impairment in PD, e.g., akinesia, the inability to perform sequential movements, impairments in the pacing of rhythmic movements, and impairments in the predictability of movements [26]. A quite novel kind of treatment of motor functions in PD patients is the combination of motor imagery and real practice, which seems to be effective, especially for reducing bradykinesia [27].

Information about quality of life in patients with PD is important for a neurologist, as it can help him to make appropriate decisions. Hence, it is important to pay attention to study findings in this group of patients and to continue exploring the variables which can indicate changes in their quality of life. To improve the overall health status of the patients and to maintain their independence and active life is one of the challenges in neurology.

1.2 Impact of Parkinson's disease on their quality of life

PD is not a fatal diagnosis by itself, but in people seriously disabled, suffering from the disease several years, it will influence their general

physical and mental conditions as well as their social functioning, which could decrease the patient's quality of life and also reduce the length of his/her life [4,28]. After 2–5 years from the onset of disease, up to 50% of PD patients develop motor complications which include regular visits of neurologist and intensive rehabilitation [29]. The progressive nature of PD and its increasing prevalence have resulted in a substantial economic burden to society, health care providers, individual patients and their families [29,30].

Physical domain

The poorer quality of life of PD patients is mainly associated with functional status and disease severity [25,**31,**32], a fact confirmed by several studies. In a 4-year follow-up study, disease severity was significantly the most important factor for a lower QoL [33]. Altered gait and postural instability also contributed to the worsened QoL of these patients [32,34].

Psychological domain

There are several psychological aspects associated with PD decreasing QoL in patients. The presence of fatigue in PD patients predicts the worsening of all QoL domains measured by the Parkinson's Disease Questionnaire-long form (PDQ-39), a disease specific measurement; that is, primarily bodily discomfort, mobility and emotional well-being [35]. Depression is the major contributor to the explanation of the variance in QoL scores [2,36-38]. The rate of depression in community-based samples of patients with PD is approximately 30–40%, ranging from 20 to 70%, but only a minority of these patients (approximately 2.7 to 7.7%) fulfills the criteria of DSM IV for depression [39]. Physical impairment due to disease, such as increased disease severity, recent disease deterioration and the occurrence of falls, is a condition for higher levels of depression in PD patients. It was also found that depression is more strongly associated with patients' perception of being handicapped than by actual disability and can reflect a pessimistic outlook on the future [36,37]. Worse overall mental condition and patients' memory complaints are also significant factors associated with lower QoL [2,32,37]. Personality traits, such as extroversion, neuroticism or Type D personality, were till now not examined in the context of Parkinson's disease.

Social domain

The social aspect of PD most negatively influencing the social domain of QoL of patients is isolation, which is due to the embarrassment caused by the symptoms and problems with communication [40]. Patients mentioned that major social problems associated with the *disease* were the loss *of* social contact, behavioral problems, family members under strain and communication problems within the family [41].

1.3 Measuring quality of life in patients with Parkinson's disease

For measuring QoL in patients with PD, disease specific instruments and generic instruments can be used. The use of this variety of instruments is resulting into difficulties in comparing QoL of PD patients from different studies on the one hand and with other groups of chronically ill patients on the other hand.

Disease specific measurements
Disease-specific instruments widely used are the Parkinson's Disease Questionnaire (PDQ-39) designed by Peto et al. (1995) and the Parkinson's Disease Quality of Life questionnaire (PDQL) developed by De Boer et al. (1996) [42,43]. In several studies also the Parkinson's Impact Scale (PIMS) was used, useful in identifying potential problems areas, and the Parkinson LebensQualität (Parkinson QoL questionnaire) (PLQ) used mostly in German studies [44].

Generic measurements
There are also generic (disease non-specific) instruments used to compare PD patients to the general population, or to other disease groups. Predominantly the Medical Outcome Study Short Form (SF-36) and the EuroQoL 5D (EQ-5D) are used, mostly successfully used in many studies where different groups of patients were compared.

1.4 Conceptual framework

QoL is a complex and multidimensional construct that has been defined as *"a concept encompassing a broad range of physical and psychological characteristics and limitations which describe an individual's ability to function and to derive satisfaction from doing so"* [45]. It includes the following domains: the physical, encompassing the ability to conduct activities of daily living; the psychological or emotional; and the social, encompassing interactions with family, friends, and community [46].

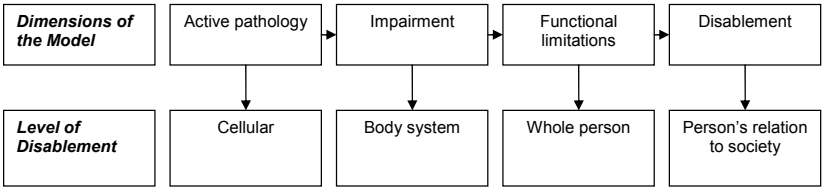
Various factors are influencing QoL in chronically ill patients. Clinical and socio-demographical factors, which are most frequently examined, are not the only factors predicting QoL. In practice, individual differences between patients were observed – patients with the same level of symptoms (objectively with the same score in neurological scales) informed the neurologist about different satisfaction with their lives.

There were several models in previous decades, which tried to explain the disablement process. Saad Nagi, a sociologist from Egyptian origin, started in the sixties of the twentieth century with this type of modeling, by introducing a dynamic view on disablement [47-49]. His

model describes the disablement process through concepts as are shown in Figure 1.1. Main terms are:

- *active pathology* – a state of the body's defences and coping mechanisms caused by infections, traumas or other pathologies
- *impairment* – a loss of or abnormality of the tissue, organ and body system level
- *functional limitations* - limitations in an individual's ability to perform the tasks and obligations of his ususal roles and daily activities
- *disablement* - limitations in performing socially defined roles, e.g. employment or self-care

Figure 1.1 Nagi's model of disablement and functional consequences of a pathological process in the body [48]



In 1976 the WHO published an upgraded model which analyzed, described and classified the consequences of disease and which distinguish between impairment, disability and handicap. It was named International Classification of Impairments, Disabilities and Handicaps (ICIDH) [50]. It sees impairment, disability and handicap as three different levels of pathology consequences of pathological processes, which are related to different levels of experience and individual awareness [49].

The conceptual framework of this study follows the ICF model – the International Classification of Functioning, Disability and Health (ICF). The ICF is the WHO's model for measuring health and disability at both individual and population levels. This widely used model was translated into several languages and it was used in studies from 191 countries and defines disablement as the result of the interaction among the domains of body, individual, and environment [51].

The ICF model is composed from 2 parts, each with 2 components (see Figure 1.2):

- part I: – Functioning and Disability

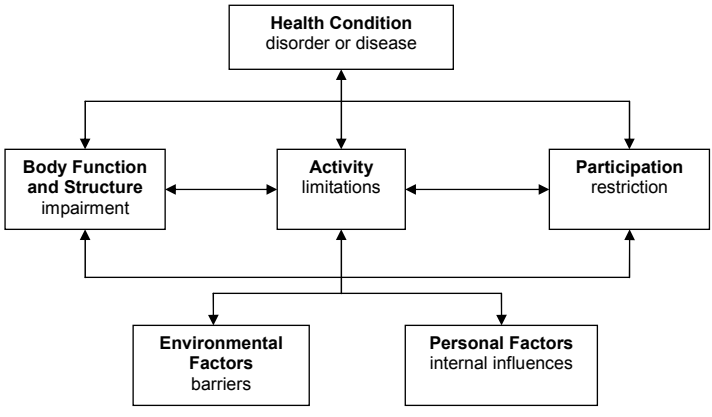
a) Body functions and Structures – physiological and anatomical changes

b) Activities and Participations – the capacity to executing tasks in a standard environment and the performance to executing tasks in the current environment

- part II: – Contextual factors
a) Environmental Factors – external influences on functioning and disability
b) Personal Factors – internal influences on functioning and disability

Figure 1.2 The WHO model of the International Classification of Functioning, Disability and Health [51]

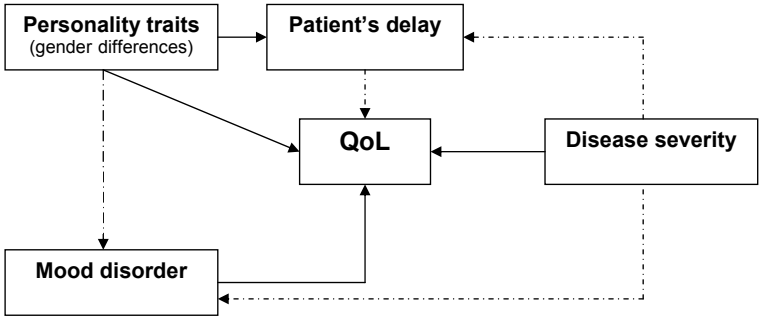
The ICF could be applied in a wide range of scientific and also practical areas, e.g. social security, management of health care, prevention and health promotion on a national, but also on an international level [51].



1.5 Aims of the study and research questions

The main aim of this cross-sectional study was to explore psychological factors (which are included in the *personal factors* of the ICF model) associated with quality of life – neuroticism, extroversion, negative affectivity, social inhibition, Type D personality and mood disorders (anxiety, depression). Associations explored in the study were derived from the theoretical background from theories dealing with the concept of QoL (Figure 1.3).

Figure 1.3 Design of the variables used in the thesis



The main objectives of the thesis therefore include:

1) to explore whether psychological factors were associated with the perception of quality of life in patients with Parkinson's disease;
2) to investigate whether psychological factors of patient's help-seeking behavior may be associated with quality of life of patients with Parkinson's disease.

The objectives led to the following general research questions (RQ):

1) to explore the associations between various personality traits, neuroticism, extroversion, negative affectivity, social inhibition and Type D personality and quality of life in Parkinson's disease patients. In addition, gender differences were examined as well *(Chapter 2 and Chapter 3)*;
2) to explore differences between delayers and non-delayers regarding psychological factors associated with quality of life in patients with Parkinson's disease and the impact of fear and anxiety on help-seeking behavior in non-parkinsonian diseases *(Chapter 4 and Chapter 5)*;
3) to compare the role of the association of psychological factors – Type D personality, anxiety and depression – with quality of life in patients with Parkinson's disease and multiple sclerosis (MS) *(Chapter 6)*.

1.6 Structure of the thesis and summary of contents

In *Chapter 1* a General Introduction on Parkinson's disease and the patient's quality of life was presented.

In *Chapter 2* the associations between extraversion, neuroticism and quality of life were presented. In this chapter personality traits for women and for men will be analyzed separately.

Chapter 3 is focused on Type D personality, negative affectivity and social inhibition as predictors of perceived quality of life. Gender differences in models for men and women will be presented as well.

Patient's delay is associated with decreasing of quality of life in many diagnoses. In *Chapter 4* a systematic review was performed for to explore, how fear, and its intensity, was associated with patient's delay in chronic and also acute disease.

Personality traits could influence decision making in help seeking, as well. In *Chapter 5* differences in personality traits between delayers and non-delayers in patients with PD were explored.

In *Chapter 6* we are comparing patients with Parkinson's disease with patients with multiple sclerosis regarding personality and depression and anxiety.

In *Chapter 7* we summarized the results of this study and discussed them. Furthermore we are trying to outline practical implication of the results of the research in neurological practice. Results of our research lead to the suggestions for further research of the quality of life in patients with Parkinson's disease.

References

[1] Freeman WD. The future of neurology. *Neurologic Clinics* 2010; **28:** 537-561.

[2] Roth J, Sekyrova M, Ruzicka E, Dvorak J, Kanovsky P, Rektorova I, Ristovska H. Parkinsonova nemoc. [Parkinson's disease]. Praha: Maxdorf, 1999.

[3] Parkinson J. An essay on the Shaking Palsy. *Journal of Neuropsychiatry and Clinical Neurosciences* 2002; **14:** 223-236.

[4] Karlsen KH, Tandberg E, Arsland D, Larsen JP. Health related quality of life in Parkinson's disease: a prospective longitudinal study. *Journal of Neurology, Neurosurgery and Psychiatry* 2000; **69:** 584 –589.

[5] Macleod M. Inequalities in the incidence and management of, and outcome from, neurological diseases in older people. *Reviews in Clinical Gerontology* 2004; **13:** 261-268.

[6] Rajput AH, Offord KP, Beard CM, Kurland LT. Epidemiology of parkinsonism: Incidence, classification, and mortality. *Annals of Neurology* 1984; 16: 278–282.

[7] van den Eeden SK, Tanner CM, Bernstein AL, *et al.* Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *American Journal of Epidemiology* 2003; **157:** 1015-1022.

[8] Shulman LM. Gender differences in Parkinson's disease. *Gender Medicine* 2007; **4:** 8-18.

[9] Muangpaisan W, Hori H, Brayne C. Systematic review of the prevalence and incidence of Parkinson's disease in Asia. *Journal of Epidemiology* 2009; **19:** 281-293.
[10] Okubadejo NU, Bower JH, Rocca WA, Maraganore DM. Parkinson's disease in Africa: A systematic review of epidemiologic and genetic studies. *Movement Disorders* 2006; **21:** 2150-2156.
[11] von Campenhausen S, Bornschein B, Wick R, *et al.* Prevalence and incidence of Parkinson's disease in Europe. *European Neuropsychopharmacology* 2005; **15:** 473-490.
[12] Baldereschi M, Di Carlo A, Rocca WA, *et al.* Parkinson's disease and parkinsonism in a longitudinal study: two-fold higher incidence in men. ILSA Working Group. Italian longitudinal study on aging, *Neurology* 2000; **55**: 1358–1363.
[13] Damiano AM, Snyder C, Strausser B, Willian MK. A review of health-related quality of life concepts and measures for Parkinson's disease. *Quality of Life Research* 1999; **8:** 235-43.
[14] Macphee GJA, Stewart DA. Parkinson's disease. *Reviews of Clinical Gerontology* 2006; **16:** 1-21.
[15] Simons G, Thompson SB, Smith-Pasqualini MC. An innovative education program for people with Parkinson's disease and their carers. *Parkinsonism and Related Disorders* 2006; **12:** 478-485.
[16] Cole SA, Woodard JL, Juncos JL, Kogos JL. Depression and disability in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neurosciences* 1996; **8:** 20-25.
[17] Papapetropoulos S, Mash DC. Psychotic symptoms in Parkinson's disease. From description to etiology. *Journal of Neurology* 2005; **252:** 753-764.
[18] Pezzoli G, Zini M. Levodopa in Parkinson's disease: from the past to the future. *Expert Opinion On Pharmacotherapy* 2010; **11:** 627-635.
[19] Dunnett SB, Björklund A, Lindvall O. Cell therapy in Parkinson's disease - stop or go? *Nature Reviews Neuroscience* 2001; **2:** 365-369.
[20] Grosset D, Taurah L, Burn DJ, *et al.* A multicentre longitudinal observational study of changes in self reported health status in people with Parkinson's disease left untreated at diagnosis. *Journal of Neurology, Neurosurgery and Psychiatry* 2009; **78:** 465-469.
[21] Brandt-Christensen, M, Kvist, K, Nilsson, FM, Andersen, PK, Kessing, LV. Treatment with antiparkinson and antidepressant drugs: a register-based, pharmaco-epidemiological study. *Movement Disorder* 2007; **22:** 2037-2042.
[22] Carr J, Kies B, Fine J, Movement Disorders Group of South Africa. Guideline for the treatment of Parkinson's disease. *South African Medical Journal* 2009; **99:** 755-756.
[23] Horstink M, Tolosa E, Bonuccelli U, *et al.* European Federation of Neurological Societies; Movement Disorder Society-European

Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. *European Journal of Neurology* 2006; **13:** 1170-1185. a

[24] Horstink M, Tolosa E, Bonuccelli U, *et al.*European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). Part II: late (complicated) Parkinson's disease. *European Journal of Neurology* 2006; **13:** 1186-1202. b

[25] Dubayova T, Nagyova I, Havlikova E, Rosenberger J, Gdovinova Z, Middel B, van Dijk, JP, Groothoff JW. Neuroticism and extraversion in association with quality of life in patients with Parkinson's disease. *Quality of Life Research* 2009; **18:** 33-42.

[26] Hömberg V. Motor training in the therapy of Parkinson's disease. *Neurology* 1993; **43**(Suppl 6)**:** S45-S46.

[27] Tamir R, Dickstein R, Huberman M. Integration of Motor Imagery and Physical Practice in Group Treatment Applied to Subjects With Parkinson's Disease. *Neurorehabilitation & Neural Repair* 2007; **21:** 68-75.

[28] Mylne AQ, Griffiths C, Rooney C, Doyle P. Trends in Parkinson's disease related mortality in England and Wales, 1993-2006. *European Journal of Neurology* 2009; **16:** 1010-1016.

[29] Winter Y, von Campenhausen S, Brozova H, *et al.* Costs of Parkinson's disease in Eastern Europe: A Czech cohort study. *Parkinsonism and Related Disorders* 2010; **16:** 51-56.

[30] Whetten-Goldstein K, Sloan F, Kulas E, Cutson T, Schenkman M. The burden of Parkinson's disease on society, family, and the individual. *Journal of American Geriatric Society* 1997; 45: 844–849.

[31] Hobson P, Holden A, Meara J. Measuring the impact of Parkinson's disease with the Parkinson's Disease Quality of Life questionnaire. *Age and Ageing* 1999; **28:** 341-346.

[32] Gómez-Esteban JC, Zarranz JJ, Lezcano E, Tijero B, Luna A, Velasco F, Rouco I, Garamendi I. Influence of motor symptoms upon the quality of life of patients with Parkinson's Disease. *European Neurology* 2007; **57:** 161-165.

[33] Karlsen KH, Tandberg E, Arsland D, Larsen JP. Health related quality of life in Parkinson's disease: a prospective longitudinal study. *Journal of Neurology, Neurosurgery and Psychiatry* 1999; **69:** 584-589.

[34] Behari M, Srivastava AK, Pandey RM. Quality of life in patients with Parkinson's disease. *Parkinsonism and Related Disorders* 2005; **11:** 221–226.

[35] Havlikova E, Rosenberger J, Nagyova I, Middel B, Dubayova T, Gdovinova Z, van Dijk, JP, Groothoff JW. Impact of fatigue on quality of life in patients with Parkinson's disease. *European Journal of Neurology* 2008; **15:** 475-480.
[36] Schrag A, Jahanshahi M, Quinn NP. What contributes to depression in Parkinson's disease? *Psychological Medicine* 2001; **31:** 65-73.
[37] Cubo E, Rojo A, Ramos S, Quintana S, Gonzalez M, Kompoliti K, Aguilar M. The importance of educational and psychological factors in Parkinson's disease quality of life. *European Journal of Neurology* 2002; **9:** 589–593.
[38] Slawek J, Derejko M, Lass P. Factors affecting the quality of life of patients with idiopathic Parkinson's disease – a cross-sectional study in outpatient clinic attendees. *Parkinsonism and Related Disorders* 2005; **11:** 465–468.
[39] Tandberg E, Larsen JP, Aarsland D, Cummings JL. The occurrence of depression in Parkinson's disease. A community-based study, *Archives of Neurology* 1996; **53:** 175–179.
[40] van der Bruggen H, Widdershoven G. Being a Parkinson's patient: immobile and unpredictably whimsical literature and existential analysis. *Medicine, Healthcare and Philosophy* 2004; **7:** 289-301.
[41] Lee KS, Merriman A, Owen A, Chew B, Tan TC. The medical, social, and functional profile of Parkinson's disease patients. *Singapore Medical Journal* 1994; **35:** 265-268.
[42] Peto V, Jenkinson C, Fitzpatrick R, *et al.* The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Quality of Life Research* 1995; **4:** 241–248.
[43] de Boer AG, Wijker W, Speelman JD, *et al.* Quality of life in patients with Parkinson's disease: development of a questionnaire. *Journal of Neurology, Neurosurgery and Psychiatry* 1996; **61:** 70–74.
[44] Marinus J, Ramaker C, van Hilten JJ, Stiggelbout AM. Health related quality of life in Parkinson's disease: A systematic review of disease specific instruments. *Journal of Neurology, Neurosurgery and Psychiatry* 2002; **72:** 241-248.
[45] Stepanski E, Zorick F, Roehrs T, Young D, Roth T. Daytime alertness in patients with chronic insomnia compared with asymptomatic control subjects. *Journal of Sleep Research and Sleep Medicine* 1988; **11:** 54–60.
[46] Walker SR, Rosser R. Quality of life: assessment and application. Lancaster: MTP Press, 1988.
[47] Nagi SZ. Some conceptual issues in disability and rehabilitation. In: Sussman MB (ed.) Sociology and rehabilitation. Washington, DC: American Sociological Association; 1965.
[48] Nagi SZ. An epidemiology of disability among adults in the United States. *Milbank Quarterly* 1976; **54:** 439–467.

[49] Masala C, Petretto DR. From disablement to enablement: conceptual models of disability in the 20th century. *Disability and Rehabilitation* 2008, **30:** 1233-1244.
[50] World Health Organization. International Classification of Impairments, Disabilities and Handicaps: A manual of classification relating to the consequences of diseases, published in accordance with resolution WHA 29.35 of the 29th World Health Assembly, May 1976. Geneva: World Health Organization, 1980.
[51] World Health Organisation (WHO). International classification of functioning, disability, and health (ICF). Geneva, World Health Organization; 2001.

Chapter 2

Neuroticism and extraversion in association with quality of life in atients with Parkinson's disease

Tatiana Dubayova, Iveta Nagyova, Eva Havlikova, Jaroslav Rosenberger, Zuzana Gdovinova,
Berrie Middel, Jitse P. van Dijk, and Johan W. Groothoff

(Quality of Life Research, 2009, 18:33-42)

Abstract

Purpose: Personality traits appear as determinants of quality of life (QoL) in most chronic diseases. The aim of this study is to explore whether neuroticism and extraversion contribute to the variance in QoL in patients with Parkinson's disease (PD) when controlled for age, functional status and disease duration.
Methods: The Parkinson's Disease Quality of Life Questionnaire (PDQ-39) was used to assess QoL and the Unified Parkinson's Disease Rating Scale (UPDRS) for disease severity. Neuroticism and extraversion were measured with the Eysenck Personality Questionnaire (EPQR-A). Multiple linear regression analysis was then used to assess the contribution of neuroticism and extraversion to QoL.
Results: The sample consisted of 153 PD patients (48.4% women; 67.9±9.3 years; mean disease duration 7.5±5.8 years). Neuroticism was, after disease severity, the second most important variable associated with QoL in PD patients, in particular for domains associated with psychological processes: *emotional well-being*, *social support*, *stigma* and *communication*. A higher score in extraversion was significantly associated with better *emotional well-being* in males, but surprisingly, with worse *emotional well-being* in females.
Conclusions: After functional status, personality traits were clearly associated with QoL in PD patients. Therefore, they should be taken into account by healthcare professionals in their appraisal of patient complaints.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease that affects 1% of all people over 60 years of age and around 2% of the population over 80 years of age. It includes both physical and mental symptoms which have an impact on the quality of life (QoL) of those with the disease [1,2]. The physical symptoms of PD typically affecting QoL are tremor, rigidity, slowness, a blank stare (the so-called "Parkinson's mask") and troubles with manual dexterity [3]. Mental symptoms may include depression, sleep disorders, hallucinations and delirium, some of which may be related to therapy using dopaminergic drugs [4,5]. The social components of PD involve isolation due to the embarrassment caused by the symptoms and problems with communication [6].

With regard to basic sociodemographic and clinical variables, increasing age and higher disease duration have been found to be associated with decreased QoL in PD patients [7]. In addition, mildly significant differences in disability and QoL have been noted between the

genders in general: women have reported greater disability and reduction of QoL than men [8]. Gender differences are also present in the incidence of PD: the disease occurs more frequently in men than in women in every decade of life [9]. One of the various theories explaining these differences is that they may result from the neuroprotective effects of estrogen [8,10,11].

Some personality traits, such as neuroticism and extraversion, are assumed to be factors that contribute to the perception of health status and thus lead to a worse perception of QoL by people with several chronic diseases [12-14]. People who score high on the neuroticism scale manifest more worries, uncertainties and anxiety [15]. Because these people are more likely to behave overly emotionally and react too strongly to all sorts of stimuli, their neuroticism seems to be associated with psychological dysfunction [15,16]. Some authors have reported that neuroticism also appears to be associated with the tendency to recall physical symptoms as being worse than they really were [17,18], thus indirectly contributing to a lower perceived QoL [19]. Quality of life of patients with chronic diseases may also be influenced indirectly by extraversion. Extravertly oriented people have a tendency to be sociable and to prefer changes, and there is a high probability that they will crave excitement and act impulsively [15]. It has been observed that people with a low score in extraversion are more self-centered and are more sensitive to stress than extraverted people [20]. Therefore, it might be hypothesized that extraversion influences the level of coping with chronic disease and can thus also influence the level of QoL [20,21].

The QoL of patients with PD is frequently studied, but very little is known about the associations between personality traits and QoL in these patients. The aim of this study, therefore, is to explore whether personality traits (neuroticism and extraversion) contribute to the variance in QoL in patients with PD when controlled for disease severity, disease duration and age. In addition, this study analyzes whether gender differences in the QoL of PD patients can be attributed to gender-related differences in extraversion and neuroticism in these patients.

Methods

Subjects and procedure

Data collection took place between February 2004 and February 2006. One hospital in Bratislava as well as 4 hospitals and 17 outpatient neurology clinics in the eastern part of the Slovak Republic cooperated in this study.

Questionnaires were sent to patients diagnosed with Parkinson's disease three weeks before the interview. All patients were diagnosed according to the United Kingdom Parkinson's Disease Society Brain Clinical Criteria [22]. Exclusion criteria were defined as follows: a)

patients older than 85 years, because of the high probability of other co-morbidities and movement disabilities of a non-parkinsonian character and b) an MMSE score lower than 23 points.

An interview with each patient took place three weeks after the invitation. After each interview, a neurologist assessed the severity of the patient's disease using the Unified Parkinson's Disease Rating Scale (UPDRS Version 3.0) [23]. The patients' mental status was assessed with the Mini-Mental State Examination (MMSE) [24]. The structured interview consisted of questions about the patient's medical history and subjective feelings that were not part of the questionnaire. Sociodemographic data were derived from medical records and from questionnaires filled in by the patients themselves.

The study was conducted after informed consent was obtained from the patients prior to the study. The local Ethics Committee of the University Hospital in Kosice approved the study in Kosice on 17 December 2002.

Measures

Disease severity

The Unified Parkinson's Disease Rating Scale (UPDRS) is currently used as a standard reference scale in clinical practice and in research for assessing disease severity in patients with PD. Ratings are observation-based, and scores are obtained by interview and physical examination. The scale consists of four parts: mentation and mood (part 1), activities of daily living (part 2), motor function (part 3) and complications resulting from dopaminergic therapy, including motor fluctuations and dyskinesias (part 4). Parts 1, 2 and 4 are interview-based, while part 3 is based on a clinical examination by a health professional and represents the patient's condition at the time of the examination. Patients can score from 0 to 176, with higher scores indicating increased disease severity [23].

Extraversion and neuroticism

The Eysenck Personality Questionnaire Revised Abbreviated (EPQR-A) was used for measuring Extraversion and Neuroticism [25]. The questionnaire was validated in the Czech Republic in a sample of 3565 people [26]. The Slovak and Czech languages are similar, and today's Czech and Slovak Republics were, prior to 1993, united in a single country. Thus, results from Czech Republic could be valid also for the needs of this research. The questionnaire consists of 24 items divided into 4 subscales: extraversion, neuroticism, psychoticism and the lie scale. Items are scored on a Yes (=1) No (=0) basis, and the overall score for each subscale ranges from between 0–6, with higher scores indicating higher levels for the personality traits.

Internal reliability found across the samples was .74-.84 for the extraversion subscale and .70-.77 for neuroticism [27]. In the present study Cronbach's alpha was .85 for extraversion and .72 for neuroticism.

Quality of life

The Parkinson's Disease Questionnaire - long form (PDQ-39) is a disease-specific instrument developed for measuring health-related quality of life in patients with Parkinson's disease. Its 39 items are divided into 8 scales: *mobility* (10 items), *activities of daily living* (6 items), *emotional well-being* (6 items), *stigma* (4 items), *social support* (3 items), *cognition* (4 items), *communication* (3 items) and *bodily discomfort* (3 items). In response to each question, respondents select from answers ranging from *never* (0), *occasionally* (1), *sometimes* (2), *often* (3) and a*lways* (4). Each scale and the summary index were transformed in order to have a range from 0 (=no problem at all) to 100 (=maximum level of a problem) [28]. We translated the questionnaire from its original source [28] into the Slovak language and then translated it back into English using another translator. Two Slovak native speakers with mastery of the English language first translated the questionnaires from English into Slovak. The questionnaires were then re-translated from Slovak back into English, this time by a native English speaker with mastery of the Slovak language. The discrepancies between the different versions of the questionnaires were then discussed. We checked the basic psychometric characteristics of the scale, but these have not yet been published. In the present study, the Cronbach's alphas were as follows: .93 (*mobility*), .91 (*activities of daily living*), .85 (*emotional well-being*), .88 (*stigma*), .75 (*social support*), .67 (*cognition*), .76 (*communication*) and .80 (*bodily discomfort*).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS 14.0.1.) software was used to analyze the data. Firstly, independent sample t-tests were conducted to assess differences between the genders in disease severity, age, disease duration, extraversion and neuroticism. As a second step, a difference of proportions test (CIA) was used to assess gender differences in partnership and education [29]. Thirdly, Pearson's correlation coefficients were used to determine the strengths of the relationships between the study variables. Finally, multiple linear regression analyses were used to assess the contribution of the independent variables age, gender, disease duration, functional status (UPDRS) and personality traits (E and N) and to explain the variance of the dependent variables - the dimensions of the PDQ-39. Identical multiple linear regression analysis was performed for males and females separately.

Results

Out of 512 patients with Parkinson's disease, 160 agreed to participate and filled in the questionnaires. Forty-one of the 512 refused to participate, and 311 did not respond to the invitation. Seven patients were excluded after the personal interview because of the exclusion criteria. The final sample consisted of 153 patients (response rate 31.3%). Non-respondents differed significantly from the analyzed group in age (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39), and there were significantly more women than men among the non-respondents (difference -0.0110; SE=.041; 95% CI -.091 – .069).

Descriptive statistics

Females made up 48.6% of the participants and males 51.4%, with a mean age of 67.9±9.3 years (range 44-83). The mean disease duration was 7.5 ± 5.8 years (range 0-34). One hundred and four patients from the sample (68%) lived with a partner, and 49 patients (32%) were widowed, divorced or single. Fifty-two patients (34%) had completed elementary education, 84 patients (55%) secondary education and 17 patients (11%) had a university education. Disease severity in the patients varied from 5 points to 97, with a mean score (38.8) on the UPDRS representing medium disease severity.

All patients used antiparkinsonian therapy according to international guidelines [30,31].

Gender differences in the study variables

Males and females did not differ in age, disease duration and disease severity. No differences between genders were found with regard to the psychological variables extraversion and neuroticism. There were no differences between genders in the scores of the overall QoL and in PDQ-39 dimensions, except for *bodily discomfort* (*P*=.05), where women scored significantly higher (Table 2.1).

Results of correlation analyses

Table 2.2 presents the correlations between the PDQ-39 and age, disease duration, disease severity, extraversion and neuroticism for males and females separately. Disease severity significantly correlated with all scales of the PDQ-39, except for satisfaction with *social support* in men. In women it played a less important role.

Examining the relationships between variables by means of Pearson's coefficients showed significant correlations between extraversion on one hand and *mobility* and *activities of daily living* on the other. Females with higher scores for extraversion reported better QoL in the dimension of *activities of daily living*, in contrast to males, for whom extraversion did not

appear to be important for any of the study variables.

The correlations show a strong relationship between nearly every sub-scale of PDQ-39 and neuroticism. For females, neuroticism is the main variable correlating with the QoL scales.

Overall QoL, represented by the PDQ-39 summary index, correlated with disease severity in both genders. In females it also correlated with neuroticism, and in males with disease duration.

Table 2.1 Characteristics of the sample – percentages, means and standard deviations (SD) of study variables.

	Males	Females	Total sample	t-tests/CIA
Number of subjects (%)	79 (51.6)	74 (48.4)	153 (100)	
Mean age in years (SD)	68.5 (9.2)	67.3 (9.3)	67.9 (9.3)	ns
Mean disease duration in years (SD)	7.7 (5.7)	7.4 (5.8)	7.5 (5.8)	ns
Disease severity – UPDRS (SD)	38.8 (22.2)	34.9 (18.7)	36.9 (20.6)	ns
Married or living with a partner (%)	66 (83.5)	38 (51.4)	104 (68)	
Education elementary (%)	22 (27.8)	30 (40.5)	52 (34)	
secondary (%)	44 (55.7)	40 (54.1)	84 (55)	
university (%)	13 (16.5)	4 (5.4)	17 (11)	
Quality of Life – PDQ-39 total (SD)	56.9 (17.4)	61.2 (16.4)	58.9 (17.0)	ns
Mobility (SD)	60.2 (25.0)	66.4 (23.4)	63.2 (24.4)	ns
Activities of daily living (SD)	58.2 (26.0)	57.5 (27.3)	57.9 (26.6)	ns
Emotional well-being (SD)	59.9 (20.6)	65.5 (19.8)	62.6 (20.4)	ns
Stigma (SD)	53.7 (25.0)	54.5 (27.3)	54.1 (26.0)	ns
Social support (SD)	38.8 (18.0)	42.2 (20.7)	40.4 (19.4)	ns
Cognition (SD)	57.2 (20.1)	60.6 (18.6)	58.9 (19.4)	ns
Communication (SD)	49.9 (21.4)	48.9 (20.3)	49.4 (22.6)	ns
Bodily discomfort (SD)	69.7 (23.5)	80.9 (20.2)	75.2 (22.6)	$t \leq .05$
Extraversion (SD)	2.7 (2.2)	2.7 (2.3)	2.7 (2.2)	ns
Neuroticism (SD)	2.1 (1.8)	2.7 (1.9)	2.4 (1.9)	ns

Abbreviations: SD – standard deviation, ns – non-significant

Model of predictors of QoL

Multiple linear regression analyses were performed in order to identify how much the variance of the dependent variables (*mobility*, *activities of daily living*, *emotional well-being*, *stigma*, *social support*, *cognition*, *communication* and *bodily discomfort*) could be explained by the personality traits if controlled for the relevant sociodemographic and clinical variables (Table 2.3). Table 2.3 (and also Table 2.4) shows the beta values, which reveal the relationships between the dimension and each value in the model.

Table 2.2 Intercorrelations between the study variables for males and females

PDQ-39 subscales	age		disease duration		disease severity		extraversion		neuroticism	
	M	F	M	F	M	F	M	F	M	F
mobility	.03	**.33****	**.42****	.06	**.70****	**.72****	-.18	-.17	.10	.21
CI	(-.70;-.39)	(-.24;.22)	(-.02;.40)	(-.67;-.33)	(.67;.85)	(.71;.88)	(-.50;-.10)	(-.52;-.12)	(-.62;-.26)	(-.46;-.03)
activity of daily living	.05	**.25***	**.44****	.10	**.83****	**.75****	-.17	**-.25***	.07	**.28***
CI	(-.67;-.35)	(-.39;.05)	(.03;.44)	(-.62;-.25)	(.90;.96)	(.77;.90)	(-.52;-.12)	(-.39;.05)	(-.65;-.32)	(-.34;.11)
emotional well-being	-.11	.18	**.33****	.13	**.41****	**.43***	-.21	.07	**.37****	**.52****
CI	(-.60;-.42)	(-.50;-.10)	(-.23;.21)	(-.58;-.20)	(-.05;.38)	(-.01;.43)	(-.46;-.04)	(-.66;-.31)	(-.14;.30)	(.22;.60)
stigma	-.06	-.22	**.24***	.13	**.29***	.20	-.21	-.06	.14	**.30****
CI	(-.66;-.33)	(-.45;-.01)	(-.40;.02)	(-.58;-.20)	(-.31;.13)	(-.48;-.06)	(-.46;-.04)	(-.67;-.33)	(-.56;-.18)	(-.30;.16)
social support	.00	**-.29***	**.23***	.14	.16	.02	-.12	.05	.22	**.33****
CI	(-.73;-.44)	(-.32;.14)	(-.42;5.9)	(-.57;-.18)	(-.53;.14)	(-.71;-.40)	(-.59;-.22)	(-.68;-.35)	(-.44;-.02)	(-.24;.22)
cognition	**.29***	**.31****	**.44****	-.02	**.38****	**.50****	-.18	-.11	.00	.14
CI	(-.31;.13)	(-.28;.18)	(.03;.44)	(-.71;-.40)	(-.12;.32)	(.17;.56)	(-.50;-.10)	(-.61;-.24)	(-.73;-.44)	(-.57;-.18)
communication	.09	.19	**.40****	.17	**.56****	.27	-.21	-.22	.06	.18
CI	(-.62;-.28)	(-.49;-.08)	(-.07;.36)	(-.52;-.12)	(.33;.66)	(-.36;.09)	(-.46;-.04)	(-.45;-.01)	(-.66;-.33)	(-.50;-.10)
bodily discomfort	-.08	.11	**.23***	.04	**.47****	.13	-.04	.07	.19	**.30****
CI	(-.64;-.30)	(-.61;-.24)	(-.42;5.9)	(-.69;-.36)	(.10;.50)	(-.58;-.20)	(-.68;-.37)	(-.66;-.31)	(-.49;-.08)	(-.30;.16)
PDQ-39 summary index CI	.01 (-.72;-.42)	.15 (-.55;-.16)	**.48**** (.13;.52)	.15 (-.55;-.16)	**.67**** (.61;.82)	**.63**** (.50;.77)	-.20 (-.47;-.06)	-.14 (-.57;-.18)	.20 (-.47;-.06)	**.43**** (-.01;.43)

* P≤.05, ** P≤.01; Abbreviations: M – males, F – females, CI – confidential interval

Table 2.3 Hierarchical multiple linear regression analyses. Age, disease duration, UPDRS, extraversion and neuroticism related to PDQ-39 subscales and PDQ-39 summary index

	PDQ-39 subscales																PDQ-39 summary index	
	mobility		activities of daily living		emotional well-being		stigma		social support		cognition		communication		bodily discomfort			
Variables	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β
age	.01	.02	.00	-.06	.00	.06	.02	-.13	.03	-.11	.07	**.24***	.04	**.18***	.01	-.06	.00	-.01
disease duration	.07	-.01	.09	-.02	.07	.13	.02	.06	.02	.14	.05	.09	.09	**.18***	.02	.04	.11	.11
UPDRS	.40	**.66*****	.54	**.78*****	.10	**.29*****	.04	.16	.00	-.02	.07	**.26****	.08	**.24****	.06	**.24***	.29	.53***
E	.00	-.07	.01	-.09	.00	-.01	.03	-.17	.00	-.06	.01	-.11	.05	**-.23****	.00	.05	.01	-.13
N	.01	.11	.01	.11	.24	**.50*****	.05	**.23***	.07	**.27****	.01	.12	.02	**.16***	.05	**.24****	.11	**.34*****
Model	Adj. R^2 = .46 F-value=21.5***		Adj. R^2 = .64 F-value=43.4***		Adj. R^2 = .38 F-value=15.6***		Adj. R^2 = .12 F-value=4.2***		Adj. R^2 = .09 F-value=3.3**		Adj. R^2 = .17 F-value=6.0***		Adj. R^2 = .24 F-value=8.7***		Adj. R^2 = .10 F-value=3.7**		Adj. R^2 = .50 F-value=24.4***	

* p≤.05, ** p≤.01, *** p≤.001; Abbreviations: UPDRS – disease severity, E – extraversion, N – neuroticism

Table 2.4 Hierarchical multiple linear regression analyses separately for males and females. Age, disease duration, UPDRS, extraversion and neuroticism related to PDQ-39 subscales and PDQ-39 summary index

	PDQ-39 subscales																PDQ-39 summary index	
	mobility		activities of daily living		emotional well-being		stigma		social support		cognition		communication		bodily discomfort			
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
age	.03	.07	-.04	-.09	.07	.08	.08	**-.31***	.16	**-.28***	**.33****	.16	**.27***	.18	-.04	.09	.12	-.09
disease duration	-.04	-.03	-.06	.02	.08	.14	-.01	.11	.08	.14	**.43****	-.13	.13	.15	-.09	.05	.08	.11
UPDRS	.69***	.69***	.86***	**.73*****	**.28***	**.39*****	.22	.22	.06	.04	.02	**.44*****	**.43*****	.08	**.47****	.04	**.58****	**.57*****
E	-.16	-.01	-.03	-.15	**-.27***	**.25****	-.23	-.14	-.23	.03	-.15	-.04	**-.24***	**-.25***	-.02	.07	**-.22***	-.07
N	.09	.09	.08	.13	**.42*****	**.59*****	.21	**.25***	**.26***	**.29***	.09	.07	.12	.18	.15	**.33***	**.26***	**.39*****
Model	$Adj.R^2_M$ = .46		$Adj.R^2_M$ = .68		$Adj.R^2_M$ = .33		$Adj.R^2_M$ = .07		$Adj.R^2_M$ = .07		$Adj.R^2_M$ = .28		$Adj.R^2_M$ = .38		$Adj.R^2_M$ = .15		$Adj.R^2_M$ = .53	
	$Adj.R^2_F$ = .49		$Adj.R^2_F$ = .58		$Adj.R^2_F$ = .54		$Adj.R^2_F$ = .16		$Adj.R^2_F$ = .12		$Adj.R^2_F$ = .21		$Adj.R^2_F$ = .11		$Adj.R^2_F$ = .04		$Adj.R^2_F$ = .52	
	$F\text{-value}_M$=11.1***		$F\text{-value}_M$=26.1***		$F\text{-value}_M$=6.8***		$F\text{-value}_M$=1.9		$F\text{-value}_M$=1.8		$F\text{-value}_M$=5.6***		$F\text{-value}_M$=8.5***		$F\text{-value}_M$=3.0*		$F\text{-value}_M$=14.0***	
	$F\text{-value}_F$=12.4***		$F\text{-value}_F$=17.4***		$F\text{-value}_F$=14.6***		$F\text{-value}_F$=3.3*		$F\text{-value}_F$=2.6*		$F\text{-value}_F$=4.2**		$F\text{-value}_F$=2.4*		$F\text{-value}_F$=1.4		$F\text{-value}_F$=13.2***	

Displayed values are Betas. * p≤.05, ** p≤.01, *** p≤.001;

Abbreviations: M – males, F – females, ADL – activities of daily living, UPDRS – disease severity, E – extraversion, N – neuroticism

The standardized Beta values were all measured in standard deviation units and so are directly comparable; e.g. a Beta of 0.78 means that increases of 1 point on the UPDRS total score is associated with an increase of .78 point on the ADL scale.

The analyses were controlled for both disease variables (disease severity and disease duration) and for age. Higher age predicted worse scores in the subscales *cognition* and *communication*. Disease duration explained some of the variance, but only in *communication*. As expected, disease severity was the strongest predictor in almost all dimensions of PDQ-39, particularly in *activities of daily living*, *mobility*, *emotional well-being*, *cognition*, *communication*, and *bodily discomfort,* but it did not appear to be associated with the dimensions of *social support* and *stigmatization*.

The model for overall QoL was fully covered only by disease severity and neuroticism. Extraversion appeared to be a significant factor only for the dimension *communication*. Neuroticism was important mostly in the domains which are associated with some kind of psychological processes: *emotional well-being*, *stigma, social support* and *communication*. However, neuroticism also explained some of the variance in *activities of daily living* and *bodily discomfort*.

Gender differences in predictors of QoL

Table 2.4 presents the results of multiple linear regression analyses for men and women separately. Significant gender differences were found in the predictors of the PDQ-39 sub-scales and for its summary index.

Out of all sociodemographic variables only age appeared to contribute significantly to the total explained variance. Lower age was significantly associated with *stigmatization by illness* and *social support* in women. Higher age was closely connected with lower scores in the domains *cognition* and *communication* in men. Disease duration had an impact on QoL only in the *cognition* subscale in men. Functional status was the only factor of the domains *mobility*, *activities of daily living* and *emotional well-being* in both genders. In males it also had an impact on *communication* and *bodily discomfort*, whereas in females it was connected with worse *cognition*.

Overall QoL was associated in both genders with disease severity and neuroticism. In men, 3.3% of the variance was also explained by extraversion. Extraversion explained 4.7% variance in *communication* in men and 6.4% in women. For both genders extraversion was an important part of the model of *emotional well-being*, though the observed relations were in the opposite direction. In women a high score for extraversion was associated with lower QoL in *emotional well-being*, whereas in men a higher score in extraversion was associated with a better score in this dimension. Neuroticism played an important role in *emotional well-being* and *social support* in both genders. In women neuroticism was also associated with *stigmatization by illness* and *bodily discomfort*.

Discussion

The aim of this study was to explore the contribution of personality traits (neuroticism and extraversion) to QoL in patients with PD and the contribution of possible gender differences in extraversion and neuroticism to QoL.

Disability, as expected, was the fundamental variable for QoL. In the intercorrelations between the variables, associations were found between disease duration and all PDQ-39 scales in men, but none in women. However, disease duration did not significantly contribute to the models for each scale, except *cognition* in men. In addition to disease severity, the second most important factor for QoL in PD patients was neuroticism. Patients with higher scores on the neuroticism scale reported significantly worse status in the domains of *emotional well-being*, *stigma*, *social support* and *bodily discomfort*. However, in separate models for males and females, neuroticism remained important only in the subscale of *emotional well-being* in both genders. Neuroticism played a role in the subscales of *stigma* and *social support* in women, but it did not appear to be important in men due to the low validity of the *social support* model for men.

Our results for neuroticism correspond with studies focusing on other patient groups, including patients with cognitive impairments, chronic pain and depression. A high level of neuroticism predicts the use of ineffective passive coping strategies, and those patients reported worse perception of their health problems [32-34]. It seems that due to societal influences, males and females develop different ways of coping and experiencing the world [34]. This phenomenon was also found by researchers who observed that a different score in neuroticism reflects socially learned behaviour rather than biological differences. Gender-role rather than gender had greater explanatory power with regard to neuroticism [35].

Extraversion was associated only with the subscale of *communication*: patients scoring higher on the extraversion scale seem to have fewer problems with communication skills. This corresponds with the study by Eysenck (1991) [15], where to be talkative is one of the characteristics of an extravertly-oriented person. However, there were differences between males and females in the model of *emotional well-being*. For both genders, extraversion is an important variable, but in the opposite direction. Extraverted males perceived their *emotional well-being as* better, but a higher score in extraversion was associated with worse *emotional well-being* in females. An explanation might be the associations between extraversion and coping strategies which have been found in several studies [20,21]. These differences could be explained by the supposed use of different coping strategies by males and females [36]. Our results support the

findings of one Spanish study, which confirmed a close association between extraversion and active coping strategies, which are used mostly by males [20].

Analysis presented in this paper explains only part of the variance in the QoL of patients with PD. The construct of QoL of those patients appears to be too complicated to be explained by psychological variables such as personality traits. Models of *stigma*, *social support*, *cognition* and *bodily discomfort* were significant in general, but the adjusted R2 explains only a relatively small part of the variance. However, the relationships between study variables and these dimensions are significant. Differences in the significance between models for men and women suggest possible differences in the model variables. It can be hypothesized that models of QoL for men and women, especially in the dimensions *stigma*, *social support*, *cognition* and *bodily discomfort*, are composed from different variables. The gender aspect of QoL appears to be an important focus for further studies.

A limitation of this study was the relatively low response rate, which may have an impact on generalizations of the results to the total population of PD patients. Non-respondents were older than respondents, so one might hypothesize that they refused to participate in the study because of serious motor complications in the advanced stages of PD and because of an increased need for help from their social surroundings. Regrettably, we have no information about the disease duration and the disease severity of the non-respondents.

Future research should concentrate on explaining how PD patients cope with health problems. The impact of personality traits on QoL is known from different studies on several chronic diseases. For example, close associations between extraversion, neuroticism and mental condition of the patients were confirmed in hemodialysis patients [21]. However, in the field of PD this is a relatively new idea.

Currently, the management of patients with PD is primarily aimed at prolonging life expectancy and diminishing motor disabilities [37]. The results of this study show that psychological traits are clearly associated with QoL as well and therefore should be taken into account by healthcare professionals in their appraisal of patient complaints. PD patients with high scores in neuroticism, especially females, may be considered as a population at risk for lower QoL.

Effective management of PD patients should include a specific approach to improve QoL in the course of treatment. Our results are important for neurologists; they could use them in the phase of diagnosis where patients with higher scores in neuroticism could aggravate their symptoms, and also in the phase of the treatment where patients could differ in their perception of the efficacy of the treatment.

Acknowledgements

This work was supported by the Slovak Research and Development Agency under contract No. APVV-20-038305.

References

[1] Macphee GJA, Stewart DA. Parkinson's disease. *Reviews in Clinical Gerontology* 2006; **16:** 1-21.
[2] Damiano AM, Snyder C, Strausser B, Willian MK. A review of health-related quality of life concepts and measures for Parkinson's disease. *Quality of Life Research* 1999; **8:** 235-243.
[3] Simons G, Thompson SB, Smith-Pasqualini MC. An innovative education program for people with Parkinson's disease and their carers. *Parkinsonism and related Disorders* 2006; **12:** 478-485.
[4] Cole SA, Woodard JL, Juncos JL, Kogos JL. Depression and disability in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neurosciences* 1996; **8:** 20-25.
[5] Papapetropoulos S, Mash DC. Psychotic symptoms in Parkinson's disease. From description to etiology. *Journal of Neurology* 2005; **252:** 753-764.
[6] van der Bruggen H, Widdershoven G. Being a Parkinson's patient: immobile and unpredictably whimsical literature and existential analysis. *Medicine, Health Care, and Philosophy* 2004; **7:** 289-301.
[7] Wielinski CL, Erickson-Davis C, Wichmann R, Walde-Douglas M, Parashos SA. Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. *Movement Disorders* 2005; **20:** 410-415.
[8] Shulman LM. Gender differencies in Parkinson's disease. *Gender Medicine* 2007; **4:** 8-18.
[9] Rajput AH, Offord KP, Beard CM, Kurland LT. Epidemiology of parkinsonism: Incidence, classification, and mortality. *Annals of Neurology* 1984; **16:** 278-282.
[10] van den Eeden SK, Tanner CM, Bernstein AL, *et al.* Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *American Journal of Epidemiology* 2003; **157:** 1015-1022.
[11] Haaxma CA, Bloem BR, Borm GF, *et al.* Gender differences in Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry* 2007; **78:** 819-824.
[12] Kempen GIJM, Jelicic M, Ormel J. Personality, chronic medical morbidity, and health-related quality of life among older persons. *Health Psychology* 1997; **16:** 539-546.

[13] Jelicic M, Kempen GI, Passchier J. Psychological well-being in older adults suffering from chronic headache. *Headache* 1998; **38:** 292-294.
[14] Ranchor AV, Sanderman R, Steptoe A. Pre-morbid predictors of psychological adjustment to cancer. *Quality of Life Research* 2002; **11:** 101-113.
[15] Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Inventory. London: London University of London Press, 1994.
[16] Ruggeri M, Pacati P, Goldberg G. Neurotics are dissatisfied with life, but not with services. The South Verona Outcome Project 7. *General Hospital Psychiatry* 2003; **25:** 338-344.
[17] Costa PT, McCrae RR. Neuroticism, somatic complaints and disease: Is the bark worse than the bite? *Journal of Personality* 1987; **55:** 299-316.
[18] Watson D, Pennebaker JW. Health complaints, stress and distress: Exploring the central role of negative affectivity. *Psychological review* 1989; **96:** 234-254.
[19] Larsen RJ. Neuroticism and selective encoding and recall of symptoms: Evidence from a combined concurrent-retrospective study. *Journal of Personality and Social Psychology* 1992; **62:** 480-488.
[20] Ramírez-Maestre C, Martinez AEL, Zarazaga RE. Personality characteristics as differential variables of the pain experience. *Journal of Behavioral Medicine* 2004; **27:** 147-165.
[21] Kidachi R, Kikuchi A, Nishizawa Y, Hiruma T, Kaneko S. Personality types and coping style in hemodialysis patients. *Psychiatry and Clinical Neurosciences* 2007; **61:** 339-347.
[22] Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery and Psychiatry* 1992; **55:** 181-184.
[23] van Hilten JJ, van der Zwan AD, Zwinderman AH, Ross RA. Rating imparment and disability in Parkinson's disease: evaluation of the Unified Parkinson's disease Rating Scale. *Movement Disorders* 1994; **9:** 84-88.
[24] Folstein MF, Folstein SE, McHough PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. *Journal Psychiatric Research* 1975; **12:** 189-198.
[25] Francis LJ, Brown LB, Philipchalk R. The development of an abbreviated form of the Revised Eysenck Personality Questionnaire (EPQR-A): its use among students in England, Canada, The USA and Australia. *Personality and Individual Differences* 1992; **13:** 443-449.
[26] Kozeny J. Faktorová struktura 24 položkové formy dotazníku EPQR-A [Factor structure of the 24 items questionnaire EPQ-A]. *Československá psychologie* 2001; **45:** 289-301.

[27] Forrest S, Lewis CA, Shevlin M. Examining the factor structure and differential functioning of the Eysenck personality questionnaire revised-abbreviated. *Personality and Individual Differences* 2000; **29:** 579-588.
[28] Peto V, Jenkinson C, Fitzpatrick R. PDQ-39: a review of the development, validation and application of a Parkinson's disease quality of life questionnaire and its associated measures. *Journal of Neurology* 1998; **245**(Suppl 1)**:** S10-14.
[29] Newcombe RG, Altman DG. Proportions and their differences. In: Altman DG, Machin D, Bryant TN, eds. Statistic with confidence. London: BMJ Books, 2000.
[30] Horstink M, Tolosa E, Bonuccelli U, *et al.* European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. *European Journal of Neurology* 2006; 13:1170-1185. a
[31] Horstink M, Tolosa E, Bonuccelli U, *et al.*. European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). Part II: late (complicated) Parkinson's disease. *European Journal of Neurology* 2006; 13:1186-1202. b
[32] van den Heuvel N, Smits CHM, Deeg DJH. Personality: A moderator of the relation between cognitive functioning and depression in adults aged 55-85? *Journal of Affective Disorders* 1996; **41:** 229-240.
[33] Merlijn VPBM, Hunfeld JAM, van der Wouden JC, Hazebroek-Kampschreur AA, Koes BW, Passchier J. Psychosocial factors associated with chronic pain in adolescents. *Pain* 2003; **101:** 33-34.
[34] Goodwin RD, Gotlib IH. Gender differences in depression: the role of personality factors. *Psychiatry Research* 2004; **126:** 135-142.
[35] Shevlin M, Bailey F, Adamson G. Examining the factor structure and sources of differential functioning of the Eysenck Personality Questionnaire Revised – Abbreviated. *Personality and Individual Differences* 2002; **32:** 479-487.
[36] Carver C, Scheier M, Weintraub J. Assessing coping strategies: a theoretically based approach. *Journal of Personality and Social Psychology* 1989; **56:** 267-283.
[37] Behari M, Srivastava AK, Pandey RM. Quality of life in patients with Parkinson's disease. *Parkinsonism and Related Disorders* 2005; **11:** 221-226.

Chapter 3

The association of type D personality with quality of life in patients with Parkinson's disease

Tatiana Dubayova, Iveta Nagyova, Eva Havlikova,
Jaroslav Rosenberger, Zuzana Gdovinova,
Berrie Middel, Jitse P. van Dijk, and Johan W. Groothoff

(Aging and Mental Health, 2009, 13:905-912)

Abstract

Objectives: Personality traits appear as determinants of quality of life (QoL) in most chronic diseases. Type D personality is characterized by ineffective coping strategies that reduce QoL in patients with coronary heart disease. The aim of this study was to evaluate whether Type D personality also predicts QoL in patients with Parkinson's disease (PD). In addition, gender differences in Type D personalities are explored.
Methods: The sample consisted of 153 PD patients (51.4% males; mean age 67.9±9.3 years). DS-14 was used to measure Type D personality, negative affectivity (NA) and social inhibition (SI). The Parkinson's Disease Quality of Life Questionnaire (PDQ-39) was used to assess QoL, and the Unified Parkinson's Disease Rating Scale (UPDRS) was used to assess functional status. The regression model consisted of disease severity, disease duration, age and DS-14 and its two scales (NA and SI).
Results: Type D is negatively associated with overall QoL in PD patients and most subscales of the PDQ-39. Type D explained *emotional well-being* in both genders but was significant in the models for *stigma*, *cognition* and *communication* only in men. NA and SI played a less important role in women in comparison with men.
Conclusion: Type D personality is an important part of the QoL model in PD patients of both genders, especially in the NA scale. The gender differences suggest that male and female PD patients require different coping strategies.

Introduction

Parkinson's disease (PD) obviously has a serious impact on a patient's quality of life (QoL), predominantly in the physical and social domains [1,2]. Symptoms of PD that are likely to affect physical functioning are tremor, rigidity, slowness, gait disorders, freezing, falling, troubles with manual ability, constipation, dysphagia, fatigue, painful spasms and dyskinesias [3]. Problems affecting the mental functioning of PD patients include depression, sleep disorders, cognitive problems and sometimes hallucinations and delirium, which are related to therapy with dopaminergic drugs [4,5]. PD also interferes with social functioning, since PD patients have a higher risk of communication problems, are likely to become unemployed and often avoid social contact, as they may feel embarrassment due to their symptoms becoming manifest [6]. The diversity of symptoms associated with PD and its management leads to worse physical, mental and social well-being in comparison with people of the same age without symptoms of Parkinsonism [7].

With regard to basic sociodemographic and clinical variables, increasing age and longer disease duration were found to be associated with decreased QoL in PD patients [8]. In addition, mildly significant differences in disability and QoL were noted between the genders in general: women reported greater disability and reduction of QoL than did men [9].

Disease severity, especially in the context of motor function impairment of PD patients, significantly reduces QoL and increases difficulties in activities of daily living [10,11]. However, some personality traits were assumed to contribute to the perception of health status and thus led to a worse perception of QoL in people with several chronic diseases as well [12,13]. The psychological variables frequently used in clinical studies are extroversion, neuroticism, anxiety and depression. It has been shown that these variables are assumed to be important contributing factors to QoL and perceived health status in healthy people as well as in people with a disease [14,15]. Differences between genders were also found in these variables, for example, in neuroticism: women consistently scored significantly higher in neuroticism than men [16,17].

The construct of the Type D personality is related to poor cardiac prognosis in patients with coronary heart disease. The interaction between NA (which is closely related to neuroticism) and SI is associated with an increased risk of depressive symptoms, a higher number of reinfarctions and higher mortality rates [18]. About 10-20% of subjects from the normal population can be classified as Type D, and this number increases to 30% in patients with coronary disease and to more than 50% in patients with hypertension [19,20]. Type D has also been characterized by ineffective coping strategies that reduce the QoL of patients with this type of personality [21].

Type D personality may be associated with health-related quality of life not only in cardiovascular diseases, but also in patients with other diseases [19]. The aim of this study was to evaluate whether the Type D personality, after controlling for disease severity, disease duration and age, explains QoL in patients with PD. In addition, gender differences in Type D are explored. The final aim of this study was to evaluate whether there are gender differences in the association of NA and SI personality traits and QoL in patients with PD.

Methods

Subjects and procedure

Data collection took place between February 2004 and February 2006. One hospital in Bratislava and 4 hospitals and 17 outpatient neurologists/clinics in the eastern part of the Slovak Republic gave us access to their

databases of patients with Parkinson's disease. Neurologists from these institutions, using the United Kingdom Parkinson's Disease Society Brain Clinical Criteria [22], had previously diagnosed all patients included in the sample as suffering from Parkinson's Disease.

Questionnaires were sent to these PD patients three weeks before an interview with the researchers. Exclusion criteria were defined as follows: a) patients older than 85 years (prior to sending invitations to patients for a personal examination) because of the high probability of other co-morbidities and movement disabilities of a non-parkinsonian character, and b) patients with an MMSE score below 23 points.

Each patient was interviewed three weeks after receipt of the invitation. After the interview with a psychologist (T.D.), one neurologist from the research team (E.H.) confirmed the initial diagnosis of PD and assessed each patient's disease severity using the Unified Parkinson's Disease Rating Scale (UPDRS Version 3.0) [23]. The patient's cognitive status was assessed using the Mini-Mental State Examination (MMSE) [24]. The structured interview consisted of questions on the patient's medical history and subjective feelings that were not part of the questionnaire. Sociodemographic data were derived from questionnaires filled in by patients themselves and data about antiparkinsonian therapy from medical records.

Participation in the research was voluntary. The study was conducted only after informed consent was obtained from the patients prior to the interview. The local Ethics Committee of the University Hospital in Kosice approved the study in Kosice on 17 December 2002.

Measures

Disease severity

The Unified Parkinson's Disease Rating Scale (UPDRS) is a tool for assessing disease severity in patients with Parkinson's disease and consists of four parts: mentation and mood (Part 1), activities for daily living (Part 2), motor function (Part 3) and complications from dopaminergic therapy (Part 4), including motor fluctuations and dyskinesias. Parts 1, 2, and 4 are interview-based, while Part 3 is based on a clinical examination by a health care professional and represents the patient's condition at the time of examination. A neurologist scores patients on a scale from 0 to 176, where a higher score is indicative of increased disease severity [23].

Type D personality

The DS-14 was used to assess Type D personality and its two constituent subscales, negative affectivity (NA) and social inhibition (SI). NA means

the tendency to experience negative emotions, like anger, dysphoria, irritability, hostile feelings, depressed affect and anxiety. The SI scale covers discomfort in social interactions, reticence and lack of social poise [25]. The construct of Type D personality is stable when compared to the gender effect [20, 25, 26, 27]. Subjects rated these aspects of their personality on a 5-point Likert scale ranging from 0=false, 1=rather false, 2=neutral, 3=rather true to 4=true. The NA and SI scales were then scored as continuous variables (range 0-28). A cutoff of 10 on both scales was used to classify subjects as Type D (NA ≥ 10 and SI ≥ 10) [25]. Cronbach's alpha in the original study was 0.88 for NA and 0.86 for SI. In the current study, DS-14 showed a good internal consistency (with Cronbach's alphas of .77 for NA and .76 for SI).

Quality of life

The Parkinson's Disease Questionnaire-long form (PDQ-39) is a disease-specific instrument developed for measuring health-related quality of life in patients with Parkinson's disease. Its 39 items are divided into 8 scales: *mobility* (10 items), *activities of daily living* (6 items), *emotional well-being* (6 items), *stigma* (4 items), *social support* (3 items), *cognition* (4 items), *communication* (3 items) and *bodily discomfort* (3 items). Respondents selected answers to each question ranging from never (0), occasionally (1), sometimes (2), often (3) and always (4). Each scale and the summary index were then adjusted to have a range from 0 (no problem at all) to 100 (maximum level of problem) [28]. The summary index represents the overall QoL.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS 14.0.1.) was used to analyze the data. Firstly, independent sample t-tests were conducted to assess differences between genders in disease severity, disease duration, age, Type D, NA and SI. In addition, the difference of proportions test (CIA) was used to assess gender differences in partnership and education [29]. Next, multiple linear regression analyses were used to assess the contribution of the independent variables (disease severity (UPDRS), disease duration, age, and the Type D personality trait) on the explained variance of the dependent variables (dimensions of the PDQ-39 and overall QoL). Thirdly, an identical regression analysis was performed for males and females separately. Finally, regression analyses for males and females were performed separately with the NA and SI scales instead of Type D.

Results

Descriptive statistics

Out of 512 patients with Parkinson's disease, 160 agreed to participate and filled in the questionnaires. Non-respondents included 41 patients who refused to participate and 311 who did not respond to the invitation. Seven patients were excluded after the personal interview because of the exclusion criteria. The final sample thus consisted of 153 patients (29.8%). Non-respondents differed significantly from the analyzed group in age (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39) and there were significantly more women than men among the non-respondents (difference -0.0110; SE=.041; 95% CI -.091 – .069) (Table 3.1).

All patients used antiparkinsonian therapy according international guidelines [30,31]. Twelve percent of patients used only L-dopa, 24% used only dopamine agonists, 25.3% used L-dopa in combination with COMT inhibitors, 20% used L-dopa with dopamine agonists and 16% used a combination of L-dopa, a COMT inhibitor and dopamine agonists.

Both questionnaires, PDQ-39 and DS-14, showed good internal consistency. Cronbach's alphas in the present study for PDQ-39 were as follows: .93 (*mobility*), .91 (*activities of daily living*), .82 (*bodily discomfort*), .86 (*emotional well-being*), .87 (*stigma*), .75 (*social support*), .69 (*cognition*) and .79 (*communication*). Cronbach's alpha for DS-14 in the original study was 0.88 for NA and 0.86 for SI. In the current study, these figures were .77 and .76, respectively.

Model of predictors of QoL

Multiple regression analyses were performed in order to identify how much the variance of the dependent variables (*mobility*, *activities of daily living*, *emotional well-being*, *stigma*, *social support*, *cognition*, *communication*, *bodily discomfort* and the summary score for the PDQ-39) may be explained by Type D and the selected disease and demographic variables.

Type D was strongly associated with all dimensions except *mobility*, *activities of daily living* and *bodily discomfort*, which were explained only by UPDRS. Being Type D was associated with a high score in these dimensions (meaning worse QoL). After UPDRS, Type D also explained most of the variance in the overall model of QoL for PD patients. (Table 3.2)

Table 3.1 Characteristics sample – means and standard deviations (SD) of demographic and study variables.

		Males	Females	Total sample	
Number of subjects (%)		79 (51.6)	74 (48.4)	153 (100)	
Mean age in years (SD)		68.5 (9.2)	67.3 (9.3)	67.9 (9.3)	ns[#]
Mean disease duration (SD)		7.7 (5.7)	7.4 (5.8)	7.5 (5.8)	ns[#]
Disease severity – UPDRS (SD)		38.8 (22.2)	34.9 (18.7)	36.9 (20.6)	ns[#]
Quality of Life – PDQ-39 total (SD)		444.3 (128.9)	475.9 (119.2)	459.5 (124.9)	ns[#]
Married or living with a partner (%)		66 (83.5)	38 (51.4)	104 (68)	95% CI 8.2-46.2
Education	elementary (%)	22 (27.8)	30 (40.5)	52 (34)	ns[α]
	secondary (%)	44 (55.7)	40 (54.1)	84 (55)	ns [α]
	university (%)	13 (16.5)	4 (5.4)	17 (11)	95% CI 1.4-20.7
Type D personality (%)		39 (49.4)	41 (55.4)	80 (52.3)	ns[α]
Negative affectivity (SD)		12.6 (6.1)	13.6 (6.3)	13.1 (6.2)	ns[#]
Social inhibition (SD)		13.0 (5.7)	14.0 (6.5)	16.5 (6.1)	ns[#]

Abbreviations: SD – standard deviation, ns - not significant

[#] t-tests

[α] difference of proportion test

Gender differences in predictors of QoL

UPDRS was an important predictor in the overall model of QoL in both genders and had a relatively high explanatory power particularly in the models of *mobility* and *activities of daily living*. In *cognition* UDPRS was the only important factor, explaining 22% of the model's variance in women. The factors selected for the model were not relevant for explaining the models of *stigma*, *social support* and *bodily discomfort* in either gender, nor the model of *communication* in women.

Type D explained *emotional well-being* in both genders. Among men, Type D was an important factor in the models of *stigmatization by illness*, *cognition* and *communication* but played no role in these models among women. Type D personality did remain an important part of the model in the overall QoL score, however.

In Table 3.3 both scales contributing to Type D are also analyzed separately. NA was found to be significantly associated in both genders with *emotional well-being*. In men it was the only illness-related factor for feeling *stigma*. In women, a higher NA explained the higher dissatisfaction with *social support*. For overall QoL, NA explained 13.2% ($P<0.001$) of the variance in males and 9.3% ($P<0.01$) of the variance in females. SI also explained a maximum of 5.5% ($P<0.05$) of the variance in *communication* in men and 7.3% ($P<0.05$) *stigma* in women.

Table 3.2 Hierarchical multiple regression analysis. Disability (UPDRS), disease duration, age, Type D on PDQ-39 total score and subscales

	mobility		ADL		emotional well-being		stigma		social support		cognition		communication		bodily discomfort		PDQ-39 summary index	
Variables	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β	Δ R2	β
UPDRS	.47	**.67*** **	.63	**.81*** **	.15	**.27** **	.04	.17	.00	-.03	.15	**.27** **	.16	**.26** **	.07	**.26***	.39	**.54*** **
disease duration	.00	-.02	.00	-.02	.01	.10	.00	.05	.02	.12	.00	.76	.02	**.17***	.00	.02	.01	.09
age	.00	-.01	.01	-.09	.00	-.01	.04	-.16	.03	-.16	.04	**.23** **	.02	**.17***	.01	-.11	.01	-.06
Type D	.01	-.08	.00	-.05	.16	**-.42*** **	.07	**-.26** **	.05	**-.24** **	.04	**-.21***	.07	**-.27*** **	.00	-.07	.08	**-.29*** **
Model	Adj. R2 =.46 F-value=26.7***		Adj. R2 =.63 F-value=52.1***		Adj. R2 =.31 F-value=14.9***		Adj. R2 =.12 F-value=5.0***		Adj. R2 =.08 F-value=3.47**		Adj. R2 =.21 F-value=8.8***		Adj. R2 =.25 F-value=10.9***		Adj. R2 =.05 F-value=2.7*		Adj. R2 =.47 F-value=26.9***	

*p≤.05, ** p≤.01, *** p≤.001

Abbreviations: ADL – activities of daily living, UPDRS – functional status, NA – negative affectivity, SI – social inhibition

Table 3.3 Multiple regression analyses of disability (UPDRS), disease duration, age, Type D, NA and SI on dimensions of PDQ-39 and PDQ-39 summary index in men and women

	mobility		ADL		emotional well-being		stigma		social support		cognition		communication		bodily discomfort		PDQ-39 summary index	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
UPDRS	**.67*** **	**.72*** **	**.85*** **	**.79*** **	.19	.38	.15	**.28***	-.01	.06	.01	**.46*** **	**.37****	.15	.48**	.09	**.54*** **	**.63*** **
disease duration	-.03	-.04	-.07	.01	.11	.11	.00	.09	.11	.13	**.40****	-.14	.15	.14	-.09	.04	.10	.08
age	.00	.04	-.07	-.12	.00	.01	.03	**-.35****	.09	**-.32***	**.34****	.15	**.24***	.15	-.09	.03	.07	-.15
Type D	-.18	.07	-.10	-.01	**-.48*** **	**-.34****	**-.35****	-.22	-.24	-.24	**-.32****	-.05	**-.32****	-.21	-.05	-.03	**-.35*** **	**-.22***
Model	$Adj.R^2_M$=.49		$Adj.R^2_M$=.70		$Adj.R^2_M$=.34		$Adj.R^2_M$=.11		$Adj.R^2_M$=.02		$Adj.R^2_M$=.36		$Adj.R^2_M$=.42		$Adj.R^2_M$=.15		$Adj.R^2_M$=.56	
	$Adj.R^2_F$=.50		$Adj.R^2_F$=.55		$Adj.R^2_F$=.27		$Adj.R^2_F$=.14		$Adj.R^2_F$=.11		$Adj.R^2_F$=.22		$Adj.R^2_F$=.07		$Adj.R^2_F$=.05		$Adj.R^2_F$=.41	
	$F\text{-value}_M$=15.0***		$F\text{-value}_M$=35.6***		$F\text{-value}_M$=8.6***		$F\text{-value}_M$=2.9*		$F\text{-value}_M$=1.3		$F\text{-value}_M$=9.5***		$F\text{-value}_M$=11.6***		$F\text{-value}_M$=3.6*		$F\text{-value}_M$=19.8***	
	$F\text{-value}_F$=15.6***		$F\text{-value}_F$=18.8***		$F\text{-value}_F$=6.5***		$F\text{-value}_F$=3.4*		$F\text{-value}_F$=2.9*		$F\text{-value}_F$=5.2***		$F\text{-value}_F$=2.14		$F\text{-value}_F$=.2		$F\text{-value}_F$=10.9***	

	mobility		ADL		emotional well-being		stigma		social support		cognition		communication		bodily discomfort		PDQ-39 summary index	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
UPDRS	**.68*** **	**.71*** **	**.83*** **	**.79*** **	.16	**.25***	.10	.23	.02	-.02	-.02	**.44*** **	**.37****	.10	**.46****	.05	**.56*** **	**.51*** **
disease duration	-.02	-.05	-.07	-.00	.12	.14	.01	.07	.14	.06	**.40****	-.15	.14	.12	-.09	.07	.09	.10
age	-.01	.05	-.06	-.11	.01	.08	.05	**-.32***	.07	**-.28***	**.35*** **	.16	**.24***	.18	-.08	.05	-.11	.08
NA	.07	-.05	.23	-.05	**.49*** **	**.61*** **	**.46*** **	.06	.12	**.41****	**.31***	.01	.15	.09	.12	.23	**.25***	**.37*** **
SI	.06	.07	-.09	.09	.07	.06	.02	**.30***	-.02	-.02	.11	.13	**.28***	.26	-.04	-.12	.19	.03
Model	$Adj.R^2_M$=.46		$Adj.R^2_M$=.72		$Adj.R^2_M$=.37		$Adj.R^2_M$=.20		$Adj.R^2_M$=.04		$Adj.R^2_M$=.39		$Adj.R^2_M$=.45		$Adj.R^2_M$=.14		$Adj.R^2_M$=.58	
	$Adj.R^2_F$=.49		$Adj.R^2_F$=.55		$Adj.R^2_F$=.54		$Adj.R^2_F$=.18		$Adj.R^2_F$=20		$Adj.R^2_F$=.22		$Adj.R^2_F$=.11		$Adj.R^2_F$=.04		$Adj.R^2_F$=.48	
	$F\text{-value}_M$=10.9***		$F\text{-value}_M$=32.5***		$F\text{-value}_M$=8.0***		$F\text{-value}_M$=4.0**		$F\text{-value}_M$=.50		$F\text{-value}_M$=8.7***		$F\text{-value}_M$=10.6***		$F\text{-value}_M$=3.0*		$F\text{-value}_M$=17.2***	
	$F\text{-value}_F$=12.2***		$F\text{-value}_F$=15.3***		$F\text{-value}_F$=14.5***		$F\text{-value}_F$=3.6**		$F\text{-value}_F$=4.0**		$F\text{-value}_F$=4.4**		$F\text{-value}_F$=2.4*		$F\text{-value}_F$=.67		$F\text{-value}_F$=11.6***	

*p≤.05, ** p≤.01, *** p≤.001

Abbreviations: M – males, F – females, ADL – activities of daily living, NA – negative affectivity, SI – social inhibition; displayed values are Beta's

Discussion

The Type D construct is a relevant factor for assessing quality of life in patients with Parkinson's disease. Having a Type D personality was, after disease severity, the second most important part of the model of overall QoL in PD patients and is related to their worse score in the dimensions of *emotional well-being*, *stigma*, *social support*, *cognition* and *communication*, in particular. With the exception of *cognition,* all other domains associated with Type D are connected with social functioning or social life. Although both Type D scales define negative feelings and attitudes of the individual, which in turn negatively determine social behavior [25], it may be stated that people with a higher score in Type D are generally less satisfied with various aspects of their social life. Type D persons are well aware of their level of emotional distress as indicated by high scores on distress measures. It is possible that distress mediates the influence of Type D personality on QoL. Therefore, repressive coping would also have to predict clinical events beyond the effect of Type D personality [32,33].

Even though the genders did not differ in the distribution of the Type D personality in the analyses, the impact of Type D personality on quality of life is apparent by gender. In the model of overall quality of life, NA appeared to be important for both genders, contrary to SI, which does not play a role in the model. A higher score in NA was associated with a worse score in the dimensions of *stigma* and *cognition* in men, while in women it was associated with a worse score in *social support*. In both genders, NA explained the variance in *emotional well-being*. SI was important in the model of *communication* in men and *stigma* in women. In women, personality traits like NA or SI seemed to play a less important role in comparison with men, in contrast to gender differences in personality traits reported in a study by Martin and Kirkcaldy (1998). In their study, females scored generally higher in neuroticism compared with males [34]. In line with the results of this paper, it can be hypothesized that models of QoL for men and women are composed of different variables.

Only a few studies have investigated gender differences in PD patients. These studies compared both groups mainly with regard to sociodemographic characteristics, socioeconomic status and disease duration [8,35]. In one cross-sectional study of PD patients [36], no differences in PDQ-39 scores between men and women were found, and the authors found that neither age nor gender had a significant impact on quality of life in PD patients studied. On the contrary, being older, being female and belonging to lower socioeconomic groups are associated with poorer quality of life in the general population [36,37].

Our results can be compared with those from a study of older adult couples by Robb et al. (2003), in which n*euroticism* and extroversion

emerged as moderators of the association of stressors and the husband's subjective well-being [38]. The gender aspect of QoL appears to be an important topic for further research, which could go deeper into the psychological differences between men and women.

A limitation of this study was the relatively low response rate, which may have an impact on generalization of the results to the total population of PD patients. Non-respondents were older than respondents, so it may be supposed that they refused to participate in the study because of serious motor complications found in the higher stages of PD and due to the need for help from their social surroundings. Regrettably, we have no information about disease duration and disease severity of non-respondents.

The analysis presented in this paper explains just part of the variance of the QoL of patients with PD. In several models, e.g. *communication*, *bodily discomfort* or *social support*, differences between genders existed in the adjusted explained variance. These differences in the models suggest possible differences in the main variables in both genders, which suggests that the model of QoL is composed of different variables for each gender. Personality traits seem to be one of the possible ways to explain these differences.

More knowledge about the association of negative affectivity, social inhibition and quality of life in PD patients may give us a clearer view of patient complaints in the case of worsening quality of life. It is important in further research to unravel the relationship between Type D, distress and QoL. In addition, the gender aspect of QoL appears to be an important topic, contributing to our knowledge about psychological differences between men and women. Consequently, coping styles and self-management skills in both genders might also differ, as has been shown in several other studies [39,40]. Because of the possible different needs of men and women, psychological intervention programs may need to be different as well.

This study concludes that the Type D personality and its scales of negative affectivity and social inhibition are important factors that may play an important role in assessing quality of life in patients with Parkinson's disease.

Acknowledgements

This work was supported by the Slovak Research and Development Agency under contract No. APVV-20-038305.

References

[1] Chapuis S, Ouchchane L, Metz O, Gerbaud L. Impact of the motor complications of Parkinson's disease on the quality of life. *Movement Disorders* 2005; **20:** 224-230.

[2] Marinus J, Ramaker C, van Hilten JJ, Stiggelbout AM. Health related quality of life in Parkinson's disease: a systematic review of disease specific instruments. *Journal of Neurology, Neurosurgery and Psychiatry* 2002; **72:** 241-248.

[3] Simons G, Thompson SB, Smith-Pasqualini MC. An innovative education program for people with Parkinson's disease and their careers. *Parkinsonism and Related Disorders* 2006; **12:** 478-485.

[4] Cole SA, Woodard JL, Juncos JL, Kogos JL, Youngstrom EA, Watts RL. Depression and disability in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neuroscience* 1996; **8:** 20-25.

[5] Papapetropoulos S, Mash DC. Psychotic symptoms in Parkinson's disease. From description to etiology. *Journal of Neurology* 2005; **252:** 753-764.

[6] van der Bruggen H, Widdershoven G. Being a Parkinson's patient: immobile and unpredictably whimsical literature and existential analysis. *Medicine, Health Care, and Philosophy* 2004; **7:** 289-301.

[7] Damiano AM, Snyder C, Strausser B, Willian MK. A review of health-related quality of life concepts and measures for Parkinson's disease. *Quality of Life Research* 1999; **8:** 235-243.

[8] Wielinski CL, Erickson-Davis C, Wichmann R, Walde-Douglas M, Parashos SA. Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. *Movement Disorders* 2005; **20:** 410-415.

[9] Shulman LM. Gender differences in Parkinson's disease. *Gender Medicine* 2007; **4:** 8-18.

[10] Damiano AM, McGrath MM, Willian MK, Snyder CF, LeWitt PA, Reyes PF, Richter RR, Means ED. Evaluation of a measurement strategy for Parkinson's disease: assessing patient health-related quality of life. *Quality of Life Research* 2000; **9:** 87-100.

[11] Pechevis M, Clarke CE, Vierrege P. Effects of dyskinesias in Parkinson's disease on quality of life and health-related costs: A prospective European study. *European Journal of Neurology* 2005; **12:** 956-963.

[12] Jelicic M, Kempen GI, Passchier J. Psychological well-being in older adults suffering from chronic headache. *Headache* 1998; **38:** 292-294.

[13] Kempen GIJM, Jelicic M, Ormel J. Personality, chronic medical morbidity, and health-related quality of life among older persons. *Health Psychology* 1997; **16:** 539-546.

[14] Gulseren S, Gulseren L, Hekimsoy Z, Cetinay P, Ozen C, Tokatlioglu B. Depression, anxiety, health-related quality of life, and disability

in patients with overt and subclinical thyroid dysfunction. *Archives of Medical Research* 2006; **37:** 133-139.
[15] Lorenz D. Quality of life and personality in essential tremor patients. *Movement Disorders* 2006; **21:** 1114-1118.
[16] Costa PT, Terracciano A, McCrae RR. Gender differences in personality traits across cultures: Robust and surprising findings. *Journal of Personality and Social Psychology* 2001; **81:** 322-331.
[17] McCrae RR, Terracciano A. Universal features of personality traits from observer's perspective: Data from 50 cultures. *Journal of Personality and Social Psychology* 2005; **88:** 547-561.
[18] Pedersen SS, Denollet J. Validity of the Type D personality construct in Danish post-MI patients and healthy controls. *Journal of Psychosomatic Research* 2004; 57: 265-572.
[19] Bartels, H., Middel, B., Pedersen, S.S., Staal, M.J., & Albers, F.W.J. (2009) The distressed (type D personality) is independently associated with tinnitus adjusted for other personality characteristics: a case-control study. *Psychosomatics* (accepted for publication).
[20] Denollet J. Personality and coronary heart disease: The type D Scale-16 (DS16). *Annals of Behavioral Medicine* 1998; **20:** 209-215.
[21] Denollet J. Behavioral research on coronary disease: Where is the person? *Journal of Behavioral Medicine* 1993; **16:** 115-141.
[22] Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery and Psychiatry* 1992; **55:** 181-184.
[23] van Hilten JJ, van der Zwan AD, Zwinderman AH, Ross RA. Rating imparment and disability in Parkinson's disease: evaluation of the Unified Parkinson's disease Rating Scale. *Movement Disorders* 1994; **9:** 84-88.
[24] Folstein MF, Folstein SE, McHough PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. *Journal Psychiatric Research* 1975; **12:** 189-198.
[25] Denollet J. DS-14: Standard assessment of negative affectivity, social inhibition and Type D personality. *Psychosomatic Medicine* 2005; **67:** 89-97.
[26] Denollet J. Personality, emotional distress and coronary heart disease. *European Journal of Personality* 1997; **11:** 343-357.
[27] Habra ME, Linden W, Anderson JC, Weinberg J. Type D personality is related to cardiovascular and neuroendocrine reactivity to acute stress. *Journal of Psychosomatic Research* 2003; **55:** 235-245.
[28] Peto V, Jenkinson C, Fitzpatrick R. PDQ-39: a review of the development, validation and application of a Parkinson's disease quality of life questionnaire and its associated measures. *Journal of Neurology* 1998; **245**(Suppl 1)**:** 10-14.

[29] Newcombe RG, Altman DG. Proportions and their differences. In: Altman DG, Machin D, Bryant TN, eds. Statistic with confidence. London: BMJ Books, 2000.
[30] Horstink M, Tolosa E, Bonuccelli U, *et al.* European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. *European Journal of Neurology* 2006; 13:1170-1185. a
[31] Horstink M, Tolosa E, Bonuccelli U, *et al.*. European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). Part II: late (complicated) Parkinson's disease. *European Journal of Neurology* 2006; 13:1186-1202. b
[32] Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert T, Brutsaert DL. Personality as independent predictor of longterm mortality in patients with coronary heart disease. *Lancet* 1996; **347:** 417–421.
[33] Denollet J, Vaes J, Brutsaert DL. Inadequate response to treatment in coronary heart disease: Adverse effects of Type-D personality and younger age on 5-year prognosis and quality of life. *Circulation* 2000; **102:** 630–635.
[34] Martin T, Kirkcaldy B. Gender differences on the EPQ-R and attitudes to work. *Personality and Individual Differences* 1998; **24:** 1-5.
[35] Hariz GM, Lindberg M, Hariz MI, Bergenheim AT. Gender differences in disability and health-related quality of life in patients with Parkinson's disease treated with stereotactic surgery. *Acta Neurologica Scandinavica* 2003; **108:** 28-37.
[36] Schrag A, Jahanshahi M, Quinn N. How does Parkinson's disease affects quality of life? A comparison with quality of life in general population. *Movement Disorders* 2000; **15:** 1112-1118.
[37] de Boer AGEM, Spruijt RJ, Sprangers MAG, de Haes JCJM. Disease-specific quality of life: is it one construct? *Quality of Life Research* 1998; **7:** 135-142.
[38] Robb C, Haley WE, Becker MA, Polivka LA, Chwa H-J. Attitudes towards mental health care in younger and older adults: similarities and differences. *Aging & Mental Health* 2003; **7:** 142–152.
[39] Weir R, Browne G, Tunks E, Gafni A, Roberts J. Gender differences in psychosocial adjustment to chronic pain and expenditures for health car services used. *Clinical Journal of Pain* 1996; **12:** 277-290.
[40] Wilz G. Predictors of subjective impairment after stroke: Influence of depression, gender and severity of stroke. *Brain Injury* 2007; **21:** 39-45.

Chapter 4

The impact of the intensity of fear on patient's delay regarding health care seeking behavior: a systematic review

Tatiana Dubayova, Jitse P. van Dijk, Iveta Nagyova, Jaroslav Rosenberger, Eva Havlikova, Zuzana Gdovinova, Berrie Middel, and Johan W. Groothoff

(International Journal of Public Health, 2010, 55:459-468)

Abstract

Objectives: This systematic review focuses on the role of the intensity of fear in patient's delay in cancer and in myocardial infarction.
Methods: In a search of literature published between 1990 and June 2009, 161 articles were found. After the use of inclusion and exclusion criteria, 11 articles in cancer and 4 articles in myocardial infarction remained.
Results: High levels of fear are associated with earlier help-seeking in both diseases; for low levels of fear the picture is unclear.
Conclusion: The level of fear is an important factor which should be taken into account when facilitating help-seeking by patients.

Introduction

An early visit to the physician is sometimes a matter of life or death. The question is, what is late and what is 'in time' in health care? Early help-seeking has an impact on the success of treatment related to the moment of intervention for a particular disease. For example, the prognosis for breast cancer and melanomas is better for patients if the problem is diagnosed within 3 months [1]. Thrombolytic treatment for heart attack is more effective when given within 2 hours [2], though it works best in the first 60 minutes [3]. To achieve a reduction in mortality from the most prevalent diseases among people of working age (men and women from 15 to 64 years of age [4]) in European countries (acute myocardial infarction (AMI) and cancer), a better understanding of the reasons for late and delayed diagnosis and consequent treatment in patients with potential symptoms of these diseases is required [5,6].

Patient's delay is most frequently described as the "length of delay between the onset/discovery/recognition of signs and symptoms and a patient's first visit to a health care/medical provider" [7,8], but more simple descriptions like "time to first presentation of signs or symptoms to a physician" can be found as well [9,10]. Also, the terms 'help-seeking delay' or 'help-seeking behavior' are frequently used in the literature as a synonym for 'patient's delay'.

In many studies patient's delay is associated mainly with sociodemographic factors such as gender, age, socioeconomic status (SES) or marital status, though the findings are equivocal. The strongest evidence exists for longer patient's delay being associated with age and SES (without regard to diagnosis). Older people [1,11-13] and people from low SES groups [5,12,14,15] had a tendency to hesitate in consulting an expert. The relationship between gender and patient's delay is not so strong and varies from 'women had a higher tendency to delay' (in cases of AMI and cases of melanoma) [11,14,16-18] to 'there is no correlation

between patient's delay and gender' (in cases of AMI) [19, 20]. The same holds true for education; several studies confirmed the association between a lower level of education and a greater tendency to hesitate in seeking help [5,13,18,21], but approximately the same number of studies refuted this association [8,22-24].

Not only sociodemographic factors influence patient's delay; clinical variables also appear to be important for making a decision on accessing health care. In many cases, *previous medical history* has an opposite effect on an early visit to surgery or emergency center. Women with a personal history of benign forms of breast cancer delayed longer in comparison with women without a history of a benign disease [5,25]. It was also found that patients with *typical symptoms* of a certain disease seek help sooner. Persons who identified symptoms correctly as originating from the heart received help one hour earlier compared to those who attributed their pain to other parts of the body [16,18]. Results from breast cancer studies also confirm this association between typical symptoms of the disease and earlier consulting with an expert. Women delayed longer when initial breast symptoms did not include a lump [23] compared to women who detected a breast lump, the latter group waiting significantly less time [26]. An important factor for decision-making is *knowledge*. Patients who came earlier to the emergency room had more knowledge about the cardiovascular system and cardiac symptoms, more appropriate behavior and fewer risk factors when compared with the group of patients who delayed for more than 1.5 hours [22]. This was confirmed by the finding that knowledge is a stimulating factor in the decision-making process about having a disease [27,28].

Apart from sociodemographic and clinical variables, psychological factors may also play a role in patient's delay. Several clinical studies mentioned fear as an important psychological factor associated with motivation for treatment or patient's delay [29-31]. According to the definition, fear is the emotional reaction to a specific, identifiable and immediate threat such as a dangerous animal or an injury, and it has a protective function associated with the fight or flight response [32]. Clinically, the terms fear and anxiety are frequently used interchangeably [30]. However, there are differences between these variables from a psychological point of view. Anxiety is a form of negative emotions closely related to fear and is defined as unspecified fear with no clear focus [33]. Whereas fear motivates an individual to engage in defensive behaviors, anxiety is associated with preventive behaviors, including avoidance, and may have higher intensity than actual fear. For these reasons, 'being anxious' was defined for the purposes of this paper as having a higher intensity than 'having fear'.

The connection of fear with patient's delay was well described in the Leicester review, where the authors identified two types of fear (fear

of embarrassment and fear of cancer) in a review of studies in different types of cancer [34]. In order to complete the variances of fear, fear of pain may also be included, a fact relevant mainly for diseases associated with muscular injuries or delay in the rehabilitation process [31]. Feelings such as worry, fear and anxiety can be elicited by symptom-induced pain or discomfort, presumed diagnosis and anticipated consequences of treatment, as well as by coping failures and reinterpretations of the illness condition [35]. Fear appears to be an important psychological factor in delay, and its intensity may have an influence on early arrival to a health care professional. Studies analyzing the association between patient's delay and fear in patients with cancer and AMI were selected for the review, because these two diseases are the two main causes of death in European countries [36]. The aim of this paper is to explore the role of the intensity of the perception of fear and anxiety in the help-seeking process in patients with a slow, progressive disease and in those with an acute disease.

Methods

In June 2009, the electronic databases MEDLINE and PsychINFO were searched for articles meeting the following inclusion criteria: 1) original papers on cancer or AMI, 2) written in English, 3) from the search period 1990 until June 2009 and 4) containing the key words 'patient's delay' or 'help-seeking behavior' or 'treatment-seeking behavior' or 'treatment seeking delay' or 'patient acceptance of health care' and 'fear' or 'anxiety'.

Two reviewers (TD and JPvD) independently assessed the studies that were identified during the screening based on information obtained from the title and the abstract of the publications from the first search strategy. When discrepancies appeared, the papers were independently assessed by a third reviewer (JWG). After the first search, both reviewers read the full text of the selected 15 articles.

For this systematic review we adopted and modified criteria from existing quality assessment lists [37, 38]. Two reviewers (TD and JPvD) assessed the quality of the publications as positive (+), negative (-) or unknown (?) based on the information provided in the article. Disagreements between reviewers were discussed during a consensus meeting. The following four quality criteria were chosen for evaluating the publications:

I. definition and operationalization of patient's delay – patient's delay was defined exactly using a disease-specific cutoff point which divided the sample into delayers and non-delayers (+), or patient's delay was defined as a continuous variable (-),

II. definition and operationalization of fear or anxiety – fear and anxiety were operationalized and defined (+), or they were not clearly defined (-),
III. reliability of measurements of fear or anxiety – using validated measurements for fear and anxiety (e.g. HADS, STAI-T, SCID, LEDS etc.) (+), qualitative study (+), assessing fear or anxiety only from self-reporting of patients or non-validated scales (-),
IV. sample size – adequate sample size for the statistical method used (+), inadequate sample size for the statistical method used (-)
V. statistical analyses – using t-tests, chi-square, correlations, regression analyses etc. for (+) or using descriptive statistical methods (means and percentages) (-) for assessment of the relationships between patient's delay and intensity of fear.

For each study a quality score was calculated. The paper was rated as *'strong evidence'* when it had an adequate sample size, used validated measurements and reported statistically significant differences in relation to the patient's delay or fear or used appropriate analytic techniques (qualitative studies). Papers which had an adequate sample size and used a rigorous methodology to ascertain data but used only descriptive statistical methods were rated as having a *'moderate'* level of evidence. Papers which used inappropriate methods of collecting relevant data about patient's delay or fear and used insufficient analysis were considered as *'insufficient'*.

Results

Using the first search strategy 158 articles were found. Additional screening based on authors detected another 16 articles which were not included in the MEDLINE or the PsychINFO database. Three of the 19 authors consulted also mailed a reference to 3 other articles related to the topic of patient's delay. Thus the total number of articles found was 177.

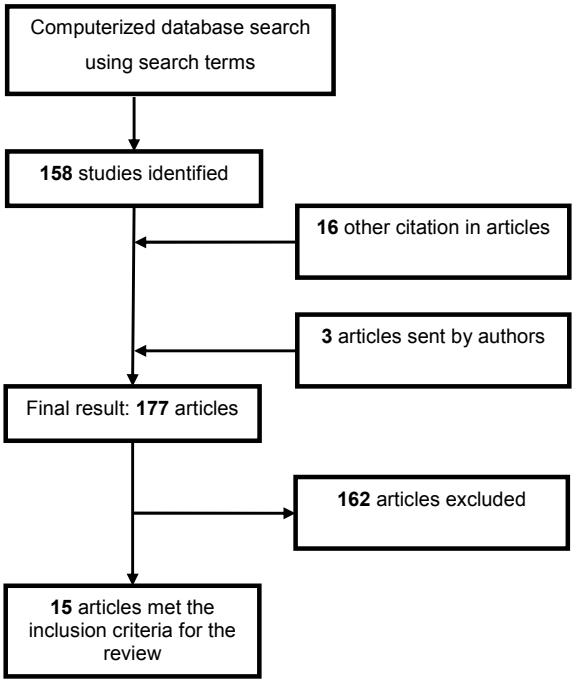
From these 177 articles, 162 were excluded because: they contained irrelevant content; involved studies of children and adolescents; were case reports; were books or book chapters; and because they:

- focused only on the association between patient's delay and progression of disease or the effectiveness of treatment;
- reported on the effectiveness of educational programs for reducing patient's delay;
- concentrated only on the association of patient's delay with sociodemographic factors (e.g. age, gender, educational level, occupation);

- focused only on measuring the time from first signs until first contact with a medical doctor without any further explanation.

The process of applying these criteria is shown in Figure 1; 15 articles remained for review.

Figure 4.1 Flow diagram of the selection process



Disagreement occurred mainly because of reading errors and differences in the interpretation of the list of criteria, but after the consensus meeting no disagreements persisted. The third reviewer was not asked for a final decision.

Quality assessment

Only one of the fifteen selected studies was rated as 'insufficient'. Eleven were considered as having a 'moderate' level of evidence and three were rated as studies with a 'strong level of evidence'. (Table 4.1)

Table 4.1 The ratings of the 15 studies

Study, reference	Disease	I	II	III	IV	V	Evaluation of the study	
Mor et al., 1990	cancer	+	-	-	+	-	2/5	M*
Burgess et al., 1998	cancer	+	?	-	+	+	3/5	M
Burgess et al., 2000	cancer	+	+	+	+	+	5/5	S*
Nosarti et al., 2000	cancer	+	-	-	+	-	2/5	M
Brochez et al., 2001	cancer	-	-	-	+	+	2/5	M
de Nooijer et al., 2001a	cancer	+	+	+	-	-	3/5	M
de Nooijer et al., 2001b	cancer	+	+	+	-	-	3/5	M
Burgess et al., 2001	cancer	+	+	-	+	-	3/5	M
Meechan et al., 2003	cancer	-	+	+	+	+	4/5	S
Rozniatowski et al., 2005	cancer	-	+	+	+	+	4/5	S
Ristvedt et al., 2005	cancer	-	+	+	-	+	3/5	M
Dracup et al., 1997	AMI	+	-	-	+	+	3/5	M
McKinley et al., 2000	AMI	-	-	-	+	-	1/5	I*
Kentsch et al., 2002	AMI	+	-	-	+	-	2/5	M
Moser et al., 2005	AMI	-	-	-	+	+	2/5	M

*S – Strong level of evidence; M – Moderate level of evidence; I - Insufficient level of evidence; Quality criteria: I - definition and operationalization of patient's delay – patient's delay was defined exactly using disease specific cut-off point which divided sample on delayers and non-delayers (+), or patient's delay was defined as continuous variable (-); II - definition and operationalization of fear or anxiety – fear and anxiety were operationalized and defined (+), or they were not clearly defined (-); III - reliability of measurements of fear or anxiety – using validated measurements for fear and anxiety (e.g. HADS, STAI-T, SCID, LEDS etc.) (+), qualitative study (+), assessing fear or anxiety only from self-reporting of a patients or non-validated scales (-); IV - sample size – adequate sample size to the used statistic method (+), inadequate sample size to the used statistic method (-); V - statistical analyses – using t-tests, chi-square, correlations, regression analyses etc. for (+) or using descriptive statistic methods (means and percentages) (-) for assessment of the relationships between patient's delay and intensity of fear.

Study characteristics

The characteristics of the studies are presented in Table 4.2 Twelve of the 15 selected studies addressed some form of carcinoma (5 on breast cancer, 1 on cutaneous melanomas, 3 on patients with various types of carcinoma, 1 on rectal cancer and 1 on head and neck cancer) and 4 looked at acute myocardial infarction.

In the selected papers information about patient's delay was obtained from structured or semi-structured interviews with patients or from medical records. The questionnaires contained parts in which the patients were asked about delay and the reasons for delay [23, 39, 40], or the data about delay was obtained from medical records [15,26,28, 41]. Measuring the concept of fear varied in the selected articles from spontaneous sentences from patients about their fear to standardized measures, where fear was expressed in numbers. Although reliable, validated

and standardized measures to assess fear or anxiety are widely used in diagnosis and research (such as the Hospital Anxiety and Depression Scale (HADS), State-Trait Anxiety Inventory – Trait scale (STAI-T), the Structured Clinical Interview (SCID), the Response to Symptoms Questionnaire and the Bedford College Life Events and Difficulties Schedule (LEDS), such measures were used in only six of the studies [15,28,42-44]. In eleven of the fifteen analyzed studies, expressions of patients were investigated using a few items from a larger, non-standardized questionnaire or a semi-structured interview. In addition to standardized questionnaires, several authors also used qualitative measures covering many aspects of various domains of the patient's life. They offer a place for spontaneous expressions from the patient's point of view.

How does the intensity of fear influence patient's delay?
Words which described the intensity of fear varied in the reviewed studies from 'being worried' to 'have a fear', 'be anxious', 'in panic' or 'feel death anxiety'. This sequence reflects the intensity of the emotion of fear.

Cancer
Being only 'worried' by the first signs of disease is not enough stimulus for seeking help in patients with cancer. It appears that patients who were worried tended to have longer patient's delay than those who were not worried, although the difference were not statistically significant (p=0.07) [40]. But the same authors also found that patients who were worried about their lesion more frequently consulted a dermatologist than those who were not anxious at all (p=0.03). It can be hypothesized that being worried has no impact on the decision-making process to visit a specialist for the first time, but that it does have an impact on the patient's wish to be treated.

Results of the studies on 'having fear' are contradictory. In patients with different types of carcinoma, 17% of the delayers reported fear of discovering the cause of their symptoms as the reason for delaying. Delayers with breast cancer mentioned this reason more often than patients with lung or colorectal carcinoma (20.7% vs. 10.5% and 16%) [39]. It was also found that women who expressed more fear about the consequences of diagnosis and the treatment of the disease delayed longer [45]. In a different study, those who delayed were those who reported less fear after discovering the first symptoms of disease (p=0.05); but in contrast, in the same sample more psychological distress (as expressed by the GHQ-12 scores) was associated with longer delay, especially in those who did indeed turn out to have breast cancer [23,46]. In a later analysis it was found that the influence of fear on decision making is related to various aspects of treatment, the seriousness of the disease, dying or leaving relatives behind [47].

'Being anxious' appears to be a factor which stimulates decision-making in women with breast cancer [46]. This finding was confirmed in a study which shows that there was a lack of anxiety and depression symptoms in patients with large tumor lesions who delayed consultation, whereas patients with smaller lesions with a short delay presented high levels of anxiety (p=0.00001) [43]. Using a regression model, not having a breast lump (β=-0.35, t=-3.30, p=0.0001) and lower initial symptom distress (β=-0.32, t=-3.03, p=0.001) were found to be the factors most predictive of patient's delay [26]. However, in other studies, different results were found. It was not confirmed that being clinically anxious or depressed before or around the time of symptom discovery increases the risk of a woman with symptoms delaying her presentation for medical attention [42]. Similar results were reported in a study by Ristvedt and Trinkaus (2005), in which anxiety was measured with a standardized STAI-T questionnaire. Lower scores on STAI-T were associated with fewer doctor visits, so it can be hypothesized that the level of anxiety has a positive correlation with patient's delay [44]. However, in the same article the authors found that people characterized as fearful, shy, tense, and worried had a significantly shorter delay time [44].

Patients who reacted to first symptoms with 'panic' or were 'extremely alarmed' or 'anxious' sought medical help or visited the EMS within a few hours [27]. The study showed that panic stimulated patients into inferring illness from the symptoms and shortening appraisal delay as a result.

Acute myocardial infarction

Studies about worries regarding AMI itself were absent, but several studies confirmed that patients with AMI who delayed seeking assistance reported being worried about troubling others with a request for assistance (p=0.001) and feared the financial consequences of seeking help (p=0.02) [15,41]. In patients with AMI 'having fear' is associated with hesitation in seeking help and therefore with longer patient's delay [45]. Those patients with AMI who were least anxious about their symptoms delayed seeking medical attention [28]. Short decision time (< 1 hour) was associated in the case of AMI with evaluating symptoms as threatening or dangerous and causing a feeling of 'panic' and 'death anxiety' [48].

Table 4.2 Summary of reviewed studies divided in studies of cancer and AMI

Reference/country	Type of study	Study population	Disease	Quality of the study	Overall assessment and strength of evidence
Burgess et al., 1998 UK	cross-sectional	135 women with cancer 53 control study	Breast cancer	M	- delayers reported less fear on discovering symptoms (p =.05)
Burgess et al., 2000 UK	cross-sectional	158 women	Breast cancer	S	no difference between delayers and non-delayers in prevalence of full-case depression (p =.7), borderline anxiety (p =.6), or full-case anxiety (p =.3) the study found no evidence that being clinically anxious or depressed before or around the time of symptom discovery increases the risk of delaying
Nosarti et al., 2000 UK	cross-sectional	692 women	Breast cancer	M	- women who delayed because they feared a cancer diagnosis had the highest median delay long delayers were characterized by poor health awareness about hypothetical breast symptoms and by fear and high levels of psychological morbidity
Burgess et al., 2001 UK	cross-sectional	46 women	Breast cancer	M	delayers expressed more fear about the consequences of diagnosis and treatment of breast cancer
Meechan et al., 2003 New Zealand	cross-sectional	85 women	Breast cancer	S	a significant correlation was found between patient's delay and emotional response to symptom discovery – high levels of emotional response were associated with shorter delay (p =0.01) there were no association between delay time and fear of cancer treatment
Mor et al., 1990 U. S.	cross-sectional	121 patients with lung cancer 214 patients with breast cancer 290 patients with colorectal cancer	Lung cancer Breast cancer Colorectal cancer	M	17% of delayers reported fear of discovering the cause of their symptoms as a reason of delaying

de Nooijer et al., 2001a, The Netherlands	cross-sectional	23 patients	Cancer	M	panic shortened appraisal delay shame or embarrassment and lack of worry about the nature of the symptom increased patient's delay
de Nooijer et al., 2001b, The Netherlands	cross-sectional	23 patients	Cancer	M	panic and being anxious stimulated patients to consult with GP within few hours lack of worry was an impeding factor
Brochez et al., 2001 Belgium	cross-sectional	130 patients (89 women, 41 men)	Melanoma	M	worried patients tended to have a longer patient's delay, although the difference was not statistically significant patients who were worried about their lesion more frequently consulted a dermatologist than those who were not anxious ($\chi 2$=4.95, p=.03)
Rozniatowski et al., 2005 France	cross-sectional	100 patients	Head and neck cancer	S	in delayers a lack of anxiety and depressive symptoms was observed; non-delayers presented a high level of anxiety (p <.0001)
Ristvedt et al., 2005 USA	cross-sectional	69 patients	Rectal cancer	M	- low scores in anxiety in STAI-T were associated with more favorable judgments of overall prior health (p=.025) and with fewer doctor visits (p=.041), but were not associated with cancer screening.
Dracup et al., 1997 North America	cross-sectional	Patients enrolled to the GUSTO trial N = 277	AMI	M	- delayers reported being worried about troubling others with a request for assistance (p=.001) and feared of consequences of seeking help (p =.02)
McKinley et al., 2000 Australia	cross-sectional	277 North Americans 147 Australians	AMI	I	fearing the financial consequences of seeking help were associated with longer delay in North American patients, but not in Australian
Kentsch et al., 2002 Germany		739 patients	AMI	M	short decision time (< 1 hour) was associated with death anxiety and with being scared of immediate hospitalization
Moser et al., 2005	cross-sectional	194 patients	AMI	M	patients whose symptoms were perceived as serious (p =.004) and felt anxious about them (p =.04) delayed less than patients who did not view their symptoms as serious or experienced anxiety about them

A summary of the findings is presented in Table 4.3

Table 4.3 Patient's delay and stages of fear

	Results	Cancer	AMI
Worry	worry has no impact on patient's delay	Brochez et al., 2001	
Fear	fear shortened time of patient's delay	Burgess et al., 1998, Nosarti et al., 2000	
	fear prolonged time of patient's delay	Mor et al., 1990, Burgess et al., 2001	Dracup&Moser, 1997 McKinley et al., 2000
Anxiety	anxiety shortened time of patient's delay	Nosarti et al., 2000 Rozniatowski et al., 2005 Meechan et al., 2003 Ristvedt&Trinkaus, 2005	Moser et al., 2005
	anxiety prolonged time of patient's delay	Burgess et al., 2000 Ristvedt&Trinkaus, 2005	
Panic/ Death anxiety	panic or death anxiety shortened time of patient's delay	de Nooijer et al., 2001	Kentsch et al., 2002

Discussion

Summary of the main findings

This paper presents the results of 15 studies which investigated patient's delay with the intensity of fear. Levels of intensity of fear were constructed after a detailed reading of the studies. These stages of fear were: 'being worried', 'having fear', 'being anxious', 'being in panic' and 'feeling death anxiety'. Differences in fear between cancer and AMI patients were expected. 'Being worried', 'having fear', and 'being anxious' were mainly present in cancer patients. 'Being worried' is not enough for seeking help with cancer, but it starts the process of internal thinking about the possibility of being treated. The emotion 'fear' seems to be a factor for longer delay, but the decision process in patients experiencing fear was also influenced by other factors, such as embarrassment, pressure from a patient's relatives or fear of financial consequences. 'Being anxious' had a direct impact on shortening patient's delay. These emotions were not present in the case of AMI, but the feeling of 'panic' or 'death anxiety' present in cancer and AMI was associated with seeking help within a few hours of the appearance of the first symptoms of illness; the impact of this type of fear on the patient's delay was similar in both diagnoses.

Meaning of the results

The emotion of fear could lead to either help-seeking behavior or to delay, depending on the cause of the fear and the way people cope with it. The intensity of negative feelings seems to be an important predictor of a patient's help-seeking behavior. Of the defined levels of fear ('being worried', 'having fear', 'being anxious', 'in panic' and 'feeling death anxiety'), the latter two have a significantly positive effect on decision-making in help-seeking behavior. Either the first two have no influence on patient's delay (worry) or their impact is ambivalent (fear). Although there are differences in the onset of both diseases, the emotional reaction upon first signs or symptoms were similar. 'Having fear' from treatment, from the consequences of diagnose or from bothering others with bad feelings slowed help-seeking behavior in cancer and also in AMI. On the other hand, when patients feel anxiety or panic, according to the results of our review, they seek help sooner in both cases. On this basis, it can be expected that people who are more frightened will have a greater chance of getting medical help earlier than those without such a strong emotional response like in a slow progressive disease - cancer and sometimes also in the case of acute myocardial infarction.

The results of this review also show that minimizing the seriousness of symptoms was negatively correlated with the intensity of fear, making seeking treatment less urgent and producing longer delay. Some authors call this phenomenon health-related 'defensive bias' [5], 'optimistic bias' [10] or 'denial' [49], which leads to longer patient's delay. On the other hand, these behavioral variables were found to be associated with the degree of patient's understanding of the treatment, which is why some authors suggest speaking about 'indecision' rather than about 'denial' [50,51].

Another explanation for the connection between fear and patient's delay is that people also differ in their perception of symptoms. Some people simply have more symptoms than others, or they differ in the sensation they experience from the same symptom [27]. It was observed that some people focus on bodily symptoms more intensely than other people, leading to increased reports of symptoms [52]. Recognizing pain symptoms has a positive effect on rising anxiety and thus on decision-making in patients with acute myocardial infarction and breast cancer [5,16], but this was not proven in all of the studies [35]. The considerable difference between acute pain in cases of acute myocardial infarction and chronic pain in breast cancer occurring in later stages of the disease also has to be taken into account. In the variables of patient's delay between patients with acute myocardial infarction experiencing pain and those without pain, no significant correlations were found [15]. Similar results were found in women with breast cancer [26].

Strengths and limitations

This study is the first which systematically summarizes the influence of the intensity of fear in patient's delay in both a slow, progressive disease and in an acute disease. A limitation of this study was that the analyzed studies did not use the same instruments for measuring fear or anxiety. They varied from standardized instruments like STAI-T, HADS or LEDS to information from semi-structured interviews or self-created questionnaires. Measurement of fear was not the primary aim in several analyzed studies; therefore, the authors did not pay such detailed attention to analyzing the connection of fear or anxiety with patient's delay. Another limitation of the analyses of fear is that, like in all studies examining the relationship between level of fear/anxiety and delay, all patients were assessed retrospectively after they had been admitted to the hospital. The generalizibility of the results may be limited by a potential publication bias towards positive findings.

The qualitative evaluation of studies may be also interpreted. Only six of the fifteen selected articles use validated measurements of fear or anxiety. In the remaining cases, fear was not the main aim of the study, but it was one of the possible reasons for patient's delay. In six cases, the authors used the patient's delay as continuous variable in the analyses, a fact viewed as a negative factor in this paper. Patient's delay should be interpreted from a disease-specific point of view, which is why it is preferable to speak about patient's delay only in cases when a patient comes to a health professional after a certain moment which is related to the diagnose. A lack of operationalization of fear or anxiety was observed especially in studies where the author did not used validated measurements. Patients in these studies just reported fear for various reasons, but its intensity or specification is missing. The results of the evaluation of the studies reviewed in this paper should inspire us to be more focused primarily on the association between patient's delay and fear and anxiety.

Conclusion

There are two ways of coping with fear – fight or flight. The avoidance behavior associated with reduction of fear and anxiety seems to be helpful in the short term because of the reduction of negative feelings, but it may be counterproductive in the long run [30]. Our data explored the possible reasons for patient's delay. The lack of emotional response on symptom discovery can lead to patient's delay in both AMI and cancer. The level of fear evidently influences the decision-making process in patients on help-seeking and hence, this important factor should be taken into account when facilitating help-seeking by patients, and especially in cases of low level of fear, encouraging them to seek out medical care. Results of the study suggest that fear might not be disease specific and might have a

similar impact on the decision making process in acute as well as slow progressive diagnoses. Unfortunately, the results needed to clarify this point regarding other diseases are missing.

Knowledge about factors associated with patient's delay also could be used in preparing educational programs. Studies suggest that psychological rather than demographic factors are the main predictors of delay time [46]. Therefore, information about clinical variables could be included in the content of such programs, though knowledge about psychological phenomena such as fear and worry can be a more meaningful factor affecting their efficiency. It was observed that health education about cancer mostly tells people how to identify cancer symptoms but provides little about the consequences of a cancer diagnosis [45]. Moreover, it was shown that when patients are prepared to anticipate an aversive situation, they are more likely to cope effectively [15]. Further successful cooperation after a patient's first visit to the medical doctor is conditioned by doctor's communicative skills and his/her proper counseling [53]. Health programs for early help-seeking in case of the appearance of the first symptoms of cancer which are oriented only on information about the disease and not on the positive aspects of early diagnosis may increase the fear of a certain diagnosis, which may lead to two types of behavior: denying the initial symptoms or being hypersensitive to any type of small discomforts in the body. Both reactions are strategies with low efficacy for coping with the disease process and may lead to difficulties in help-seeking behavior, a delay which in turn does not contribute to the reduction in mortality aimed for by health policy in most countries.

Acknowledgements

This work was supported by the Slovak Research and Development Agency under contract No. APVV-20-038305.

References

[1] Arndt V, Sturmer T, Stegmaier C, Ziegler H, Dhom G, Brenner H. Patient delay and stage of diagnosis among breast cancer patients in Germany: a population based study. *British Journal of Cancer* 2002; **86:** 1034-1040.

[2] Davalos A. Thrombolysis in acute ischemic stroke: successes, failures and new hopes. *Cerebrovascular Diseases* 2005; **20**(suppl 2)**:** S135-139.

[3] Warnes CA, Williams RG, Bashore TM, Child JS, Connolly HM, Dearani JA, Del Nido P, Fasules JW, Graham TP Jr, Hijazi ZM, Hunt SA, King ME, Landzberg MJ, Miner PD, Radford MJ, Walsh EP, Webb GD. ACC/AHA 2008 guidelines for the management of adults with

congenital heart disease. *Journal of the American College of Cardiology* 2008; **52:** e1-121.
[4] Eurostat. The social situation in the European Union 2007. Statistical books 2008. 15.06.2009
[5] Caplan LS, Helzlsouer KJ. Delay in breast cancer: A review of the literature. *Public Health Reviews* 1992; **20:** 187-214.
[6] Moser DK, Kimble LP, Alberts MJ, *et al.* Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on Cardiovascular Nursing and Stroke Council. *Journal of Cardiovascular Nursing* 2007; **22:** 326-343.
[7] Thongsuksai P, Chongsuvivatwong V, Sriplung H. Delay in breast cancer care: a study of Thai women. *Medical Care* 2000; **38:** 108-114.
[8] Demissie M, Lindtjorn B, Berhane Y. Patient and health service delay in diagnosis of pulmonary tuberculosis in Ethiopia. *BMC Public Health* 2002; **2:** 23.
[9] Young CJ, Sweeney JL, Hunter A. Implication of delayed diagnosis in colorectal cancer. *ANZ Journal of Surgery* 2000; **70:** 635-638.
[10] Andersen BL, Cacioppo J, Roberts DC. Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *British Journal of Social Psychology* 1995; **34:** 33-52.
[11] Ottesen MM, Kober L, Jorgensen S, Torp-Pedersen C. Determinants of delay between symptoms and hospital admission in 5978 patients with acute myocardial infarction. *European Heart Journal* 1996; **17:** 429-437.
[12] Facione NC, Miaskowski C, Dodd MJ, Paul SM. The self-reported likelihood of patient delay in breast cancer: new thoughts for early detection. *Preventive Medicine* 2002; **34:** 397-407.
[13] Montella M, Crispo A, Botti G, De Marco M, de Bellis G, Fabbrocini G, Pizzorusso M, Tamburini M, D'Aiuto G. An assessment of delays in obtaining definitive breast cancer treatment in Southern Italy. *Breast Cancer Research And Treatment* 2001; **66:** 209-215. a
[14] Schmidt SB, Borsch MA. The prehospital phase of acute myocardial infarction in the era of thrombolysis. *American Journal of Cardiology* 1990; 65: 1411-1415.
[15] Dracup K, Moser D. Beyond socio-demographic: Factors influencing to seek treatment for symptoms of acute myocardial infarction. *Heart and Lung* 1997; **26:** 253-262.
[16] Dracup K, Moser DK. Treatment seeking behavior among those with signs and symptoms of acute myocardial infarction. *Heart and Lung* 1991; **20:** 570-575.
[17] Betti R, Vergani R, Tolomio E, Santambrogio R, Crosti C. Factors of delay in the diagnosis of melanoma. *European Journal of Dermatology* 2003; **13:** 183-188.

[18] Lefler LL, Bondy KN. Women's delay in seeking treatment with myocardial infarction – a meta-synthesis. *European Journal of Cardiovascular Nursing* 2004; **19:** 251-268.
[19] Schroeder JS, Lamb IH, Hu M. The prehospital course of patients with chest pain: analysis of the prodromal, symptomatic, decision-making, transportation and emergency room periods. *American Journal of Medicine* 1978; **64:** 742.
[20] Maynard C, Althouse R, Olsufka M, Ritchie JL, Davis KB, Kennedy JW. Early versus late hospital arrival for acute myocardial infarction in the Western Washington thrombolytic therapy trials. *American Journal of Cardiology* 1989; **63:** 1296.
[21] Montella M, Crispo A, D'Aiuto G, De Marco M, de Bellis G, Fabbrocini G, Pizzorusso M, Tamburini M, Silvestra P. Determinant factors for diagnostic delay in operable breast cancer patients. *European Journal of Cancer Prevention* 2001; **37:** 843-848. b
[22] Bleeker JK, Lamers LM, Leenders IM, Kruyssen DC, Simoons ML, Trijsburg RW, Erdman RA. Psychological and knowledge factors related to delay of help-seeking by patients with acute myocardial infarction. *Psychotherapy and Psychosomatics* 1995; **36:** 151-158.
[23] Burgess CC, Ramirez AJ, Richards MA, Love SB. Who and what influences delayed presentation in breast cancer? *British Journal of Cancer* 1998; **77:** 1343-1348.
[24] Yu RF, San Jose MC, Manzanilla BM, Oris MY, Gan R. Sources and reasons for delays in the care of acute stroke patients. *Journal of Neuroscience* 2002; **199:** 49-54.
[25] Dracup K, Moser DK, Eisenberg M, Meischke H, Alonzo AA, Braslow A. Causes of delay in seeking treatment for heart attack symptoms. *Social Science and Medicine* 1995; **40:** 379-392.
[26] Meechan G, Collins J, Petrie KJ. The relationship of symptoms and psychological factors to delay in seeking medical care for breast symptoms. *Preventive Medicine* 2003; **36:** 374-378.
[27] de Nooijer J, Lechner L, de Vries H. A qualitative study on detecting cancer symptoms and seeking medical help; an application of Andersen's model of total delay. *Patient Education and Counseling* 2001; **42:** 145-157. b
[28] Moser DK, McKinley S, Dracup K, Chung ML. Gender differences in reason patients delay in seeking treatment for acute myocardial infarction symptoms. *Patient Education and Counseling* 2005; **56:** 45-54.
[29] Bish A, Ramirez A, Burgess C, Hunter M. Understanding why women delay in seeking help for breast cancer symptoms. *Journal of Psychosomatic Research* 2005; **58:** 321-326.
[30] Leeuw M, Goossens MEJB, Linton SJ, Crombez G, Boersma K, Vlaeyen WS. The fear-avoidance model of musculosceletal pain: current state of scientific evidence. *Journal of Behavioral Medicine* 2006; **30:** 77-94.

[31] George SZ, Dover GC, Fillingim RB. Fear of pain influences outcomes after exercise-induced delay onset muscle soreness at the shoulder. *Clinical Journal of Pain* 2007; **23:** 76-84.
[32] Rachman, S. Anxiety. Hove: Psychological Press, 1989.
[33. Hartl P, Hartlova H. Psychologicky slovnik. (Lexicon of Psychology). Praha: Portal, 2004.
[34] Smith LK, Pope C, Botha JL. Patient's help-seeking experiences and delay in cancer presentation: a qualitative synthesis. *Lancet* 2005; **366:** 825-831.
[35] Cameron L, Leventhal EA, Leventhal H. Symptom representations and affect as determinant of care seeking in a community-dwelling, adult sample population. *Health Psychology* 1993; **12:** 171-9.
[36] Mackenbach JP, Stirbu I, Roskam A-JR, Schaap MM, Menvielle G, Leinsalu M, Kunst AE. Socioeconomic inequalities in health in 22 European countries. *New England Journal of Medicine* 2008; **358:** 2468-2481.
[37] van der Mei SF, Krol B, van Son WJ, de Jong PE, Groothoff JW, van den Heuvel WJ. Social participation and employment status after kidney transplantation: a systematic review. *Quality of Life Research* 2006; **15:** 979-994.
[38] den Oudsten BL, van Heck, GL, de Vries J. Quality of life and related concepts in Parkinson's disease: a systematic review. *Movement Disorders* 2007; **11:** 1528-1537.
[39] Mor V, Masterson-Allen S, Goldberg R, Guadagnoli E, Wool MS. Pre-diagnostic symptom recognition and help seeking among cancer patients. *Journal of Community Health* 1990; **15:** 253-266.
[40] Brochez L, Verhaeghe E, Bleyen L, Naeyaert JM. Time delays and related factors in the diagnosis of cutaneous melanoma. *European Journal of Cancer* 2001; **37:** 843-848.
[41] McKinley S, Moser DK, Dracup K. Treatment-seeking behavior for acute myocardial infarction symptoms in North America and Australia. *Heart and Lung* 2000; **29:** 237-247.
[42] Burgess CC, Ramirez AJ, Smith P, Richards MA. Do adverse life events and mood disorders influence delayed presentation of breast cancer? *Journal of PsychosomaticResearch* 2000; **48:** 171-175.
[43] Rozniatowski O, Reich M, Mallet Y, Penel N. Psychosocial factors involved in delay consultation by patients with head and neck cancer. *Head and Neck* 2005; **4:** 274-280.
[44] Ristvedt SL, Trinkaus KM. Psychological factors related to delay in consultation for cancer symptoms. *Psycho-Oncology* 2005; **14:** 339-350.
[45] Burgess CC, Hunter MS, Ramirez AJ. A qualitative study of delay among women reporting symptoms of breast cancer. *British Journal of General Practice* 2001; **51:** 967-971.

[46] Nosarti C, Crayford T, Roberts JV, Elias E, McKenzie K, David AS. Delay in presentation of symptomatic referrals to a breast clinic: patient and system factors. *British Journal of Cancer* 2000; **82:** 742-748.
[47] de Nooijer J, Lechner L, de Vries H. Help-seeking behavior for cancer symptoms: perceptions of patients and general practitioners. *Psycho-Oncology* 2001; **10:** 469-478. a
[48] Kentsch M, Rodemerk U, Rodemerk G, Schnoor U, Münzel T, Ittel TH, Mitusch R. Emotional attitudes toward symptoms and inadequate coping strategies are major determinants of patient delay in acute myocardial infarction. Zeitschrift Für Kardiologie 2002; **91:** 147-155.
[49] Moyer A, Levine EG. Clarification of the conceptualization and measurement of denial in psychosocial oncology research. *Annals of Behavioral Medicine* 1999; **20:** 149-160.
[50] Temoshok L, diClemente RJ, Sweet DM, Blois MS, Sagebiel RW. Factors related to patient delay in seeking medical attention for cutaneous malignant melanoma. *Cancer* 1984; **54:** 3048-53.
[51] Leslie WS, Urie A, Hooper J, Morrison CE. Delay in calling for help during myocardial infarction: reasons for the delay and subsequent pattern of accessing care. *Heart* 2000; **84:** 137-141.
[52] Pennebaker JW. The psychology of physical symptoms. New York: Springer – Verlag, 1982.
[53] Matejic B, Kesic V, Markovic M, Topic L. Communication about cervical cancer between women and gynecologists in Serbia. *International Journal of Public Health* 2008, **53:** 245-251.

Chapter 5

Differences in quality of life by personality traits among delayers and non-delayers with Parkinson's disease

Tatiana Dubayova, Jitse P. van Dijk, Iveta Nagyova, Eva Havlikova, Jaroslav Rosenberger, Zuzana Gdovinova, Berrie Middel, and Johan W. Groothoff

(submitted)

Abstract

Objectives: The aim of the paper is to explore whether quality of life (QoL) in patients with Parkinson's disease (PD) who delayed in seeking help is associated with personality traits.
Methods: The sample consisted of 142 patients (average age 67.6±9.2 years; 51.4% men; mean disease duration 7.6±5.9 years). Patient's delay was dichotomized at the cut-off point of 1 year. The Eysenck Personality Questionnaire (EPQR-A) was used for measuring extroversion (E) and neuroticism (N). Health-related quality of life (HRQOL) was assessed using the Thirty-six Item Short Form Health Survey (SF-36) and its two summary scores: the physical health component summary score (PHC) and the mental health component summary score (MHC). T-tests and multiple linear regression analyses were used to analyze the data.
Results: Increased neuroticism was related to lower scores in PHC and MHC in delayers and in non-delayers. Conversely, non-delayers scored higher in extroversion, which was associated with better scores in PHC and MHC.
Conclusion: Social interactions, associated with an extrovertly oriented personality, can force decision making on help-seeking. Factors contributing to early help-seeking behavior in PD patients may result in a greater chance of limiting impairment of their quality of life.

Introduction

Parkinson's disease (PD) is a chronic progressive neurodegenerative disorder influencing many aspects of a patient's life, primarily in terms of mobility and independence. The diversity of symptoms associated with PD (e.g. tremor, rigidity, bradykinesia, falls, as well as non-motor symptoms like painful spasms, depression, sleep problems and fatigue) leads to worse physical, mental and social well-being in comparison with people of the same age without symptoms of Parkinsonism, even when the disease is treated properly [1-3].

In the case of life-threatening diseases like stroke, heart attack or cancer, seeking medical care sooner has a positive impact on the success of treatment [4-6]. The consequence of delay in seeking help for these diseases on a patient's quality of life (QoL) is evident [7,8]. However, there is a lack of literature answering the question of whether delay in seeking help and treatment is associated with later QoL in chronic diseases such as Parkinson's disease. In PD a patient's QoL corresponds with the decision regarding when to start with drug treatment, whether the decision to take a "wait and see" approach or to start with drug treatment immediately

upon identifying the diagnosis might make a difference for improving the patient's self-reported QoL [9]. In patients with PD, health-related quality of life (HRQOL) is determined mainly by physical mobility and progression of the disease [10]. However, quality of life in the elderly can be influenced also by non-clinical factors, for example life satisfaction or happiness [11,12].

The association between patients' delay and personality traits has still not been adequately explained. Many studies on the non-clinical factors of patients' delay have focused mostly on the social, cognitive and emotional factors of delay in life threatening diseases, but studies into the association between personality traits and patients' delay are missing.

The aim of this paper is to explore 1) the relationship between delay and quality of life in patients with PD; 2) the association of personality traits and quality of life in patients with PD, stratified by delay.

Methods

Subjects and procedure

The patients for this cross-sectional study were recruited from the databases of 4 hospitals and 17 outpatient neurologists in the eastern part of the Slovak Republic between February 2004 and February 2006. Neurologists from the mentioned institutions diagnosed all patients included in the sample as suffering from Parkinson's disease according to the United Kingdom Parkinson's Disease Society Brain Clinical Criteria [13].

Exclusion criteria were defined as follows: a) patients older than 85 years because of the high probability of other co-morbidities and movement disabilities of a non-parkinsonian character, and b) patients with a Mini-Mental State Examination (MMSE) score [14] below 23 points.

Each patient was assessed individually by a neurologist from the research team (E.H.) using the Unified Parkinson's Disease Rating Scale (UPDRS Version 3.0) [15]. A patient's cognitive status was assessed using the MMSE [14]. The structured interview consisted of questions on the patient's medical history and subjective feelings that were not part of the questionnaire. Sociodemographic data were derived from questionnaires filled in by the patients themselves and data about antiparkinsonian therapy from their medical records.

The study was conducted after informed consent was obtained from the patients prior to the interview. Participation in the research was voluntary. The local Ethics Committee of the University Hospital in Kosice approved the study in Kosice on 17 December 2002.

Measures

Patient's delay

The length of patient's delay was assessed according to two questions: 'When did the first signs of the disease appear?' and 'How long did you delay the first consultation with your general practitioner (GP)?' The answer to the latter question was recorded as the number of months. Patients were also asked for the approximate date of verification of PD diagnosis: 'When was the diagnosis of PD confirmed?' In cases of uncertainty, the medical records were checked for information regarding the first consultation of a health professional. Because of the intermittent occurrence and slow progress of symptoms in the first phase of the disease, in several cases patients who sought medical help within 1 year of the appearance of the first signs and symptoms of the disease were marked as 'non-delayers' and those over 1 year as 'delayers'. This period was defined on the basis of interviews with patients – when the initial signs were not dramatic, people attributed them frequently to 'stress'. When delaying more than 1 year after the first signs appeared, the delay becomes more serious: Patients cannot attribute these signs to any cause other than disease and should have visited a physician.

Disease severity

The Unified Parkinson's Disease Rating Scale (UPDRS) was used in research for assessing disease severity in patients with PD. The UPDRS consists of four parts, pertaining to: mentation and mood (Part 1), activities of daily living (Part 2), motor function (Part 3) and complications of dopaminergic therapy (Part 4), including motor fluctuations and dyskinesias. Parts 1, 2, and 4 are interview-based; Part 3 is based on a clinical examination by a health care professional and represents the patient's condition at the time of the examination. A neurologist can score patients from 0 to 176, where higher scores indicate increased disease severity [15].

SF-36

The thirty-six item Short Form Health Survey (SF-36) was designed to measure health-related quality of life (HRQOL) from the patient's point of view as part of the Medical Outcome Study (MOS). It assesses 8 health concepts: a) physical functioning; b) role limitations because of physical health problems; c) bodily pain; d) general health perception; e) vitality (energy/fatigue); f) social functioning; g) role limitations because of emotional problems; and h) general mental health [16]. These scales were further combined into 2 summary scores: a physical health component summary score (PHC) (subscales a-d) and a mental health component

summary score (MHC) (subscales e-h). All item scores are transformed into a scale from 0 (poor health) to 100 (optimal health) [17]. Cronbach's alphas for the subscales were .94 for physical functioning, .84 for role limitations because of physical health problems, .91 for bodily pain, .69 for general health perception, .71 for vitality (energy/fatigue), .74 for social functioning, .81 for role limitations because of emotional problems and .75 for general mental health. Cronbach's alphas for the summary scores were .87 for PHC and .78 for MHC.

Extroversion and neuroticism

The Eysenck Personality Questionnaire Revised Abbreviated was used for measuring Extroversion and Neuroticism (EPQR-A) [18]. The questionnaire was validated in the Czech Republic in a sample of 3565 people [19]. The Slovak and Czech languages are very similar. The questionnaire consists of 24 items divided into 4 subscales: extroversion, neuroticism, psychoticism and the lie scale, from which we used extroversion and neuroticism. Items are scored on a Yes (=1) / No (=0) basis, and the overall score for each subscale ranges between 0–6. Higher scores indicate higher levels of the personality traits. Internal reliability found across the samples was .74-.84 for the subscales of extroversion and .70-.77 for neuroticism [20]. In the present study Cronbach's alpha was .85 for extroversion and .72 for neuroticism.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS 14.0.1.) software was used to analyze the data. Summary scores MHC and PHC of SF-36 as well as the UPDRS score were calculated according the scoring algorithm [15,17]. Independent samples were subjected to t-tests to assess the differences between delayers and non-delayers in terms of disease severity, disease duration, age, MHC and PHC. CIA software was used to test the difference of proportions for assessing differences between tested groups in partnership and education [21]. Multiple linear regression analyses were used to assess the contribution of the independent variables – disease severity (UPDRS), age at the time of diagnosis, and extroversion and neuroticism – to the explained variance of the dependent variables – MHC and PHC – in 2 groups of patients: those who sought help within 1 year of the first signs and symptoms appearing and those who delayed more than 1 year before seeking medical care.

Results

Descriptive statistic

Out of 512 patients with Parkinson's disease, 160 agreed to participate and completed the questionnaires. Among the non-participants, 41

patients refused to participate and 311 did not respond to the invitation. Seven patients were excluded after the personal interview because of the exclusion criteria, and 11 questionnaires could not be analyzed because of missing data. Non-participants differed significantly from the analyzed group regarding age (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39) and there were significantly more women than men among the non-participants (difference -0.0110; SE=.041; 95% CI -.091 – .069).

The final sample consisted of 142 patients (51.4% men, 48.6% women) with a mean disease duration of 7.6 years (SD=5.9). Ninety-six patients from the sample (67.6%) lived with a partner, and 46 patients (32.4%) were widowed, divorced or single. Gender differences appeared in patient's delay; women registered the first signs of the disease significantly later and more than half of delayers were women. Otherwise there were no significant differences in age, disease duration and functional status (measured by UPDRS) between men and women. Delayers and non-delayers significantly differed in marital status (70.9% of the non-delayers lived with a partner), in disease severity (non-delayers had worse scores on the UPDRS) and non-delayers perceived their health status as worse.

Delayers and non-delayers differed regarding age achieved as of the date of data collection, but there were no differences in their age at the time of providing the diagnosis. In non-delayers there were more patients with an elementary education and in delayers there were more patients with secondary education. The samples did not differ in the number of patients with a university education. Patients who delayed longer had significantly shorter disease duration ($p \leq 0.001$) and achieved significantly lower scores on the UPDRS ($p \leq 0.001$) than non-delayers. In MHC there were no differences between the two groups, but in PHC the delayers scored higher ($p \leq 0.05$).

All patients used antiparkinsonian therapy according international guidelines [22, 23]. Twelve percent used only L-dopa, and 24% used only dopamine agonists. L-dopa in combination with Catechol-O-Methyl-Trasnsferase (COMT) inhibitors were used by 25.3% of the patients and L-dopa with dopamine agonists were used by 20% of the patients. The combination of L-dopa, a COMT inhibitor and dopamine agonists was used by 16% of the patients from our sample.

Physical and mental quality of life in delayers and non-delayers

Results of the linear regression are displayed in Table 5.2 In delayers and in non-delayers high scores on the UPDRS and neuroticism were associated with low scores in PHC and MHC.

Table 5.1 Characteristics of the sample by length of delay – means and standard deviations (SD) or N (%) on demographic and study variables

		delay < 1 year (non-delayers)	delay > 1 year (delayers)	Total sample	p / 95% CI
Number of subjects (%)		79 (55.6)	63 (44.4)	142 (100)	
Gender	Males (%)	47 (59.5)	26 (41.3)	73 (51.4)	
	Females (%)	32 (40.5)	37 (58.7)	69 (48.6)	
Mean age in years (SD)		69.4 (8.6)	65.4 (9.6)	67.6 (9.2)	p≤0.01
Mean age at onset signs (SD)		62.5 (11.0)	59.9 (10.7)	61.3 (10.9)	ns#
Married or living with a partner (%)		56 (70.9)	40 (63.5)	96 (67.6)	-.08; .23 ns α
Education	elementary (%)	32 (40.5)	15 (23.8)	47 (33.1)	.02; .32 α
	secondary (%)	35 (44.3)	44 (69.8)	79 (55.6)	-.41; -.10 α
	university (%)	12 (15.2)	4 (6.3)	16 (11.3)	-.01; .12 ns α
Disease duration (SD)		9.2 (6.4)	5.6 (4.3)	7.6 (5.9)	p≤0.001
UPDRS (SD)		43.1 (21.3)	29.1(15.8)	36.9 (20.2)	p≤0.001
Personality	Neuroticism (SD)	2.2 (1.9)	2.7 (1.9)	2.4 (1.9)	ns#
	Extroversion (SD)	2.6 (2.3)	2.9 (2.2)	2.7 (2.2)	ns#
Mental health summary score (SD)		48.7 (16.0)	53.6 (18.8)	50.9 (17.4)	ns#
Physical health summary score (SD)		33.6 (18.0)	42.5 (25.5)	37.6 (22.0)	p≤0.05

Abbreviations: SD – standard deviation, ns - not significant; # t-tests; difference of proportion test

In non-delayers extroversion was an important part of the model explaining MHC. A higher score in extroversion explained 11.2% of the variance in MHC – that is, being more extroverted means a better score in MHC. Age at onset, education and disease duration up to the time of the research were not relevant variables in either model.

Table 5.2 Multiple regression analyses of mental and physical summary score in delayers and non-delayers with disability (UPDRS), age, disease duration, education, extroversion and neuroticism

	Mental summary score		Physical summary score	
Variables	delay < 1 year	delay > 1 year	delay < 1 year	delay > 1 year
UPDRS	-.39***	-.31*	-.62***	-.55***
age at onset signs	.04	-.09	.01	-.09
education	.04	.07	.16	.12
disease duration	.10	-.02	.19	-.01
extroversion	.32**	.12	.07	-.09
neuroticism	-.36**	-.40**	-.22*	-.27*
Model	Adj.R^2=.36 F-value=7.0***	Adj.R^2=.41 F-value=5.0***	Adj.R^2=.39 F-value=7.9***	Adj.R^2=.49 F-value=8.7***

*p≤.05, ** p≤.01, *** p≤.001; displayed values are Beta's

Discussion

Patients with PD who came earlier to see a health care professional had a significantly lower physical quality of life than delayers, but they did not differ in their mental quality of life. It is supposed, that delayers were less affected by the disease which might have been the reason for the longer delay, and also for the higher physical quality of life.

In both models analyzing MHC and PHC, neuroticism, after disease severity, contributed substantially to the models for non-delayers and delayers. Neuroticism was negatively related to both the mental health and the physical health component of the HRQOL. It can be hypothesized that neuroticism is a reaction to getting a chronic and quality-of-life decreasing disease such Parkinson's disease. This idea is supported by the findings of a large British study [24]. The feelings of anxiety and worry are rather stable components of neurological diseases in comparison with healthy control samples. A high score in neuroticism was in several studies also mentioned as a factor closely related to depression, which is one of the symptoms of PD patients, but it is also associated with other neurological diseases [24-26].

Extroversion was associated with the prediction of a better score in MHC in non-delayers. Extroverted people are sociable; they prefer changes, crave excitement and act impulsively [27]. Several studies found that the possibility of sharing feelings with somebody has a significant impact on the decision to consult a specialist. In one British study, among the important factors associated with longer patient delay was not disclosing the discovery of the breast symptom immediately to someone else and seeking help only after being prompted by others [28]. A positive correlation was found between 'asking others for advice' and the decision to visit a specialist early also in studies from various countries [29,30]. This association was confirmed indirectly by a French study of 100 patients with head and neck cancer, where 43% of the patients who lived alone and 21% of those who lived with a partner delayed consultation. In the same study 'living with a partner' correlated with higher anxiety, which implies that anxiety caused by the partner's observations may have been the motivating factor that induced the patients to seek consultation earlier [31]. The other person could facilitate the recognition of the potential seriousness of the situation and the decision to seek medical advice [32]. This corresponds with the results of Smith and colleagues (2005), who mentioned that others noticed changes, such as weight loss and lethargy, and they made the connection between symptoms and illness for the patient, who discussed his or her vague symptoms with them [33]. Consequently, it can be hypothesized, that extroverts have more social interactions which can lead to earlier help-seeking behavior.

A limitation of this study was the relatively low response rate, which

may have an impact on generalization of the results to the total population of PD patients. Non-respondents were older than respondents, and a possible reason for refusing participation in the study could be the presence of more serious motor complications associated with higher stages of PD and the increasing need for help from their social surroundings compared with the participants. We are regrettably missing information about disease duration and disease severity in the non-respondents.

Our study showed that personality traits, especially extroversion and neuroticism, are closely associated with HRQOL in patients with PD. More sociable patients have a greater chance of getting medical help sooner than patients who are isolated. Disease severity and the number of social interactions associated with an extrovertly oriented personality seem to be important for decision-making. It is also evident that neuroticism is associated with a decrease in overall perception of quality of life in patients with Parkinson's disease, but it is not associated with patient's delay. Recent treatment of PD patients is primarily concerned with the improvement of motor functioning and on symptoms that lower quality of life decreasing [34]. Currently, treatment options for neurodegenerative diseases, including parkinsonism, are limited and mainly affect only the symptoms of a disease and have no significant disease-modifying effect [35]. Early help-seeking behavior will be important in the future, when a neuroprotective therapy is developed for patients having PD [36]. Under such conditions, seeking help sooner will mean better chances to limit the progress of the disease in its early phase, when the impact of the disease on a patient's quality of life is not yet very significant.

Acknowledgements

This work was supported by the Slovak Research and Development Agency under contract No. APVV-20-038305.

References

[1] Damiano AM, Snyder C, Strausser B, Willian MK. A review of health-related quality of life concepts and measures for Parkinson's disease. *Quality of Life Research* 1999; **8:** 235-243.

[2] Schrag A, Jahanshahi M, Quinn N. How does Parkinson's disease affects quality of life? A comparison with quality of life in general population. *Movement Disorders* 2000; 15: 1112-1118.

[3] Simons G, Thompson SB, Smith-Pasqualini MC. An innovative education program for people with Parkinson's disease and their careers. *Parkinsonism and Related Disorders* 2006; **12:** 478-485.

[4] Arndt V, Sturmer T, Stegmaier C, Ziegler H, Dhom G, Brenner H. Patient delay and stage of diagnosis among breast cancer patients in Germany: a population based study. *British Journal of Cancer* 2002; **86:** 1034-1040.

[5] Davalos A. Thrombolysis in acute ischemic stroke: successes, failures and new hopes. *Cerebrovascular Diseases* 2005; **20**(suppl 2)**:** 135-139.

[6] Hirvonen TP, Halinen MO, Kala RA, Olkinuora JT. Delays in thrombolytic therapy for acute myocardial infarction in Finland. Results of a national thrombolytic therapy delay study. Finish Hospitals' Thrombolysis Survey Group. *European Heart Journal* 1998; **19:** 885-892.

[7] Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999; **353:** 1119-1126.

[8] Moser DK, Kimble LP, Alberts MJ, *et al.* Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: A scientific statement from the American Heart Association council on cardiovascular nursing and stroke council. *Journal of Cardiovascular Nursing* 2007; **22:** 326-343.

[9] Grosset D, Taurah L, Burn DJ, *et al.* A multicentre longitudinal observational study of changes in self reported health status in people with Parkinson's disease left untreated at diagnosis. *Journal of Neurology, Neurosurgery, and Psychiatry* 2009; **78:** 465-469.

[10] Forsaa EB, Larsen JP, Wentzel-Larsen T, Herlofson K, Alves G. Predictors and course of health-related quality of life in Parkinson's disease. *Movement Disorders* 2008; **23:** 1420-1427.

[11] McDowell I, Newell C. Measuring health: A guide to rating scales and questionnaires (2nd ed.). New York: Oxford University Press, 1996.

[12] Kai I, Ohi G, Kobayashi Y, Ishizaki T, Hisata M, Kiuchi M. A possible health index for elderly. *Asi-Pacific Journal of Public Health* 1991; **5:** 221-227.

[13] Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery and Psychiatry* 1992; **55:** 181-184.

[14] Folstein MF, Folstein SE, McHough PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. *Journal Psychiatric Research* 1975; **12:** 189-198.

[15] van Hilten JJ, van der Zwan AD, Zwinderman AH, Ross RA. Rating imparment and disability in Parkinson's disease: evaluation of the Unified Parkinson's disease Rating Scale. *Movement Disorders* 1994; **9:** 84-88.

[16] Ware J, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). *Medical care*1992; **30:** 473-483.
[17] Ware J, Snow K, Kosinski M, Gandek B. SF-36 Health Survey: manual and interpretation guide. Boston: The Health Institute, New England Medical Center, 1993.
[18] Francis LJ, Brown LB, Philipchalk R. The development of an abbreviated form of the Revised Eysenck Personality Questionnaire (EPQR-A): its use among students in England, Canada, The USA and Australia. *Personality and Individual Differences* 1992; **13:** 443-449.
[19] Kozeny J. Faktorová struktura 24 položkové formy dotazníku EPQR-A [Factor structure of the 24 items questionnaire EPQ-A]. *Československá psychologie* 2001; **45:** 289-301.
[20] Forrest S, Lewis CA, Shevlin M. Examining the factor structure and differential functioning of the Eysenck personality questionnaire revised-abbreviated. *Personality and Individual Differences* 2000; **29:** 579-588.
[21] Newcombe RG, Altman DG. Proportions and their differences. In: Altman DG, Machin D, Bryant TN, eds. Statistic with confidence. London: BMJ Books, 2000.
[22] Horstink M, Tolosa E, Bonuccelli U, *et al.* European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. *European Journal of Neurology* 2006; 13:1170-1185. a
[23] Horstink M, Tolosa E, Bonuccelli U, *et al.*. European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). Part II: late (complicated) Parkinson's disease. *European Journal of Neurology* 2006; 13:1186-1202. b
[24] Ishihara-Paul L, Wainwright NWJ, Khaw K-T, Luben RN, Welch AA, Day NE, Brayne C, Surtees PG. Prospective association between emotional health and clinical evidence of Parkinson's disease. *European Journal of Neurology* 1992; **15:** 1148-1154.
[25] Morris PL, Robinson RG, Samuels J. Depression, introversion and mortality following stroke. *Australian and New Zealand Journal of Psychiatry* 1993; **27:** 443-449.
[26] Morris PLP, Robinson RG. Personality neuroticism and depression after stroke. *International Journal of Psychiatry in Medicine* 1995; **25:** 93-102.

[27] Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Inventory. London: London University of London Press, 1994.
[28] Burgess CC, Ramirez AJ, Richards MA, Love SB. Who and what influences delayed presentation in breast cancer? *British Journal of Cancer* 1998; **77:** 1343-1348.
[29] de Nooijer J, Lechner L, de Vries H. A qualitative study on detecting cancer symptoms and seeking medical help; an application of Andersen's model of total delay. *Patient Education and Counseling* 2001; **42:** 145-157.
[30] Kentsch M, Rodemerk U, Müller-Esch G, Schnoor U, Münzel T, Ittel TH, Mitusch R. Emotional attitudes toward symptoms and inadequate coping strategies are major determinants of patient delay in acute myocardial infarction. *Zeitschrift Für Kardiologie* 2002; **91:** 147-155.
[31] Rozniatowski O, Reich M, Mallet Y, Penel N. Psychosocial factors involved in delay consultation by patients with head and neck cancer. *Head Neck* 2005; **4:** 274-280.
[32] Burgess CC, Hunter MS, Ramirez AJ. A qualitative study of delay among women reporting symptoms of breast cancer. *British Journal of General Practice* 2001; **51:** 967-971.
[33] Smith LK, Pope C, Botha JL. Patient's help-seeking experiences and delay in cancer presentation: a qualitative synthesis. *Lancet* 2005; **366:** 825-831.
[34] Behari M, Srivastava AK, Pandey RM. Quality of life in patients with Parkinson's disease. *Parkinsonism and Related Disorders* 2005; **11:** 221-226.
[35] Abdin AA, Hamouda HE. Mechanism of the neuroprotective role of coenzyme Q10 with or without L-dopa in rotenone-induced parkinsonism. *Neuropharmacology* 2008; **55:** 1340-1346.
[36] Schapira AHV, Olanow CW. Neuroprotection in Parkinson's Disease: Mysteries, Myths, and Misconceptions. *JAMA: Journal of the American Medical Association* 2004; **291:** 358-364.

Chapter 6

Type D, depression and anxiety in association with quality of life in patients with Parkinson's disease and with multiple sclerosis

Tatiana Dubayova, Martina Krokavcova, Iveta Nagyova, Jaroslav Rosenberger, Zuzana Gdovinova, Berrie Middel, Johan W. Groothoff, and Jitse P. van Dijk

(submitted)

Abstract

Background: The present study examines the role of Type D personality, anxiety and depression in quality of life (QoL) in patients of two chronic neurological diseases – Parkinson's disease (PD) and multiple sclerosis (MS).
Methods: This cross-sectional study included 142 PD patients (73% males; mean age 67.6±9.2 years) and 198 patients with MS (32.3% males; 38.4±10.8 years). Multiple regression analyses were used to analyze the association of UDPRS (PD patients) or EDSS (MS patients), Type D personality (DS-14) and anxiety and depression (HADS) with the physical (PCS) and mental summary (MCS) of QoL, as measured by the SF-36.
Results: In PD patients, Type D was significantly associated with MCS only; in MS patients Type D was significantly associated with both dimensions - MCS and PCS. After adding anxiety and depression, the importance of Type D for the QoL model dramatically decreased. Anxiety and depression were strongly associated with lower scores in MCS and PCS in both PD and MS patients.
Conclusions: The actual mood of PD and MS patients – the level of anxiety or depression – might have a greater impact on patients' QoL than their personality. Further longitudinal research should focus on how the pathway consisting of personality traits, anxiety and depression, and QoL might be constructed.

Introduction

The major clinical symptoms of Parkinson's disease (PD) and multiple sclerosis (MS) significantly affect a patient's quality of life. Symptoms associated with PD are tremor, rigidity, bradykinesia and falls, as well as non-motor symptoms like painful spasms, depression, sleep problems and fatigue [1,2]. Multiple sclerosis (MS) is a disorder of the central nervous system (brain and spinal cord) caused by demyelinations in the white matter of the central nervous system. It is marked by lack of muscle coordination, muscle weakness, speech problems, paresthesia, and visual impairments [3,4]. MS is characterized by recurrent attacks of neurological symptoms followed by a remission [4]. Other forms of MS are secondary progressive, primary progressive, progressive relapsing and the malignant course of the disease [5]. In both diseases, the symptoms lead to worse physical, mental and social well-being in comparison with people of the same age without symptoms of Parkinsonism or MS [2,6-10].

Mood disorders, especially depression, are among the clinical symptoms of both diseases. In PD patients, the prevalence of depression ranges from 20% to 40% [11,12], while depression affects 27-54% of MS patients [13,14]. Both diseases are often associated with higher scores in

anxiety [15,16]. A recent study by Goretti and colleagues clearly presented that depression had a negative impact on all QoL domains and anxiety on the mental domains in MS patients [17]. Anxiety and depression, even at moderate levels, were *also* positively linked with poor *QoL in studies about PD [12,18]*.

Other psychological factors have been identified as important variables in QoL models. Personality traits, mostly high levels of neuroticism and low levels of extraversion, contributed to a worse perception of QoL in several diseases [19-26]. The construct of the Type D personality was primarily designed for measuring personality traits in coronary heart disease patients associated with an increased risk of depressive symptoms, a higher number of reinfarctions and higher mortality rates [27,28]. In further studies, its validity among non-cardiovascular diseases was also shown. Type D was associated with poor physical and mental health status among patients with melanoma, Parkinson's disease, mild traumatic brain injury, vertigo complaints, tinnitus or sleep apnoe [29-31]. The DS-14 questionnaire, which measures Type D, was evaluated as a valid instrument for assessing and comparing Type-D personality across clinical groups as well [32].

In a previous study we concluded that Type D personality plays an important role in QoL assessment in PD patients. Having a Type D personality was, after disease severity, the second most important determinant of overall QoL and was related to the patient's worse score in the dimensions associated with mental status, as measured by Parkinson's Disease Questionnaire (PDQ-39) [30].

Neurologists should be aware of factors associated with a patient's QoL in order to be able to choose the most effective interventions in the framework of treatment. For this study, Type D personality, anxiety and depression were assumed to be the variables associated with the perception of health status and thus might lead to a worse perception of QoL among patients with Parkinson's disease and patients with multiple sclerosis. The aim of this study is to explore whether Type D was associated with the mental and physical health status of quality of life in PD and MS patients even when depression and anxiety are added to the model.

Methods

Participants and sample size

Patients with PD and MS in this cross-sectional study were recruited from the databases of 4 hospitals and 17 outpatient neurologists and also from MS society in the eastern part of the Slovakia between February 2004 and February 2006. Neurologists from the above mentioned institutions diagnosed all patients included in the sample as suffering from PD according to the United Kingdom Parkinson's Disease Society

Brain Clinical Criteria [33]. MS patients were diagnosed by neurologists according to the diagnostic criteria for MS [4]. Data collection of MS patients took place between December 2003 and July 2006.

Exclusion criteria for both diseases were defined as follows: a) patients with a Mini-Mental State Examination (MMSE) score [34] below 23 points, b) co-morbidities and movement disabilities not caused by MS or PD.

Sociodemographic data were derived from questionnaires filled in by the patients themselves, and data about neurological treatment from their medical records. Disability in each patient was assessed by a neurologist. The study was conducted after informed consent was obtained from the patients prior to the interview. Participation in the research was voluntary. The local Ethics Committee of the University Hospital in Kosice approved the study in Kosice on 17 December 2002.

Measures

Disease severity

Disease severity was measured using the Unified Parkinson's Disease Rating Scale (UPDRS) in PD patients and the Kurtzke Expanded Disability Status Scale (EDSS) in MS patients. The UPDRS and EDSS remain the most frequently used scoring systems in PD and MS neurological practice.

The UPDRS consists of four parts, pertaining to: mentation and mood (Part 1), activities of daily living (Part 2), motor function (Part 3) and complications of dopaminergic therapy (Part 4), including motor fluctuations and dyskinesias. Parts 1, 2, and 4 are interview-based; Part 3 is based on a clinical examination by a health care professional and represents the patient's condition at the time of the examination. A neurologist can score patients from 0 to 176, where higher scores indicate increased disease severity [35].

The EDSS is based on testing functional systems: pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, mental and "other". Disability caused by SM is graded on a continuum from 0 (normal neurological examination) to 10 (death caused by MS) [36].

Type D personality

For assessing Type D personality the DS-14 was used with its constituent subscales, negative affectivity (NA) and social inhibition (SI) [28]. NA means the tendency to experience negative emotions, like anger, dysphoria, irritability, hostile feelings, depressed affect and anxiety. SI is the tendency to inhibit these emotions in social interactions [28]. Subjects rated these aspects of their personality on a 5-point Likert scale ranging from 0=false to 4=true. The NA and SI scales were scored as continuous

variables (range 0-28). A cut-off of 10 on both scales (NA ≥ 10 and SI ≥ 10) was used to classify subjects as Type D [28]. Cronbach's alpha in the original study was 0.88 for NA and 0.86 for SI. In the current study, DS-14 had good internal consistency in both diseases: Cronbach's alpha in PD patients was .77 for NA and .76 for SI, and for MS patients it was .84 for NA and .83 for SI.

HADS

The fourteen-item Hospital Anxiety and Depression Scale (HADS) was used for assessing anxiety and depression in non-psychiatric hospital departments [37]. Seven items are related to the depression and 7 to anxiety. Patients responded on a 4-point scale (from 0=absent to 3=definitely present/severe). Scores ranged from 0 to 21 for each scale, where a higher score implied more depression or anxiety. Cronbach's alpha for depression was .79 for both MS and PD patients, and for anxiety it was .81 for MS and .69 for PD patients.

SF-36

The thirty-six item Short Form Health Survey (SF-36) was designed to measure health-related quality of life (HRQOL) from the patient's point of view as part of the Medical Outcome Study (MOS). It assesses 8 health concepts: a) physical functioning; b) role limitations because of physical health problems; c) bodily pain; d) general health perception; e) vitality (energy/fatigue); f) social functioning; g) role limitations because of emotional problems; and h) general mental health [38]. These scales are further combined into 2 scales: a physical component summary score PCS (subscales a-d), which contains information about physical heath status (PHS), and a mental component summary score (MCS) (subscales e-h), which informs about mental health status (MHS). All item scores are transformed into a scale from 0 (poor health) to 100 (optimal health) [39]. Cronbach's alphas for the summary scores were .87 for PCS and .78 for MCS in PD patients, and .89 for PCS and .89 MCS for patients with MS.

Statistical analyses

Independent sample t-tests were conducted to assess differences between the sample of MS and PD patients in age, disease duration, anxiety, depression, PCS and MCS. Also the difference of proportions test (CIA) was used for assessing gender differences in partnership, Type D and education [40]. Next, linear regression analyses were used for assessing the contribution of the independent variables in 3 models. The first model included disease severity, gender, age, education and disease duration. In the second model Type D personality was added. The third model

contained also the variables anxiety and depression.

Data were analyzed using the software Statistical Package for the Social Sciences (SPSS 16.0).

Results

Descriptive statistics

Out of 512 invited patients with Parkinson's disease, 160 patients agreed to participate and filled in the questionnaires, but 7 patients were excluded after the personal interview because of the exclusion criteria. The final sample thus consisted of 153 patients (response rate 31.3%). Non-respondents were on average older compared to the analyzed group in age (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39) and there were significantly more women than men among non-respondents (difference -0.0110; SE=.041; 95% CI -.091 – .069).

From 412 MS patients who were asked to participate in the study, 207 patients were interviewed (52%), and 205 patients did not respond. There were no statistically significant differences between non-respondents and participants regarding gender, disease duration and clinical course of MS. However, the non-respondents were on average older than the participants (mean difference 1.69 yrs., SE=.87; t=-1.95; 95% CI .010 – -3.39).

Eleven patients with PD and nine patients with MS were removed from the sample because of missing data. The study ultimately involved 142 PD patients (73% males; mean age 67.6±9.2 years) and 198 patients with MS (32.3% males; 38.4±10.8). The majority of MS patients belonged to the relapsing-remitting clinical course (RR-MS; 70.2%).

All PD patients used antiparkinsonian therapy according international guidelines [41,42]. Fifty-six per cent of MS patients in this study were being treated with Interferon beta therapy.

Disease severity, Personality, Depression and Anxiety and Quality of Life

Three models were constructed to explore the contribution to the variance of PCS and MCS.

In Model 1, which consisted of disease severity, gender, age, education, and disease duration, worse disease severity was associated with a worse score in mental and in physical health status in PD patients, and female gender was associated with a worse PCS, as well. Older age and more serious disease severity were the main predictors of MCS and PCS in MS patients (Table 6.2).

Table 6.1 Characteristics of the sample – means and standard deviations (SD) or N (%) on demographic and study variables

		Parkinson's disease	Multiple sclerosis	p / 95% CI
Number of subjects (%)		142 (41.8)	198 (58.2)	
Gender	Males (%)	73 (51.4)	64 (32.3)	.09; .29 $^{\alpha}$
	Females (%)	69 (48.6)	134 (67.7)	-.29; -.09 $^{\alpha}$
Mean age in years (SD)		67.6 (9.2)	38.4 (10.8)	p≤0.001$^{\#}$
Married or living with a partner (%)		96 (67.6)	121 (61.1)	-.03; .17 ns $^{\alpha}$
Education	elementary (%)	47 (33.1)	11 (5.6)	.19; .36 $^{\alpha}$
	secondary (%)	79 (55.6)	152 (76.8)	-.31; -.11 $^{\alpha}$
	university (%)	16 (11.3)	35 (17.7)	-.14; .01 ns $^{\alpha}$
Disease duration (SD)		7.6 (5.9)	2.6 (0.8)	p≤0.001$^{\#}$
UPDRS (SD)		36.9 (20.2)	-	-
EDSS (SD)		-	3.0 (1.5)	-
Clinical course of MS	relapsing-remitting (%)	-	139 (70.2)	-
	secondary progressive (%)	-	27 (13.6)	-
	primary progressive (%)	-	29 (14.6)	-
Personality	Negative affectivity (SD)	13.2 (6.3)	12.1 (6.3)	ns$^{\#}$
	Social inhibition (SD)	13.5 (6.2)	12.0 (6.3)	p≤0.05$^{\#}$
	Type D (%)	75 (52.8)	89 (44.5)	-.03; .18 ns $^{\alpha}$
Depression (SD)		6.6 (3.6)	4.4 (3.5)	p≤0.001$^{\#}$
Anxiety (SD)		8.2 (3.9)	7.2 (4.2)	p≤0.05$^{\#}$
Physical component summary (SD)		37.6 (22.0)	48.5 (20.4)	p≤0.001$^{\#}$
Mental component summary (SD)		50.9 (17.4)	56.5 (15.7)	p≤0.01$^{\#}$

Abbreviations: SD – standard deviation, ns - not significant. $^{\#}$ t-tests; $^{\alpha}$ difference of proportion test

When Type D was added (Model 2), the strength of the model increased for MCS and PCS in both diseases. In PD patients, Type D was significantly associated with MCS only. However, Type D was significantly associated with the MCS and PCS of QoL for MS patients. Except disease severity, which remained significantly associated with both domains in both diseases, age was the second most important variable in the model of PCS and MCS in MS patients only (Table 6.2).

Model 3 showed a further increase in explained variance for both diseases when the variables anxiety and depression were added (Model 3). Anxiety and depression were strongly associated with lower scores in both subscales of the SF-36 in both groups of patients. Disease severity remained significantly associated with both domains in both diseases. Type D personality, female gender and longer disease duration were associated with PCS in PD patients (p≤.05). In MS patients higher age remained significantly associated with PCS (Table 6.2).

Table 6.2 Multiple regression analyses of disability (UPDRS in PD patients, EDSS in MS patients), gender, age, education, disability and disease duration (Model 1), Type D personality (Model 2) and anxiety and depression (Model 3) in MCS and PCS of SF-36 in PD and MS patients

	Model 1				Model 2				Model 3			
	MCS		PCS		MCS		PCS		MCS		PCS	
	PD	MS	PD	MS	PD	MS	PD	MS	PD	MS	PD	MS
UPDRS/EDSS	-.48***	-.19*	-.66***	-.47***	-.43***	-.21**	-.66***	-.48***	-.37***	-.19***	-.61***	-.47***
gender	.14	.14	.20**	.08	.10	.11	.18*	.06	.06	.04	.14*	.02
age	.05	-.29***	-.05	-.30***	.03	-.26***	-.04	-.28***	.05	-.10	-.07	-.20***
education	.03	.10	.12	.11	.01	.07	.12	.10	.01	.02	.10	.08
disease duration	.05	.16*	.13	.07	.08	.14*	.15*	.06	.08	.09	.15*	.03
Type D personality					-.32***	-.31***	-.05	-.17**	-.05	-.05	.16*	-.04
anxiety									-.23**	-.31***	-.33***	-.17**
depression									-.39***	-.46***	-.17*	-.20**
Adj.R^2	.19	.13	.42	.38	.28	.22	.41	.40	.47	.59	.53	.48
F-value	6.6***	7.0***	17.6***	24.5***	8.6***	10.2***	14.5***	22.5***	13.7***	35.0***	17.0***	23.1***

Abbreviations: UPDRS - Unified Parkinson's Disease Rating Scale, EDSS - Expanded Disability Status Scale, PD – Parkinson's disease, MS – multiple sclerosis

Discussion

Our findings demonstrate a significant association between Type D personality and the mental health status of both PD patients and MS patients. Type D personality was associated with both dimensions of QoL – PCS and MCS. However, this association disappeared in both dimensions in MS and in the mental dimension in PD when the variables anxiety and depression were added to the model. Higher scores in anxiety and depression were strongly associated with QoL in both diseases. We might suppose that the actual mood status influences a patient's perception of QoL significantly more than personality traits, which over time are mostly seen as relatively stable. Actual feelings of sadness and fear are related, with MS and PD patients both reporting worse QoL. Similar results were found in inflammatory bowel disease patients, where regression analysis showed that disease activity and psychological distress were the strongest predictors *of* QoL impairment, and that p*ersonality traits* did not play a significant role in QoL [43].

As depression is a clinical symptom for both diseases MS and PD, we included all patients into the analyses although the HADS-score could be multifactorially determined, e.g. by other organic changes in the brain or by psychological reasons associated with factors of non-parkinsonian character. To better understand this effect of the origin of the HADS, we repeated the analysis after exclusion of clinically depressed and anxious patients from the sample and in those patients only. We found that in the non-A/non-D sample not only the association between personality traits, anxiety, depression and MCS and PCS disappeared except for depression and MCS in MS, but also in both diseases the association between UDPRS/EDSS and MCS disappeared in the full model. In the clinically depressed and anxious sample the association between UDPRS/EDSS and MCS and PCS is only statistically significant in PD and not in MS. A statistically significant association between anxiety and MCS is found in PD, not in MS, but with PCS only in MS and not in PD. Depression is significantly associated with MCS in both diseases, not with PCS. These findings need further exploration. Nevertheless, having a chronic disease combined with depression is a severe disabling combination [44].

The predictive value of Type D disappeared in Model 3, although there is no doubt that its importance on QoL exists. In a previous study, the association between Type D, its subscales and QoL was explored in patients with PD [30] and other studies have reported similar results [29,31]. Thus, an important question is how personality fits into the final model consisting, besides personality, also of mood variables determining QoL in chronically ill patients. A possible answer might be that personality traits are associated indirectly with QoL via another variable. Mood variables mediating the relationship from personality to QoL was recently

suggested by Bartels et al. (2010) in the field of tinnitus. The authors in that study presented a model in which Type D personality on QoL is mediated by anxiety and depression in patients with tinnitus [31]. A similar model could be assumed for other diseases, as PD or MS.

Also coping style has been proposed as an important mediating factor with regard to adaptation to illness [17, 45-47]. Patients who more frequently used the emotional coping style reported being more disabled by their disease and suffering from poorer mental health and quality of life [48-50]. A higher level of neuroticism and a low level of extroversion were found to be related to the emotion-focused coping strategy of MS patients [51]. Also, in a sample of young adults suffering from headache, those reporting lower levels of active pain-coping showed the highest level of depressive symptoms [47]. Wahl et al. emphasized that being informed about coping strategies and their relationship to aspects of quality of life in patients with chronic diseases is important in order to establish health care interventions aimed to enhance coping skills [48].

Strengths and limitations

The study's main strength is its comparison of both chronic neurological diseases from, to our knowledge, a new point of view. The results of this study could be helpful for understanding the complexity of QoL and its factors in patients with chronic progressive neurological diseases. One of the limitations of the study is its cross-sectional design, which does not provide us with information about changes to the patient over time, and thus does not enable us to compare pathways. The low response rate might also have an impact on generalization of the results to the total population of PD and MS patients. Regrettably, we have no information about the disease duration and disease severity of non-respondents. However, it might be supposed that they refused to participate in the study because of serious motor complications found in the higher stages of PD and MS and due to the need for help from their social surroundings.

Implications

Identification of the mechanisms and consequences of functioning health perception in chronically ill patients is still a big challenge for further research. Research on QoL in patients with MS and PD should in further studies incorporate personality as an integral part of the explanatory models of quality of life; next, the relationship between mood status or psychological distress, personality traits and QoL should be explored, as well as other psychological factors which could contribute to clarify the pathways of the variables predicting quality of life of patients with chronic diseases [52]. For neurological practice the study outcomes suggest that good treatment of mood disorders could substantially contribute to a better quality of life.

Conclusion

Our findings show that actual mood status of MS and PD patients could be more important than their personality traits in assessment of QoL. To complete the model and to clarify the pathway predicting QoL, which could explain most of the variance of QoL in chronically ill patients, is a great challenge for further research. A similar model could have great meaning for clinicians, enabling them to modify their treatment style such that each patient can benefit optimally from it.

Acknowledgements

This work was supported by the Science and Technology Assistance Agency under contract No. APVV-20-038305.

References

[1] Roth J, Sekyrova M, Ruzicka E, *et al. Parkinsonova nemoc [Parkinson's disease]*. 2nd edn. Praha: Maxdorf, 1999.

[2] Simons G, Thompson SB, Smith-Pasqualini MC. An innovative education program for people with Parkinson's disease and their carers. *Parkinsonism and Related Disorders* 2006; 12: 478-85.

[3] European Commission. Some elements on the situation of multiple sclerosis in the European Union, 2004. [http://ec.europa.eu/health/ph_information/dissemination/diseases/neuro_1.pdf]

[4] McDonald WI, Compston A, Edan G, *et al*. Recommended diagnostic criteria for multiple sclerosis: Guidelines from the international panel on the diagnosis of multiple sclerosis. *Annals of Neurology* 2001; **50:**121–127.

[5] Bashir K,Whitaker JN. Handbook of Multiple Sclerosis. Philadelphia: Lipinncott Williams and Wilkins, 2002.

[6] Damiano AM, Snyder C, Strausser B, Willian MK. A review of health-related quality of life concepts and measures for Parkinson's disease. *Quality of Life Research* 1999; **8:** 235-243.

[7] Schrag A, Jahanshahi M, Quinn N. How does Parkinson's disease affects quality of life? A comparison with quality of life in general population. *Movement Disorders* 2000; **15:** 1112-1118.

[8] Benito-Leon J, Morales JM, Rivera-Navarro J, Mitchell AJ. A review about the impact of multiple sclerosis on health-related quality of life. *Disability and Rehabilitation* 2003; **25:** 1291–1303.

[9] Mitchell AJ, Benito-Leon J, Gonzalez JM, Rivera-Navarro J. Quality of life and its assessment in multiple sclerosis: Integrating physical and psychological components of well-being. *Lancet Neurology* 2005; **4:** 556–566.

[10] Riazi A, Hobart JC, Lamping DL, *et al*. Using the SF-36 measure to compare the health impact of multiple sclerosis and Parkinson's disease with normal population health profiles. *Journal of Neurology, Neurosurgery, and Psychiatry* 2003; 74: 710-714.
[11] Slaughter JR, Slaughter KA, Nichols D, Holmes SE, Martens MP. Prevalence, clinical manifestations, etiology, and treatment of depression in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neurosciences* 2001; **13:** 187–196.
[12] Schrag A. Quality of life and depression in Parkinson's disease. *Journal of the Neurological Sciences* 2006; 248: 151-157.
[13] Sadovnick AD, Remick RA, Allen J, *et al.* Depression and multiple sclerosis. *Neurology* 1996; **46:** 628–632.
[14] Chwastiak L, Ehde DM, Gibbons LE, Sullivan M, Bowen JD, Kraft GH. Depressive symptoms and severity of illness in multiple sclerosis: epidemiological study of a large community sample. *American Journal of Psychiatry* 2002; **159:** 1862–1868.
[15] Brown RF, Valpiani EM, Tennant CC, *et al.* Longitudinal assessment of anxiety, depression, and fatigue in people with multiple sclerosis. *Psychology and Psychotherapy* 2009; **82:** 41-56.
[16] Coffey CE, Cummings JL. Parkinson's disease and parkinsonism. In: Coffey CE, Cummings JL, eds. Textbook of Geriatric Neuropsychiatry. Washington DC: American Psychiatric Press, 1994: 434–456.
[17] Goretti B, Portaccio E, Zipoli V, *et al*. Coping strategies, psychological variables and their relationship with quality of life in multiple sclerosis. *Neurological Sciences* 2009; **30:** 15-20.
[18] Montel S, Bonnet A-M, Bungener C. Quality of life in relation to mood, coping strategies, and dyskinesia in Parkinson's disease. *Journal of Geriatric Psychiatry and Neurology* 2009; **22:** 95-102.
[19] Larsen RJ. Neuroticism and selective encoding and recall of symptoms: Evidence from a combined concurrent-retrospective study. *Journal of Personality and Social Psychology* 1992; **62:** 480–488.
[20] Kempen GIJM, Jelicic M, Ormel J. Personality, chronic medical morbidity, and health-related quality of life among older persons. *Health Psychology* 1997; **16:** 539–546.
[21] Jelicic M, Kempen GI, Passchier J. Psychological well-being in older adults suffering from chronic headache. *Headache* 1998; **38:** 292–294.
[22] Ranchor AV, Sanderman R, Steptoe A. Pre-morbid predictors of psychological adjustment to cancer. *Quality of Life Research* 2002; 11: 101–113.
[23] Ramirez-Maestre C, Martinez AEL, Zarazaga RE. Personality characteristics as differential variables of the pain experience. *Journal of Behavioral Medicine* 2004; **27:** 147–165.
[24] Kidachi R, Kikuchi A, Nishizawa Y, Hiruma T, Kaneko S. Personality types and coping style in hemodialysis patients. *Psychiatry and Clinical Neurosciences* 2007; **61:** 339–347.
[25] van Straten A, Cuijpers P, van Zuuren FJ, Smits N, Donker M. Personality traits and health-related quality of life in patients with mood and anxiety disorders. *Quality of Life Research* 2007; **16:** 1-8.

[26] Dubayova T, Nagyova I, Havlikova E, *et al*. Neuroticism and extraversion in association with quality of life in patients with Parkinson's disease. *Quality of Life Research* 2009; **18:** 33-42. a
[27] Pedersen SS, Denollet J. Validity of the Type D personality construct in Danish post-MI patients and healthy controls. *Journal of Psychosomatic Research* 2004; **57:** 265-572.
[28] Denollet J. DS-14: Standard assessment of negative affectivity, social inhibition and Type D personality. *Psychosomatic Medicine* 2005; **67:** 89-97.
[29] Mols F, Denollet J. Type D personality among nonvascular patient populations: a systematic review. *General Hospital Psychiatry* 2009. DOI: 10.1016/j.genhosppsych.2009.09.010 (article in press)
[30] Dubayova T, Nagyova I, Havlikova E, *et al*. The association of type D personality with quality of life in patients with Parkinson's disease. *Aging and Mental Health* 2009; 13: 905-912. b
[31] Bartels H, Pedersen SS, van der Laan BFAM, Staal MJ, Albers FWJ, Middel B. The impact of Type D personality on health-related quality of life in tinnitus patients is mainly mediated by anxiety and depression. *Otology and Neurotology* 2010; **31:** 11-18.
[32] Emons WHM, Meijer RR, Denollet J. Negative affectivity and social inhibition in cardiovascular disease: Evaluating type-D personality and its assessment using item response theory. *Journal of Psychosomatic Research* 2007; 63: 27-39.
[33] Hughes AJ, Daniel SE, Kilford L, Lees AJ. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery and Psychiatry* 1992; **55:** 181-184.
[34] Folstein MF, Folstein SE, McHough PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. *Journal Psychiatric Research* 1975; 12: 189-198.
[35] van Hilten JJ, van der Zwan AD, Zwinderman AH, Ross, RA. Rating impairment and disability in Parkinson's disease: evaluation of the Unified Parkinson's disease Rating Scale. *Movement Disorders* 1994; **9:** 84-88.
[35] Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983; **33:**1444-1452.
[37] Zigmond S, Snaith R. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica* 1983; **67:** 361-370.
[38] Ware J, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). *Medical care* 1992; **30:** 473-483.
[39] Ware JE, Snow KK, Kosinski M, Gandek M. SF-36 Health survey: manual and interpretation guide. Boston: New England Medical Center, 1993.
[40] Newcombe RG, Altman DG. Proportions and their differences. In: Altman DG, Machin D, Bryant TN, eds. Statistic with confidence. London: BMJ Books, 2000.

[41] Horstink M, Tolosa E, Bonuccelli U, *et al*. European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. *European Journal of Neurology* 2006; **13:** 1170-1185. a

[42] Horstink M, Tolosa E, Bonuccelli U, *et al*. (2006b). European Federation of Neurological Societies; Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES). Part II: late (complicated) Parkinson's disease. *European Journal of Neurology* 2006; **13:** 1186-1202. b

[43] Vidal A, Gomez-Gil E, Sans M, *et al*. Health-related quality of life in inflammatory bowel disease patients: the role of psychopathology and personality. *Inflammatory Bowel Diseases* 2008; **14:** 977-83.

[44] Andrews G, Titov N. Depression is very disabling. *The Lancet* 2007; **370:** 808-809.

[45] Allison PJ, Locker D, Feine JS. Quality of life: a dynamic construct. *Social Science and Medicine* 1997; **45:** 221-230.

[46] Hyland ME. A reformulation of quality of life for medical science. *Quality of Life Research* 1992; **1:** 267-272.

[47] Buenaver LF, Edwards RR, Smith MT, Gramling SE, Haythornthwaite JA. Catastrophizing and pain-coping in young adults: Associations with depressive symptoms and headache pain. *The Journal of Pain* 2008; **9:** 311-319.

[48] Wahl A, Hanestad BR, Wiklund I, Moum T. Coping and quality of life in patients with psoriasis. *Quality of Life Research* 1999; **8:** 427-433.

[49] Hesselink AE, Penninx BW, Schlösser MA, *et al*. The role of coping resources and coping style in quality of life of patients with asthma or COPD. *Quality of Life Research* 2004; **13:** 509-518.

[50] Folkman S, Lazarus RS. Centrality and individual differences in the meaning of daily hassles. *Journal of Personality* 1988; **56:** 743-62.

[51] Ratsep T, Kallasmaa T, Pulver A, Gross-Paju K. Personality as a predictor of coping efforts in patients with multiple sclerosis. *Multiple Sclerosis* 2000; **6:** 397–402.

[52] Havlikova E, Rosenberger J, Nagyova I, Middel B, Dubayova T, Gdovinova Z, van Dijk JP, Groothoff JW. Impact of fatigue on quality of life in patients with Parkinson's disease. *European Journal of Neurology* 2008; **15:** 475-480.

Chapter 7

General discussion and implications for practice and future research

The majority of clinical studies, focusing on quality of life of patients with Parkinson's disease, are oriented on the effect of medical treatment of motor and non-motor symptoms in terms of quality of life. Less frequently psychological factors are studied which may contribute to patients' perception of their quality of life. Although personal factors are part of the International Classification of Functioning, Disability and Health (ICF) model such factors, and among them personality, do not belong to the main factors which are taking into account in research in chronic diseases. This thesis explores the association of psychological factors with the perception of quality of life in patients with PD and, in addition, investigates whether psychological factors are associated with patient's help-seeking behavior and contribute to quality of life.

In this chapter firstly the main findings will be presented and discussed. Secondly, the study strengths and limitations of the research are mentioned. Last part is focusing on the implications of the results for practice, for the patients with Parkinson's disease and for further research.

7.1 Main findings

The main findings were organized according the main research questions.

7.1.1 The exploration of the associations between various personality traits, neuroticism, extroversion, negative affectivity, social inhibition and Type D personality and quality of life in PD patients. In addition, gender differences were examined as well.

We expected an association between personality traits (neuroticism, extroversion, negative affectivity, social inhibition and Type D personality) and quality of life in patients with Parkinson's disease. We also hypothesized, that each of the domains of quality of life is determined by different predictors. For this reason we used the PDQ-39 and its 8 scales: *mobility*, *activities of daily living*, *emotional well-being*, *stigma*, *social support*, *cognition*, *communication* and *bodily discomfort*.

Into the models variables were added, which may influence the association between personality traits and quality of life: disease severity (measured by UPDRS), disease duration and age. Despite their strong influence, the personality traits explained 8-24% of the variance of 6 dimensions of QoL (Chapter 2 and Chapter 3, Table 2.3, Table 3.3). After the UPDRS, Type D explained most of the variance in the overall model of quality of life for patients with Parkinson's disease and it was strongly associated with the dimensions *emotional well-being*, *stigma*, *social support*, *cognitions* and *communication*, but it was not significantly associated with *mobility*, *activities of daily living* and *bodily discomfort*, which were explained only by the UPDRS. Patients with higher scores on the neuroticism scale from the Eysenck Personality Questionnaire reported similarly like Type D patients a significantly worse status in the domains of *emotional well-being*, *stigma*, *social support* and also, on the contrary to Type D, in *bodily discomfort*, but not in *mobility*, *activities of daily living* and *cognitions*.

In comparisons between genders differences were found. Type D explained *emotional well-being* in both genders. Among men, Type D was an important factor in the models of *stigmatization by illness*, *cognition* and *communication* but personality played no role in these models among women. In both genders, negative affectivity (NA) and neuroticism explained 8.5-13.4 % of the variance in *emotional well-being*. A higher score in NA was associated with a worse score in the dimensions of *stigma* and *cognition* in men, while in women it was associated with a worse score in *social support*. In the model of overall quality of life, NA appeared to be important for both genders, contrary to social inhibition, which did not play a role in the model. Neuroticism played a role in the subscales of *stigma* and *social support* in women, but it did not appear to be important in men.

7.1.2 Differences between delayers and non-delayers regarding psychological factors associated with quality of life in patients with PD were explored and additionally the impact of fear and anxiety on help-seeking behavior in non-parkinsonian diseases.

Psychological factors might play a role in delaying patients and could affect QoL of such patients. The length of the patient's delay might give important information for the clinician. Because of the lack of such papers in neurological journals, we decided to do a review on delay in the field of cancer, a frequently slow developing disease, and acute myocardial infarction, an acute developing disease.

The intensity of fear is a factor, which has an impact on the decision making process of the patient. The higher the level of fear the shorter the time of the arrival to the medical doctor was. 'Being worried'

was not enough for seeking help, but probably it is starting the process of internal thinking about the possibility of being treated. 'Fear' seems to be a factor for longer delay, but the decision process in patients experiencing fear was also influenced by other factors, such as embarrassment, pressure from a patient's relatives or fear of financial consequences. 'Being anxious' and feelings of 'panic' or 'death anxiety' was associated with seeking help within a few hours.

Shortening of the patient's delay has in case of cancer and AMI impact on successfulness of treating and, indirectly, on their quality of life. The aim of our study was to explore, whether patients with PD are different in their quality of life stratified for patient's delay and whether the association of personality traits and quality of life in patients with PD is influenced by delay. Patients with PD who came earlier to see a health care professional differed from delayers by a worse functional status and they had a significantly lower physical quality of life than delayers. In neuroticism no differences were found, for both groups neuroticism was strongly associated with lower quality of life – mental and also physical. However, non-delayers were more extrovertly oriented than delayers.

7.1.3 The comparison of the role of the association of psychological factors – Type D personality, anxiety and depression – with quality of life in patients with PD and multiple sclerosis (MS).

Mood disorders, especially depression, are among the clinical symptoms of both diseases [1,2]. Because in previous studies we concluded, that personality traits (especially Type D and neuroticism) are determinants of quality of life in patients with Parkinson's disease, we explored whether Type D was associated with quality of life in PD and MS patients even when depression and anxiety was added to the model of patients' self-perceived quality of life.

Type D personality significantly associated with worse mental health status of PD patients and with decreasing scores in mental and physical domains of quality of life in MS patients. However, when the actual mood factors depression and anxiety were added, the significant association of personality traits with quality of life disappeared. This finding, the disappearing significance between personality and QoL after adding mood variables, suggests a combined pathway from personality via mood variables to quality of life.

7.2 Discussion of the main findings

Personality traits and quality of life

Findings from longitudinal studies show that Parkinson's disease affects patients' lives in a broader sense than by physical impairment, and that despite modern treatment, the impact of the disease increases as the disease progresses [3]. Personality, according the ICF model, belongs to the contextual factors, which influence patient's functioning and disability [4]. Furthermore, a review indicated that psychological and social variables influence perception of health status, mostly in case of pain, more powerfully than biological factors [5]. Several studies confirmed that personality affects patients' reports of symptoms of disease; especially neuroticism and extraversion were associated with the tendency to recall physical symptoms as being worse than they really were [6,7]. In addition, extraversion influences the level of coping with chronic disease, which influences, negatively or positively, the level of quality of life [8,9]. In this thesis it was shown, that in case of patients with Parkinson's disease, personality traits (directly, and also indirectly through the actual mood) play an important role in quality of life assessment, as well. In line with our results, we can state, that quality of life in patients with Parkinson's disease can be partially explained by personality traits.

In other studies gender differences were observed in patients with Parkinson's disease. Mildly significant differences in disability and quality of life have been noted between genders in parkinsonian patients: women reported more disability and reduction of quality of life than men [10]. Findings of Huang (2007) showed that women reported more problems in stigmatization, and men reported more problems in activities *of* daily *life*. The author also observed, that women with higher levels *of* facial expressivity felt less problems in social support and communication then women with less facial expressiveness due to the Parkinson mask *[11]*. Worse score in *social support* in women in our study was explained by negative affectivity, but it could be also associated with their worse communicational ability associated with the decreased facial expressiveness as showed by Huang's study *[11]*. The aim for further studies is to compare these results with studies in gender differences of other diseases for better understanding of the impact of psychological factors like personality on patients' complaints.

Delayers and non-delayers and quality of life

Even though Parkinson's disease has no such fatal consequences for surviving or successfulness of treatment as other diseases, e.g. acute myocardial infarction or cancer, patient's delay is an interesting phenomenon in this case. Outpatient neurologists report differences

in assessment of impairment by PD patients themselves, which may caused early or late help-seeking – patients with serious impairment sometimes do not seek help so early, as it would be expected. According to our findings delayers and non-delayers among PD patients differed, except disease severity, but also regarding extraversion (Chapter 5). Extraversion positively correlates with social activity and social support [12,13]. Therefore, patients with health complaints with a supporting environment tend to seek help sooner. The possibility of sharing feelings with somebody has a significant impact on the decision to consult a specialist [14-16]. Late help seeking could be associated with three main reasons: a) a low disease severity; b) introversion and/or lack of social contacts; c) fear from consequences of the visit medical care, leading to delay. Prevention of patient's delay in PD patients should be based on providing information how to recognize symptoms of disease and also about treatment and rehabilitation. This may lead to minimize fear from the unknown for the people involved, and for other people from society it can help to act and help to people from their surrounding.

Personality, mood disorders and quality of life

In accordance with results presented in Chapter 6 we can suppose that actual mood disorders, depression and anxiety, have more serious impact on quality of life than personality traits not only in PD patients, but also in patients with multiple sclerosis. However, predispositions to depression and anxiety are closely associated with neuroticism and extraversion. As results of several study shows, high extraversion scores may protect against depression and neuroticism reflects symptoms of depression [17-19]. Therefore, for further research in factors of quality of life can be hypothesized, that mood disorder may mediate the relationship between personality traits and quality of life. Mood variables mediating the relationship from personality to QoL was recently suggested by Bartels and colleagues in the field of tinnitus. The authors in that study presented a model in which Type D personality on quality of life is mediated by anxiety and depression in patients with tinnitus [20]. A similar model could be assumed for Parkinson's disease, as well.

7.3 Study strengths and limitations

The thesis is focused on psychological factors relevant for Parkinson's disease, a topic which is not included into most clinical studies. These factors contribute to a comprehensive picture of the total disease impact on patients' quality of life. Main strength of the thesis is the use of psychological factors as independent variables associated with quality of life in patients with Parkinson's disease. Most studies about quality of

life in those patients are focusing on the association of clinical symptoms and their influence on patient's overall quality of life or on the effect of the treatment process. Studies explaining the impact of psychological factors on perception of quality of life in this group of patients, except mood disorders, are missing. The results of our thesis could be helpful for understanding the complexity of quality of life and its factors in patients with Parkinsonism. Although the association between patients' delay and personality traits was still not been adequately explained, we try to contribute to the knowledge about this interesting phenomenon.

The low response rate was a limitation of this study. It may have an impact on generalization of the results to the total population of PD patients. Non-respondents were older than respondents, so it may be hypothesized that they refused to participate in the study because of serious motor complications found in the higher stages of PD and due to the need for help from their social surroundings. Regrettably, we have no information about disease duration and disease severity of non-respondents. Another limitation was the cross-sectional design of the study, not enabling us to explore causal relationships between variables. However, we would like also to point out, that the tendencies in the majority of the present studies are focused on the objectification of the patient's perception of quality of life and furthermore on studying factors, which could explain totally the model of quality of patient's life. However, these study approaches are not centered to the patient and his quality of life. Quality of life starts to be an abstract concept, which is related to answers of the sample of the patients with a certain diagnosis and which disease is measured by objective and valid instruments. Duchan warns against the danger of this kind of studies - our own study belongs to this type - because they could lead to ignore patient's experience as something unscientific and too subjective [21]. As was pointed out, without adequate preliminary qualitative research, quantitative research might risk a misanalysis of the target phenomenon, at the very least by the omission of relevant factors and inclusion of irrelevant ones [22].

7.4 Implications of the findings

Implications for practice

More knowledge about the association of personality traits and their contribution on patients' quality of life may give a clearer view on how to evaluate patient complaints in the case of worsening quality of life, especially in patients with Parkinson's disease. Assessment of quality of life of patients is not easy for clinicians especially because of blank stare and low mimic ("Parkinson's mask") which complicate communication

and decrease the validity of information about the well-being or the health status from the patient. Health-care providers should be aware *of* the potential relationship between facial expressiveness and the relationship with the patient, which brings implications for family, community, and therapeutic relationships *[11]*. Neurologists should be aware of factors associated with patient's quality of life in order to be able to choose the most effective interventions in the framework of treatment.

The gender aspect of quality of life appears to be an important topic, contributing to the knowledge about psychological differences between men and women. Consequently, coping styles and self-management skills in both genders might also differ, as has been shown in several studies on cancer and chronic pain [23,24]. For adjustment to the chronic pain problems the aforementioned coping styles were more important in women, whereas possessing a trusting relationship was more important for men in their adjustment process [22]. In cancer patients men are focusing on the positive sides more often than women did ($P<0.01$) [25]. Women, during stressful times, prefer to talk about it and share their feelings with others, but men with cancer would rather not [26]. Differences between men and women could be determined by cultural roles [26,27]. Different needs of men and women with PD should be taken into account in psychological intervention programs, which need to be different for both genders.

Quality of life of PD patients is closely associated with their functional status and reducing their activities of daily living, losing ability to devote to their hobbies and, consequently, reducing their participation in social life. Their social surrounding taking care on them and it could evoke feeling of guilt and dependence. Early help-seeking could prolong their active life and improve quality of life, especially in patients with diseases, which affect motor abilities, e.g. Parkinson's disease.

Recommendations for future research

One of the limitations of the study was the low response rate. Patients, even they were contacted via phone, had several problems to participate in the study. The possibility of visiting patients at home could increase their willingness to agree with participation.

For quantitative studies the ICF model helps the researcher to include all important factors to the research project and it helps to understand the concept of quality of life in a broader context. Well-designed gender studies are of importance for a profound understanding of the impact of gender on the perception of quality of life and it can improve medical care. The need to differentiate between women and men is observed also in other diseases than PD, e.g. in oncological patients [28]. Gender influences

social roles of patients with Parkinson's disease, thus it can moderate the patient's perceptions of quality of life *[11]*. Further studies are needed to explore the health and psychosocial consequences of the gender difference in self-rated social status – models of quality of life for men and women could be composed from different variables. The important question is whether gender differences are disease specific or that they are a constant phenomenon also present in other diseases. Therefore, psychological factors should be an important part of the diagnostic and treatment process of patients with Parkinson's disease, because the report of the patient about his/her symptoms may be distorted by his actual psychological status or personality and more studies based on qualitative analyses are needed. Qualitative studies could help us to interprete quantitative findings and they might help to understand the meanings, practices and context of measured variables.

Conclusion

Because of the increasing mean age of European population, it is more and more important to provide care for patients in a higher age. With increasing age a decreasing quality of life is associated not only because of the increasing occurrence of various diseases, which limit patients in his/her activities of daily living, but also because of factors associated with social conditions and psychological factors. Knowledge about factors associated with decreasing (but also increasing) quality of life in aged people means a challenge for future research and personality traits should be one of important variables of the models. Developing effective disease-management programs for patients with chronic diseases such as Parkinson's disease incorporating all possible knowledge about influencing factors is needed.

References

[1] Sadovnick AD, Remick RA, Allen J, *et al.* Depression and multiple sclerosis. *Neurology* 1996; **46:** 628–632.

[2] Slaughter JR, Slaughter KA, Nichols D, Holmes SE, Martens MP. Prevalence, clinical manifestations, etiology, and treatment of depression in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neurosciences* 2001; **13:** 187–196.

[3] Karlsen KH, Tandberg E, Arsland D, Larsen JP. Health related quality of life in Parkinson's disease: a prospective longitudinal study. *Journal of Neurology, Neurosurgery and Psychiatry* 2000; **69:** 584 –589.

[4] World Health Organisation (WHO). International classification of functioning, disability, and health (ICF). Geneva, World Health Organization; 2001.
[5] Greenspan, J. D., Craft, R. M., LeResche, L., *et al.* Studying sex and gender differences in pain and analgesia: A consensus report. *Pain* 2007; **132**(Suppl 1): S26–S45.
[6] Costa PT, McCrae RR. Neuroticism, somatic complaints and disease: Is the bark worse than the bite? *Journal of Personality* 1987; **55:** 299-316.
[7] Larsen RJ. Neuroticism and selective encoding and recall of symptoms: Evidence from a combined concurrent-retrospective study. *Journal of Personality and Social Psychology* 1992; **62:** 480-488.
[8] Ramírez-Maestre C, Martinez AEL, Zarazaga RE. Personality characteristics as differential variables of the pain experience. *Journal of Behavioral Medicine* 2004; **27:** 147-165.
[9] Kidachi R, Kikuchi A, Nishizawa Y, Hiruma T, Kaneko S. Personality types and coping style in hemodialysis patients. *Psychiatry and Clinical Neurosciences* 2007; **61:** 339-347.
[10] Shulman LM. Gender differences in Parkinson's disease. *Gender Medicine* 2007; **4:** 8-18.
[11] Huang P-Ch. Social behavior, gender, and quality of life in Parkinson's disease. Dissertation Abstracts International: Section B: The Sciences and Engineering, 70(5-B), 2009. [Dissertation]
[12] Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Inventory. London: London University of London Press, 1994.
[13] Von Dras DD, Siegler IC. Stability in extraversion and aspects of social support at midlife. *Journal of Personality and Social Psychology* 1997; **72:** 233-241.
[14] Burgess CC, Ramirez AJ, Richards MA, Love SB. Who and what influences delayed presentation in breast cancer? *British Journal of Cancer* 1998; **77:** 1343-1348.
[15] de Nooijer J, Lechner L, de Vries H. A qualitative study on detecting cancer symptoms and seeking medical help; an application of Andersen's model of total delay. *Patient Education and Counseling* 2001; **42:** 145-157.
[16] Kentsch M, Rodemerk U, Müller-Esch G, Schnoor U, Münzel T, Ittel TH, Mitusch R. Emotional attitudes toward symptoms and inadequate coping strategies are major determinants of patient delay in acute myocardial infarction. *Zeitschrift Für Kardiologie* 2002; **91:** 147-155.
[17] Jorm AF, Christensen H, Henderson AS, Jacomb PA, Korten AE, Rodgers B. Predicting anxiety and depression from personality: Is there a synergistic effect of neuroticism and extraversion? *Journal of Abnormal Psychology* 2000; **109:** 145-149.

[18] Farmer A, Redman K, Harris T, Mahmood A, Sadler S, Pickering A, McGuffin P. Neuroticism, extraversion, life events and depression: The Cardiff Depression Study. *British Journal of Psychiatry* 2002; **181:** 118-122.
[19] Jylhä P**,** Isometsä E. Temperament, character and symptoms of anxiety and depression in the general population. *European Psychiatry* 2006; **21:** 389-395.
[20] Bartels H, Pedersen SS, van der Laan BFAM, Staal MJ, Albers FWJ, Middel B. The impact of Type D personality on health-related quality of life in tinnitus patients is mainly mediated by anxiety and depression. *Otology and Neurotology* 2010; **31:** 11-18.
[21] Duchan, JF. Commentary: Where is the person in the ICF? *Advances in Speech Language Pathology* 2004; **6:** 63-65.
[22] Hawkes G, Rowe G. A characterization of the methodology of qualitative research on the nature of perceived risk: Trends and omissions. *Journal of Risk Research* 2008; **11:** 617-643.
[23] Weir R, Browne G, Tunks E, Gafni A, Roberts J. Gender differences in psychosocial adjustment to chronic pain and expenditures for health car services used. *Clinical Journal of Pain* 1996; **12:** 277-290.
[24] Wilz G. (). Predictors of subjective impairment after stroke: Influence of depression, gender and severity of stroke. *Brain Injury* 2007; **21:** 39-45.
[25] Hjörleifsdóttir E, Hallberg IR, Bolmsjö IA, Gunnarsdóttir ED. Distress and coping in cancer patients: Feasibility of the Icelandic version of BSI 18 and the WOC-CA questionnaires. *European Journal of Cancer Care* 2006; **15:** 80-89.
[26] Kiss A, Meryn S. Effect of sex and gender on psychosocial aspects of prostate and breast cancer. *British Medical Journal* 2001; **323:** 1055-1058.
[27] Behari M, Srivastava AK, Pandey RM. Quality of life in patients with Parkinson's disease. *Parkinsonism and Related Disorders* 2005; **11:** 221-226.
[28] Giesinger J, Kemmler G, Mueller V, *et al.* Are gender-associated differences in quality of life in colorectal cancer patients disease-specific? *Quality of Life Research* 2009; **18:** 547-555.

Summary

Nowadays, approximately 6 million people are affected by Parkinson's disease (PD) worldwide, but this number is not exact, because many people remain undiagnosed. The motor impairment, which is the most visible symptom of the disease, affects all domains of the patient's life – physical, psychological and social. A slow and uncertain movement, tremors and falls inhibit patients to do activities of daily living, to fully use the leisure time, and to be active in social life. Although there are many studies, which are focused on measurement the quality of life (QoL) of those patients, studies about their personality and other psychological factors associated with QoL in PD patients are scarce. In our research we focused mostly on personality (extraversion, neuroticism, type D personality, negative affectivity and social inhibition) and mood disorders (depression, anxiety) as factors associated directly with QoL or indirectly – through patient's delay (Figure 1.3).

The first aim of *Chapter 2* was to explore whether neuroticism and extraversion contribute to the variance in QoL in patients with Parkinson's disease. Multiple linear regression analyses were performed to identify how much the variance of the dependent variables, dimensions of the questionnaire PDQ-39 (*mobility*, *activities of daily living*, *emotional well-being*, *stigma*, *social support*, *cognition*, *communication* and *bodily discomfort*), could be explained by the personality traits if controlled for the relevant sociodemographic (age and gender) and clinical variables (disease severity and disease duration). After disease severity, which we expected as the most important factor influencing QoL, neuroticism was the second most important variable in the model of QoL, particularly in domains associated with psychological processes: *emotional well-being*, *social support*, *stigma* and *bodily discomfort*, explaining 5-24% of the variance of QoL. The second aim of the study was to explore gender differences in the variables in the models of QoL. A higher score in extraversion was significantly associated with better *emotional well-being* in males, but surprisingly, with worse *emotional well-being* in females. According results we can hypothesize, that neuroticism is affecting the perception of QoL and in further research gender differences - males and females develop different ways of coping and experiencing the world - can be taken into account.

In the *Chapter 3* we continued in line with results presented in *Chapter 2*. The aim of this study was to evaluate whether Type D personality, and its two subscales – negative affectivity (NA) and social inhibition (SI), predicts QoL in patients with PD and, in addition, gender differences in Type D personalities were explored. Type D was negatively

associated with overall QoL in PD patients and with all dimensions except *mobility*, *activities of daily living* and *bodily discomfort*. In women, a higher NA explained the higher dissatisfaction with *social support*. For overall QoL, NA explained 13.2% ($P<0.001$) of the variance in males and 9.3% ($P<0.01$) of the variance in females. SI also explained a maximum of 5.5% ($P<0.05$) of the variance in *communication* in men and 7.3% ($P<0.05$) *stigma* in women. In short, personality traits play an important role in the explanation of QoL in PD patients. The gender differences suggest that models of QoL for men and women are composed from different variables.

Chapter 4 presents a systematic review focusing on the role of the intensity of fear in patient's delay in seeking medical help. We used studies about rather common diseases - cancer and myocardial infarction, mostly for the reason of quantity of such kind of studies in those diseases. In a search of literature published between 1990 and June 2009, 161 articles were found. After the use of inclusion and exclusion criteria, 11 articles in cancer and 4 articles in myocardial infarction remained. Fear ranged on a scale from the lowest level of 'being worried', which is not enough to initiate the early contacting of a specialist, to the level of 'panic'. People who were extremely alarmed about the first signs of their disease were ready to consult their general practitioner (GP) within a few hours. The main result of this review was to show, that the level of fear influenced decision-making. This important factor should be taken into account when facilitating help-seeking by patients, and especially in cases of low level of fear, encouraging them to seek medical care.

Patient's delay was also the topic of *Chapter 5*. Here we explored whether QoL in PD patients who delayed in seeking help was associated with personality traits. Because of the intermittent occurrence and slow progress of symptoms in the first phase of the disease, in several cases patients who sought medical help within 1 year of the appearance of the first signs and symptoms of the disease were marked as 'non-delayers' and those over 1 year as 'delayers'. This period was defined on the basis of interviews with patients – when the onset of disease was not dramatic, people attributed them frequently to 'stress'. Non-delayers scored higher in extroversion, which was associated also with better scores in physical and mental health summary score. Results showed, that social interactions, associated with an extrovertly oriented personality, can force decision making on help-seeking.

Many studies confirmed that anxiety and depression were assumed to be the variables associated with worsening QoL in various diagnoses. Because in previous studies we concluded, that personality traits (especially Type D and neuroticism) are determinants of quality of life, in *Chapter 6* we examined whether Type D is associated with the mental and physical health status of quality of life in PD and in patients with multiple sclerosis (MS) even when depression and anxiety were added to the model.

Our findings showed that higher scores in anxiety and depression were strongly associated with QoL in both diseases. Although initially Type D personality was associated with both dimensions of QoL – physical and mental health summary score, this association disappeared in both dimensions in MS and in the mental dimension in PD when the variables anxiety and depression were added to the model. Our findings suggest a combined pathway from personality via mood variables to quality of life.

In *Chapter 7* the main findings were discussed and implications for practice and for further research were formulated. In line with our results, we can state, that quality of life in patients with Parkinson's disease can be partially explained by personality traits and also the gender aspect of quality of life appeared to be an important topic contributing to the knowledge about psychological differences between men and women with PD. Actual mood disorders, depression and anxiety, are modifying the importance of personality traits in QoL and they seem to have more serious impact on quality of life than personality traits not only in PD patients, but also in patients with multiple sclerosis. According to our findings, delayers and non-delayers among PD patients differed regarding extraversion, which positively correlates with social activity and social support. Therefore, patients extravertly oriented who have the possibility to share feelings with somebody, seek help sooner then patients with low score in extraversion.

The limitation of the study was the relatively low response rate, which may have an impact on generalization of the results to the total population of PD patients. Also using longitudinal data in further research could help us better explaining causal relationships between variables. Further research of patient's delay should also combine qualitative and quantitative research for more precise interpretation of findings. Using qualitative methods could help to understand the meanings, practices and context of measured variables. To choose the most effective interventions in the framework of treatment, neurologists should take into account their patient's personality and his actual mood or motivation, next to the worsening or improving of the symptoms of the disease.

Samenvatting

Wereldwijd zijn ongeveer 6 miljoen mensen getroffen door de ziekte van Parkinson (PD). Echter, dit aantal is niet exact, omdat veel mensen niet gediagnosticeerd zijn. De motorische stoornissen, het meest zichtbare symptoom van de ziekte, zijn van invloed op alle domeinen van het leven van de patiënt - fysiek, psychologisch en sociaal. Langzame en onzekere bewegingen, tremoren en valneigingen beperken patiënten om volop deel te nemen aan de activiteiten van het dagelijks leven, om ten volle gebruik maken van de vrije tijd, en om actief te zijn in het sociale leven. Hoewel er veel studies zijn die gericht zijn op de meting van de kwaliteit van leven van deze patiënten, zijn studies over hun persoonlijkheid en andere psychologische factoren die samenhangen met de kwaliteit van leven van PD-patiënten schaars. In ons onderzoek concentreerden we ons vooral op de persoonlijkheid (extraversie, neuroticisme, type D persoonlijkheid, negatieve affectiviteit en sociale inhibitie) en stemmingsstoornissen (depressie, angst) als factoren die direct verband houden met kwaliteit van leven van de patiënt of indirect - via uitstel van hulpzoekgedrag van de patiënt.

Het eerste doel van *Hoofdstuk 2* was te onderzoeken of neuroticisme en extraversie bijdragen aan de variantie in kwaliteit van leven bij patiënten met de ziekte van Parkinson. Multipele lineaire regressie-analyses werden uitgevoerd om te bepalen hoe groot de variantie van de afhankelijke variabelen, in casu de dimensies van de vragenlijst PDQ-39 (*mobiliteit, activiteiten van het dagelijks leven, emotioneel welzijn, stigmatisering, sociale steun, cognitie, communicatie en lichamelijk ongemak*), kunnen worden verklaard door de persoonlijkheidskenmerken gecontroleerd voor de relevante sociaal-demografische (leeftijd en geslacht) en klinische variabelen (ernst en duur van ziekte). De ernst van de ziekte was zoals verwacht de belangrijkste factor geassocieerd met kwaliteit van leven. Daarna was neuroticisme de belangrijkste variabele, in het bijzonder in de domeinen geassocieerd met psychologische processen: *emotioneel welbevinden, sociale steun*, *stigmatisering* en *lichamelijk ongemak*, met een verklaring van 5-24% van de variantie van kwaliteit van leven. Het tweede doel van het onderzoek was om sekseverschillen in de variabelen in de modellen van de kwaliteit van leven te verkennen. Een hogere score in extraversie was significant geassocieerd met een beter *emotioneel welzijn* bij mannen, maar verrassend genoeg, met een slechter *emotionele welzijn* bij vrouwen. Op basis van de resultaten mogen we veronderstellen dat neuroticisme van invloed is op de perceptie van kwaliteit van leven; in verder onderzoek moet er rekening mee worden gehouden dat sekseverschillen ten

grondslag kunnen liggen aan verschillende manieren van omgaan met en het ervaren van de wereld.

In *Hoofdstuk 3* zijn we gaan voortbouwen op de resultaten zoals gepresenteerd in *Hoofdstuk 2*. Het doel van deze studie was om te evalueren of Type D persoonlijkheid met de twee subschalen - negatieve affectiviteit (NA) en sociale inhibitie (SI) - kwaliteit van leven voorspelt bij patiënten met PD. Bovendien zijn verschillen in Type D persoonlijkheid tussen mannen en vrouwen onderzocht. Type D is negatief geassocieerd met de algemene kwaliteit van leven in PD patiënten in alle dimensies, met uitzondering van de *mobiliteit*, *activiteiten van het dagelijkse leven* en *lichamelijke ongemak*. Bij vrouwen verklaarde een hogere NA de hogere ontevredenheid met *sociale steun*. Van de variantie in de algemene kwaliteit van leven verklaarde NA 13,2% (P <0,001) bij mannen en 9,3% (P <0,01) bij vrouwen. SI verklaarde ook een maximum van 5,5% (P <0,05) van de variantie in de *communicatie* bij mannen en 7,3% (P <0,05) van de *stigmatisering* bij vrouwen. Kortom, persoonlijkheidskenmerken spelen een belangrijke rol bij het verklaren van kwaliteit van leven bij PD patiënten. De verschillen tussen mannen en vrouwen suggereren dat modellen van kwaliteit van leven voor mannen en vrouwen zijn samengesteld uit verschillende variabelen.

In *Hoofdstuk 4* wordt een systematische review beschreven die gericht is op de rol van de intensiteit van angst bij de patiënt op uitstelgedrag bij het zoeken naar medische hulp. We gebruikten onderzoeken over veel voorkomende ziekten - kanker en myocardinfarct, overwegend vanwege de reden dat dit soort studies bij deze ziekten in zekere mate is verricht. In een eerste onderzoek naar de literatuur gepubliceerd tussen 1990 en juni 2009 werden 161 artikelen gevonden. Na het gebruik van inclusie- en exclusiecriteria, bleven 11 artikelen over kanker en 4 artikelen over een myocardinfarct over. Angst varieerde op een schaal van het laagste niveau van 'ongerust zijn', dat niet voldoende is om een vroeg contact op te nemen met een specialist, tot het niveau van 'paniek'. Mensen die zeer verontrust waren over de eerste tekenen van hun ziekte waren bereid om hun huisarts binnen een paar uur te raadplegen. Het belangrijkste resultaat van dit onderzoek was aan te tonen dat het niveau van angst het uitstelgedrag beïnvloedt. Met deze belangrijke factor moet rekening worden gehouden bij het vergemakkelijken van het zoeken naar hulp door de patiënten, door vooral de niet erg verontruste patiënten aan te moedigen om medische zorg te zoeken.

Uitstelgedrag van patiënten was ook het onderwerp van *Hoofdstuk 5*. Hier hebben we onderzocht of kwaliteit van leven bij PD patiënten met uitstelgedrag was geassocieerd met persoonlijkheidskenmerken. Vanwege het intermitterende voorkomen en de trage progressie van de symptomen in de eerste fase van de ziekte zijn patiënten die medische hulp zochten binnen 1 jaar na het verschijnen van de eerste tekenen en symptomen van de ziekte gedefinieerd als '*niet-delayers*' en degenen waarbij dit langer

dan 1 jaar duurde als '*delayers*'. Deze periode is vastgesteld op basis van interviews met patiënten. Was het begin van de ziekte was niet dramatisch, dan schreven de mensen het vaak toe aan 'stress'. *Niet-delayers* scoorden hoger in extraversie, dat ook werd geassocieerd met betere scores in de samenvattende lichamelijke en geestelijke gezondheid score. De resultaten toonden aan dat sociale interacties, samen met een extrovert georiënteerde persoonlijkheid, van invloed kan zijn op het besluitvormingsproces met betrekking tot het hulpzoekgedrag van de patiënt.

Talrijke studies hebben bevestigd dat angst en depressie variabelen zijn die gepaard gaan met verslechtering van de kwaliteit van leven bij verschillende ziektebeelden. Omdat in eerdere studies geconcludeerd is, dat de persoonlijkheidskenmerken (met name Type D en neuroticisme) determinanten van kwaliteit van leven zijn, hebben we in *Hoofdstuk 6* onderzocht of Type D in verband gebracht kan worden met de geestelijke en lichamelijke gezondheidstoestand bij PD patiënten en bij patiënten met multiple sclerose (MS), zelfs als depressie en angst werden toegevoegd aan het model. Onze bevindingen toonden aan dat hogere scores van angst en depressie sterk werden geassocieerd met kwaliteit van leven bij beide ziektebeelden. Hoewel aanvankelijk Type D persoonlijkheid geassocieerd was met beide dimensies van kwaliteit van leven – de samenvattende lichamelijke en geestelijke gezondheid score - verdween deze associatie bij beide dimensies in MS en in de geestelijke dimensie in PD wanneer de variabelen angst en depressie werden toegevoegd aan het model. Onze bevindingen suggereren een gecombineerd pad van de persoonlijkheid via de stemmingsvariabelen naar kwaliteit van leven.

In *Hoofdstuk 7* worden de belangrijkste bevindingen besproken en implicaties voor de praktijk en voor verder onderzoek geformuleerd. In overeenstemming met onze resultaten, kunnen we stellen, dat de kwaliteit van leven bij patiënten met de ziekte van Parkinson gedeeltelijk kan worden verklaard door persoonlijkheidskenmerken en ook het 'gender'-aspect van de kwaliteit van het leven bleek een belangrijk onderwerp dat bijdroeg aan onze kennis over de psychologische verschillen tussen mannen en vrouwen met PD. Actuele stemmingsstoornissen, depressie en angst, kunnen het verband tussen persoonlijkheidskenmerken en kwaliteit van leven modificeren en ze lijken meer ernstige gevolgen voor de kwaliteit van leven te hebben dan persoonlijkheidskenmerken, niet alleen bij PD-patiënten, maar ook bij patiënten met multiple sclerose. Volgens onze bevindingen, verschilden '*delayers*' en '*niet-delayers*' bij PD patiënten ten aanzien van extraversie, die positief correleert met sociale activiteiten en sociale steun. Daarom zullen extrovert georiënteerde patiënten die de mogelijkheid hebben om emoties te delen met iemand anders, sneller hulp zoeken dan patiënten met een lage score in extraversie.

De beperking van de studie was de relatief lage respons, die een effect kan hebben op de generalisatie van de resultaten naar de totale populatie

van PD patiënten. Longitudinale gegevens uit verder onderzoek zouden ons kunnen helpen meer inzicht te krijgen in de causale verbanden tussen de variabelen. Nader onderzoek naar uitstelgedrag van de patiënt zou kwalitatief en kwantitatief onderzoek moeten combineren voor een meer nauwkeurige interpretatie van de bevindingen. Kwalitatieve methoden zouden kunnen bijdragen om de betekenis, handelingen en de context van de gemeten variabelen beter te begrijpen. Voor het kiezen van de meest effectieve interventies in het kader van de behandeling van PD patienten, zouden neurologen meer rekening moeten houden met de persoonlijkheidskenmerken van hun patiënt en zijn werkelijke stemming, naast de verergering of verbetering van de symptomen van de ziekte.

Zhrnutie

V súčasnosti trpí približne 6 miliónov ľudí na svete Parkinsonovou chorobou (PD). Tento odhad však nemožno považovať za presný, pretože nie všetci postihnutí ochorením sú aj diagnostikovaní. Motorické poškodenie, ktoré je najviditeľnejším symptómom ochorenia, ovplyvňuje všetky oblasti pacientovho života – fyzickú, psychickú aj sociálnu. Pomalý a neistý pohyb, tras a pády inhibujú pacienta v aktivitách každodenného života, vo voľnočasových aktivitách a v jeho/jej sociálnom živote. Aj keď sa mnohé výskumy zameriavajú na kvalitu života tejto skupiny pacientov, štúdie z pohľadu ich osobnosti a iných psychologických faktorov, ktoré s kvalitou života súvisia, sú stále zriedkavé. V našom výskume sme sa zamerali na osobnosť (extroverziu, neuroticizmus, osobnosť typu D, negatívnu afektivitu a sociálnu inhibíciu) a na poruchy nálad (depresiu a anxietu) ako na faktory súvisiace s kvalitou života priamo alebo nepriamo – prostredníctvom oddiaľovania vyhľadania odbornej starostlivosti (Schéma 1.3).

Hlavným cieľom *Kapitoly 2* bolo zistiť, či sa neuroticizmus a extroverzia podieľajú na našom modeli kvality života pacientov s Parkinsonovou chorobou. Pomocou viacnásobnej lineárnej regresie sme zisťovali, či miera variancie jednotlivých dimenzií dotazníka na meranie kvality života ľudí s PD (PDQ-39), konkrétne *mobilita*, *každodenné aktivity*, *emocionálna pohoda*, *stigma*, *sociálna opora*, *kognitívne fakory*, *komunikácia* a *telesný diskomfort*, môže byť vysvetlená pomocou osobnostných vlastností za predpokladu, že kontrolujeme model aj z hľadiska relevantných sociodemografických (vek a pohlavie) a klinických premenných (závažnosť ochorenia a dĺžka ochorenia). Hneď po faktore závažnosti ochorenia, o ktorom sme predpokladali, že bude najdôležitejším faktorom ovplyvňujúcim kvalitu života, bol druhou závažnou premennou neuroticizmus, ktorý súvisel hlavne s modelmi dimenzií súvisiacich s psychologickými procesmi: *emocionálna pohoda*, *sociálna opora*, *stigma* a *telesný diskomfort*, v ktorých vysvetľoval 5-24% variancie kvality života. Sekundárnym cieľom výskumu bolo zistiť rozdiely v modeloch kvality života medzi pohlaviami. Vyššie skóre v extroverzii signifikantne súviselo s lepším skóre v dimenzii *emocionálna pohoda* u mužov, ale, prekvapujúco, s horším skóre v tej istej dimenzii, *emocionálna pohoda*, u žien. Na základe týchto výsledkov môžeme predpokladať, že neuroticizmus ovplyvňuje vnímanie kvality života. Nasledujúci výskum v oblasti rodových rozdielov by mal preto zohľadniť odlišné kopingové stratégie mužov a žien a ich rozdielne prežívanie.

Kapitola 3 nadväzuje vo výsledkoch na *Kapitolu 2*. Cieľom tejto štúdie bolo zistiť, či osobnosť typu D a jej dve podškály, negatívna afektivita (NA)

a sociálna inhibícia (SI), predikujú kvalitu života pacientov s PD. Zisťovali sme aj rodové rozdiely v osobnostiach typu D vzhľadom na kvalitu života. Typ D negatívne asocioval s celkovým skóre kvality života a so všetkým dimenziami PDQ-39 okrem *mobility*, *aktivít každodenného života* a *telesného diskomfortu*. U žien vyššia NA vysvetľovala vyššiu nespokojnosť v dimenzii *sociálna opora*. V celkovom skóre kvality života NA vysvetľovala 13.2% (P<0.001) variancie u mužov a 9.3% (P<0.01) u žien. SI vysvetľovala najviac 5.5% (P<0.05) variancie v *komunikácii* u mužov a 7.3% (P<0.05) v dimenzii *stigma* u žien. Znamená to, že osobnostné vlastnosti hrajú dôležitú úlohu pri vysvetľovaní kvality života u pacientov s PD. Rodové rozdiely poukazujú na odlišné zloženie modelov kvality života u mužov a u žien. Je pravdepodobné, že tieto modely sú zložené z odlišných komponentov.

V *Kapitole 4* prezentujeme systematický prehľad, ktorý sa zameriava na úlohu intenzity strachu pri oneskorovaní vyhľadania zdravotnej starostlivosti pacientom. Do prehľadu sme zahrnuli články zaoberajúce sa štatisticky najčastejšími ochoreniami – rakovinou a infarktom myokardu – hlavne z dôvodu početnosti uverejnených článkov k tejto téme. Vyhľadávanie literartúry sme obmedzili na časový úsek medzi rokmi 1990 a 2009 a našli sme 161 relevantných článkov. Po použití vybraných kritérií sme do štúdie zahrnuli 11 článkov týkajúcich sa rakoviny (rôznych druhov) a 4 články týkajúce sa infarktu myokardu. Strach sa v týchto štúdiách pohyboval na škále od 'byť znepokojený', čo nestačilo na skoré kontaktovanie špecialistu, až po 'paniku'. Pacienti, ktorý boli extrémne vystrašení prvými príznakmi ochorenia, boli pripravení konzultovať ich s odborným lekárom v rámci niekoľkých hodín. Hlavným výsledkom nášho prehľadového článku bolo poukázať na to, ako miera strachu ovplyvňuje rozhodovanie pacienta. Tento dôležitý faktor by mal byť vzatý do úvahy vtedy, ak je potrebné pomôcť pacientovi pri rozhodovaní, či vyhľadať odborníka. Podpora vyhľadania zdravotnej starostlivosti je nutná najmä u pacientov pociťujúcich iba slabé znepokojenie príznakmi ochorenia.

Oneskorovanie vyhľadania zdravotnej starostlivosti bolo témou *Kapitoly 5*. V nej nás zaujímala odpoveď na výskumnú otázku, či kvalita života pacientov s PD, ktorí oddiaľovali vyhľadanie zdravotnej starostlivosti, súvisí s osobnostnými vlasnosťami. Vzhľadom na intermitentný výskyt symptómov parkinsonizmu v začiatkoch ochorenia a niekedy pozvoľný nástup ochorenia, pacienti, ktorí vyhľadali zdravotnú starostlivosť do 1 roka od spozorovania prvých príznakov ochorenia, boli označení za 'skorých' (non-delayers) a tí, ktorí ju vyhľadali po 1 roku od objavenia sa príznakov za 'neskorých' (delayers). Tento časový úsek sme zisťovali na základe rozhovoru s pacientom – pokiaľ nástup ochorenia neprebehol dramaticky, prvé symptómy ochorenia pripisovali stresu. 'Skorí' pacienti skórovali vyššie na škále extroverzie, čo tiež asociovalo s lepším skóre vo fyzickom a mentálnom výslednom skóre kvality života.

Výsledky nabádajú k vysvetleniu, že sociálne interakcie, ktoré súvisia s extrovertným správaním, môžu posilniť pacienta v jeho rozhodnutí vyhľadať odbornú starostlivosť.

Mnohé štúdie potvrdzujú, že anxieta a depresia sú faktormi, ktoré súvisia s horším vnímaním kvality života pacientami s rôznymi diagnózami. Pretože sme v predchádzajúcich kapitolách potvrdili, že osobnostné vlastnosti (prevažne osobnosť typu D a neuroticizmus) determinujú kvalitu života, v *Kapitole 6* sme skúmali, či osobnosť typu D asociuje s mentálnym a fyzickým komponentom kvality života pacientov s PD a sklerosis multiplex (SM) aj vtedy, keď k modelu ich kvality života pridáme aj premenné anxietu a depresiu. Naše zistenia potvrdzujú, že vyššie skóre anxiety a depresie silne súviselo s mierou kvality života u oboch ochorení. Napriek tomu, že osobnosť typu D asociovala s oboma dimenziami kvality života – fyzickým aj mentálnym výsledným skóre, táto asociácia zmizla u oboch dimenzií pri pacientoch so SM a v diemenzii mentálneho výsledného skóre u pacientov s PD, keď sme do modelu pridali premenné anxietu a depresiu. Z našich výsledkov vyplýva, že osobnosť síce ovplyvňuje kvalitu života, avšak nie priamo, ale prostredníctvom porúch nálad.

Kapitola 7 sa zaoberá diskusiou hlavných výsledkov výskumu a ich významom pre prax a ďalší výskum. V súlade s našimi výsledkami môžeme konštatovať, že pri hodnotení kvality života pacientov s Parkinsonovou chorobou majú vysvetľujúcu hodnotu aj osobnostné vlastnosti. Rodový aspekt je témou, ktorá sa tiež javí ako dôležitá pri skúmaní psychologických odlišností medzi mužmi a ženami s PD. Prítomnosť porúch nálad, depresie a anxiety, modifikuje vplyv osobnostných vlastností na vnímanie kvality života pacientom a zdá sa, že má vážnejší dopad na kvalitu života nielen u pacientov s Parkinsonovou chorobou, ale aj na pacientov so sclerosis multiplex. Podľa našich výsledkov, pacienti, ktorí vyhľadajú zdravotnú starostlivosť skôr (non-delayers) a pacienti oddiaľujúci vyhľadanie zdravotnej starostlivosti (delayers) sa odlišujú v miere extroverzie, ktorá pozitívne koreluje so sociálnou aktivitou a sociálnou oporou. Preto pacienti, ktorí dosahujú vyššie skóre v extroverzii a ktorí majú možnosť zdieľať svoje pocity a obavy s inými ľuďmi, vyhľadávajú zdravotnú starostlivosť skôr ako pacenti s nízkym skóre v extroverzii.

K limitáciám tohto výskumu patrila pomerne nízka návratnosť dotazníkov, ktorá môže ovplyvniť možnosť generalizácie výsledkov na celkovú populáciu pacientov s PD. Použitie longitudinálnych dát v budúcom výskume nám pomôže lepšie vysvetliť kauzálne vzťahy medzi premennými. Budúci výskum v oblasti oddiaľovania vyhľadania odbornej starostlivosti by mal obsahovať analýzu nielen kvantitatívnych, ale aj kvalitatívnych údajov, ktorá by mala zabezpečiť presnejšiu interpretáciu výsledkov. Použitie kvalitatívnych metód nám môže pomôcť objasniť významy a kontext meraných premenných. Z nášho výskumu vyplýva, že

pri výbere najefektívnejšej intervencie pri liečení pacientov s PD je nutné, aby neurológ zohľadňoval aj osobnosť pacienta a jeho aktuálnu náladu, prípadne motiváciu, nielen zlepšovanie alebo zhoršovanie klinických príznakov ochorenia.

Acknowledgements

On the first interview with my supervisors they asked me: "Are you strong enough to cope with failures?" And I answered without humility: "Of course!" This was the start of my failures, which not caused my collapse, but, surprisingly, make me stronger then ever.

Firstly, I would like to thank all brave people, who are standing behind this international cooperation – only they know, how hard were all fights on the beginning – to Jitse P. van Dijk, Berrie Middel and Johan Groothoff on the side of University Medical Centre Groningen, and Andrea Madarasova Geckova, Iveta Rajnicova Nagyova, Zuzana Gdovinova and Jaro Rosenberger on the Slovak side of our Parkinson project. My particular thanks go to the persons responsible for all important "details" – Nicol Hendrichovska, Jarmila Fristikova, Martina Sukenikova and Ivana Borysova.

I would like to thank especially also to my supervisors, who were already mentioned – Jitse, Iveta, Johan, Jaro and Berrie - for sharing with me their experiences and for teaching me how to work effectively and how to be patient. Each of them helped me to better understand what it means to be a researcher.

My special thanks are also addressed to my colleagues from the Chronic Disease team, with whom we shared all aspects of the life of a "young researcher" – Martina Chylova, Eva Havlikova and Miriam Polanova. In addition, my thanks go to all KISH PhD students, with whom we shared a lot of interesting experiences on conferences, but also in non-formal events - Martina Chylova, Maria Sarkova, Zuzana Veselska, Eva Havlikova, Maria Humenikova, Maria Bacikova, Ferdinand Salonna, Ondrej Kalina, Zuzana Skodova, Maria Majernikova, Jozef Benka and many others.

My thanks belong also to management of Faculty of Education of the University of Presov for the stimulating environment and to my colleagues from the Department of Special Education for their huge support and their ability to laugh even when life is not always easy.

I would like to express my gratitude to all patients with Parkinson's disease and neurologist as well - this project would not have been realized without their cooperation – for their willingness to donate us some hours of their lives.

Last, but not least, I want to thank my parents, my sister Maria and brother Peter, because they never doubt, that I will finish. Finally, I thank also you, A.M., for your love and trust.

About author

Tatiana Dubayova was born in October 18, 1975 in Presov, Slovak Republic. She completed secondary school in Presov in 1994 and in 2001 she achieved Master's degree in psychology on Faculty of Philosophy, University of Presov. From July 2001 till December 2002 she worked in House of care for people with physical handicap in Prešov and from February 2003 she started her PhD study on Groningen University in Groningen, The Netherlands in the field of quality of life of patients with Parkinson's disease. In years 2005-2008 she also externally worked as psychologist for association Help for Victims of Violence in Kosice. She has certifications from long-term course in *Brief therapy* (systemic approach) and in *Relaxation and imagination therapy*. From 2006 till present times she is lecturer on Department of Special Education, Faculty of Education at the University of Presov where she is teaching subjects in fields of education of mental handicapped and education of children with behavioral problems – psychology of children with special needs and foundations of psychotherapy for teachers. She is participating in the project NIL–II-022–d *"Professional ethics as a part of professional competence of supporting professions"* and she is also the coordinator of international project 2009-1-AT-LEO05-01199 *"Kid's Strengths"*.

Groningen Graduate School of Medical Sciences – Research Institute SHARE

This thesis is published within the research program **Public Health Research (PHR) of** the Research Institute SHARE of the Groningen Graduate School of Medical Sciences (embedded in the University Medical Center Groningen / University of Groningen). More information regarding the institute and its research can be obtained from our internet site: www.rug.nl/share.

Previous dissertations from the program **Public Health Research**

Bieleman A (2010) *Work participation and work capacity in early osteoarthritis of the hip and the knee*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISORS: dr FGJ Oosterveld, dr MF Reneman

Spanjer J (2010) *The Disability Assessment Structured Interview; its reliability and validity in work disability assessment*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISORS: dr B Krol, dr S Brouwer

Koopmans PC (2009) *Recurrence of sickness absence; a longitudinal study*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISOR: dr CAM Roelen

Chang CMS (2009) *Ageing with joy; the effect of a physical education programme on the well-being of older people*
SUPERVISORS: prof dr JR van Horn, prof dr JW Groothoff, prof dr MA Vreede
CO-SUPERVISOR: dr M Stevens

Krokavcová M (2009) *Perceived health status in multiple sclerosis patients*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISORS: dr JP van Dijk, dr I Nagyová, dr Z Gdovinová, dr LJ Middel

El-Sayed Hussein El-Baz N (2009) *Effect of clinical pathway implementation and patients' characteristics on outcomes of coronary artery bypass graft surgery*
SUPERVISOR: prof dr SA Reijneveld
CO-SUPERVISORS: dr LJ Middel, dr JP van Dijk, dr PW Boonstra

Buitenhuis J (2009) *The course of whiplash; its psychological determinants and consequences for work disability*
SUPERVISORS: prof dr JW Groothoff, prof dr PJ de Jong
CO-SUPERVISOR: dr JPC Jaspers

Santvoort MM van (2009) *Disability in Europe; policy, social participation and subjective well-being*
SUPERVISOR: prof dr WJA van den Heuvel
CO-SUPERVISORS: dr JP van Dijk, dr LJ Middel

Stewart RE (2009) *A multilevel perspective of patients and general practitioners*
SUPERVISORS: prof dr B Meyboom-de Jong, prof dr TAB Snijders, prof dr FM Haaijer-Ruskamp

Jong J de (2009) *The GALM effect study; changes in physical activity, health and fitness of sedentary and underactive older adults aged 55-65*
SUPERVISOR: prof dr EJA Scherder
CO-SUPERVISORS: dr KAPM Lemmink, dr M Stevens

Buist I (2008) *The GronoRun study; incidence, risk factors, and prevention of injuries in novice and recreational runners*
SUPERVISORS: prof dr RL Diercks, prof dr W van Mechelen
CO-SUPERVISOR: dr KAPM Lemmink

Škodová Z (2008) *Coronary heart disease from a psychosocial perspective: socioeconomic and ethnic inequalities among Slovak patients*
SUPERVISOR: prof dr SA Reijneveld
CO-SUPERVISORS: dr JP van Dijk, dr I Nagyová, dr LJ Middel, dr M Studencan

Havlíková E (2008) *Fatigue, mood disorders and sleep problems in patients with Parkinson's disease*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISORS: dr JP van Dijk, dr J Rosenberger, dr Z Gdovinová, dr LJ Middel

Bos EH (2008) *Evaluation of a preventive intervention among hospital workers to reduce physical load*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISOR: dr B Krol

Wagenmakers R (2008) *Physical activity after total hip arthroplasty*
SUPERVISORS: prof dr S Bulstra, prof dr JW Groothoff
CO-SUPERVISORS: dr M Stevens, dr W Zijlstra

Zuurmond RG (2008) *The bridging nail in periprosthetic fractures of the hip; incidence, biomechanics, histology and clinical outcomes*
SUPERVISOR: prof dr SK Bulstra
CO-SUPERVISORS: dr AD Verburg, dr P Pilot

Wynia K (2008) *The Multiple Sclerosis Impact Profile (MSIP), an ICF-based outcome measure for disability and disability perception in MS: development and psychometric testing*
SUPERVISORS: prof dr SA Reijneveld, prof dr JHA De Keyser
CO-SUPERVISOR: dr LJ Middel

Leeuwen RR van (2008) *Towards nursing competencies in spiritual care*
SUPERVISORS: prof dr D Post, prof dr H Jochemsen
CO-SUPERVISOR: dr LJ Tiesinga

Vogels AGC (2008) *The identification by Dutch preventive child health care of children with psychosocial problems : do short questionnaires help?*
SUPERVISORS: prof dr SA Reijneveld, prof dr SP Verloove-Vanhorick

Kort NP (2007) *Unicompartmental knee arthroplasty*
SUPERVISOR: prof dr SK Bulstra
CO-SUPERVISORS: dr JJAM van Raay, dr AD Verburg

Akker-Scheek I van den (2007) *Recovery after short-stay total hip and knee arthroplasty; evaluation of a support program and outcome determination*
SUPERVISORS: prof dr JW Groothoff, prof dr SK Bulstra
CO-SUPERVISORS: dr M Stevens, dr W Zijlstra

Mei SF van der (2007) *Social participation after kidney transplantation*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr JW Groothoff, prof dr PE de Jong
CO-SUPERVISOR: dr WJ van Son

Khan MM (2007) *Health policy analysis: the case of Pakistan*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr JW Groothoff
CO-SUPERVISOR: dr JP van Dijk

Rosenberger J (2006) *Perceived health status after kidney transplantation*
SUPERVISORS: prof dr JW Groothoff, prof dr WJA van den Heuvel
CO-SUPERVISORS: dr JP van Dijk, dr R Roland

Šléškova M (2006) *Unemployment and the health of Slovak adolescents*
SUPERVISORS: prof dr SA Reijneveld, prof dr JW Groothoff
CO-SUPERVISORS: dr JP van Dijk, dr A Madarasova-Geckova

Dumitrescu L (2006) *Palliative care in Romania*
SUPERVISOR: prof dr WJA van den Heuvel

The B (2006) *Digital radiographic preoperative planning and postoperative monitoring of total hip replacements; techniques, validation and implementation*
SUPERVISORS: prof dr RL Diercks, prof dr JR van Horn
CO-SUPERVISOR: dr ir N Verdonschot

Jutte PC (2006) *Spinal tuberculosis, a Dutch perspective; special reference to surgery*
SUPERVISOR: prof dr JR van Horn
CO-SUPERVISORS: dr JH van Loenhout-Rooyackers, dr AG Veldhuizen

Leertouwer H (2006) *Het heil van de gezonden zij onze hoogste wet; de geschiedenis van de medische afdeling bij de arbeidsinspectie*
SUPERVISORS: prof dr JW Groothoff, prof dr MJ van Lieburg, prof dr D Post

Jansen DEMC (2006) *Integrated care for intellectual disability and multilpe sclerosis*
SUPERVISORS: prof dr D Post, prof dr JW Groothoff
CO-SUPERVISOR: dr B Krol

Ham I van (2006) *De arbeidssatisfactie van de Nederlandse huisarts*
SUPERVISORS: prof dr J de Haan, prof dr JW Groothoff
CO-SUPERVISOR: dr KH Groenier

Jansen GJ (2005) *The attitude of nurses towards inpatient aggression in psychiatric care: the development of an instrument*
SUPERVISORS: prof dr SA Reijneveld, prof dr ThWN Dassen
CO-SUPERVISOR: dr LJ Middel

Post M (2005) *Return to work in the first year of sickness absence; an evaluation of the Gatekeeper Improvement Act*
SUPERVISORS: prof dr JW Groothoff, prof dr D Post
CO-SUPERVISOR: dr B Krol

Landsman-Dijkstra JJA (2005) *Building an effective short healthpromotion intervention; theory driven development, implementation and evaluation of a body awareness program for chronic a-specific psychosomatic symptoms*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISOR: dr R van Wijck

Bakker RH (2005) *De samenwerking tussen huisarts en bedrijfsarts*
SUPERVISOR: prof dr JW Groothoff
CO-SUPERVISORS: dr B Krol, dr JWJ van der Gulden

Nagyová I (2005) *Self-rated health and quality of life in Slovak rheumatoid arthritis patients*
SUPERVISOR: prof dr WJA van den Heuvel
CO-SUPERVISOR: dr JP van Dijk

Gerritsma-Bleeker CLE (2005) *Long-term follow-up of the SKI knee prosthesis.*
SUPERVISORS: prof dr JR van Horn, prof dr RL Diercks
CO-SUPERVISOR: dr NJA Tulp

Vries M de (2005) *Evaluatie Zuidoost-Drenthe HARTstikke goed!; mogelijkheden van community-based preventie van hart-en vaatziekten in Nederland*
SUPERVISORS: prof dr D Post, prof dr JW Groothoff
CO-SUPERVISOR: dr JP van Dijk

Jungbauer FHW (2004) *Wet work in relation to occupational dermatitis*
SUPERVISORS: prof dr PJ Coenraads, prof dr JW Groothoff

Post J (2004) *Grootschalige huisartsenzorg buiten kantooruren*
SUPERVISOR: prof dr J de Haan

Reneman MF (2004) *Functional capacity evaluation in patients with chronic low back pain; reliability and validity*
SUPERVISORS: prof dr JW Groothoff, prof dr JHB Geertzen
CO-SUPERVISOR: dr PU Dijkstra

Bâra-Ionilã C-A (2003) *The Romanian health care system in transition from the users' perspective*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr JAM Maarse
CO-SUPERVISOR: dr JP van Dijk

Lege W de (2002) *Medische consumptie in de huisartspraktijk op Urk*
SUPERVISORS: prof dr D Post, prof dr JW Groothoff

Hoekstra EJ (2002) *Arbeidsbemiddeling met behulp van Supported Employment als interventie bij de reïntegratie van chronisch zieken; de rol van de arbeidsbemiddelaar, chronisch zieke en werkgever*
SUPERVISORS: prof dr JW Groothoff, prof dr K Sanders, prof dr WJA van den Heuvel, prof dr D Post

Enk JG van (2002) *Determinants of use of healthcare services in childhood*
SUPERVISORS: prof dr D Post, prof dr AJP Veerman, prof dr WJA van den Heuvel

Gecková A (2002) *Inequality in health among Slovak adolescents*
SUPERVISORS: prof dr D Post, prof dr JW Groothoff
CO-SUPERVISOR: dr JP van Dijk

Dijk JP van (2001) *Gemeentelijk gezondheidsbeleid; omvang en doelgerichtheid*
SUPERVISORS:: prof dr D Post, prof dr M Herweijer, prof dr JW Groothoff

Middel LJ (2001) *Assessment of change in clinical evaluation*
SUPERVISOR: prof dr WJA van den Heuvel
CO-SUPERVISOR: dr MJL de Jongste

Bijsterveld HJ (2001) *Het ouderenperspectief op thuiszorg; wensen en behoeften van ouderen ten aanzien van de thuis(zorg)situatie in Friesland*
SUPERVISORS: prof dr D Post, prof dr B Meyboom-de Jong
CO-SUPERVISOR: dr J Greidanus

Dijkstra GJ (2001) *De indicatiestelling voor verzorgingshuizen en verpleeghuizen*
SUPERVISORS: prof dr D Post, prof dr JW Groothoff

Dalen IV van (2001) *Second opinions in orhopaedic surgery: extent, motives, and consequences*
SUPERVISORS: prof dr JR van Horn, prof dr PP Groenewegen, prof dr JW Groothoff

Beltman H (2001) *Buigen of barsten? Hoofdstukken uit de geschiedenis van de zorg aan mensen met een verstandelijke handicap in Nederland 1945-2000*
SUPERVISORS: prof dr D Post, prof dr AThG van Gennep

Pal TM (2001) *Humidifiers disease in synthetic fiber plants: an occupational health study*
SUPERVISORS: prof dr JGR de Monchy, prof dr D Post, prof dr JW Groothoff

Goossen WTF (2000) *Towards strategic use of nursing information in the Netherlands*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr ThWN Dassen, prof dr A Hasman

Hospers JJ (1999) *Allergy and airway hyperresponsiveness: risk factors for mortality*
SUPERVISORS: prof dr D Post, prof dr DS Postma, prof dr ST Weiss

Wijk P van der (1999) *Economics: Charon of Medicine?*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr L Koopmans, prof dr FFH Rutten
CO-SUPERVISOR: dr J Bouma

Dijkstra A (1998) *Care dependency: an assessment instrument for use in long-term care facilities*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr ThWN Dassen

Tuinstra J (1998) *Health in adolescence: an empirical study of social inequality in health, health risk behaviour and decision making styles*
SUPERVISORS: prof dr D Post, prof dr WJA van den Heuvel
CO-SUPERVISOR: dr JW Groothoff

Mink van der Molen AB (1997) *Carpale letsels: onderzoek naar de verzuimaspecten ten gevolgen van carpale letsels in Nederland 1990-1993*
SUPERVISOR: prof dr PH Robinson, prof WH Eisma
CO-SUPERVISORS: dr JW Groothoff, dr GJP Visser

Mulder HC (1996) *Het medisch kunnen: technieken, keuze en zeggenschap in de moderne geneeskunde*
SUPERVISOR: prof dr WJA van den Heuvel

Dekker GF (1995) *Rugklachten-management-programma bij de Nederlandse Aardolie Maatschappij B.V.: ontwerp, uitvoering en evaluatie*
SUPERVISORS: prof dr D Post, prof WH Eisma
CO-SUPERVISOR: dr JW Groothoff

Puttiger PHJ (1994) *De medische keuring bij gebruik van persluchtmaskers*
SUPERVISOR: prof dr D Post, prof dr WJA Goedhard
CO-SUPERVISOR: dr JW Groothoff

Engelsman C & Geertsma A (1994) *De kwaliteit van verwijzingen*
SUPERVISORS: prof dr WJA van den Heuvel, prof dr FM Haaijer-Ruskamp, prof dr B Meyboom-de Jong

Lucht F van der (1992) *Sociale ongelijkheid en gezondheid bij kinderen*
SUPERVISOR: prof dr WJA van den Heuvel
CO-SUPERVISOR: dr JW Groothoff

Graduate School Kosice Institute for Society and Health (KISH) and previous dissertations

The Graduate School Kosice Institute for Society and Health (KISH) was established in 2004. The Graduate School KISH is hosted by the Faculty of Medicine of the University of Pavol Jozef Safarik in Kosice (Slovakia). KISH researchers originate from the Medical Faculty, the University Hospital and other hospitals, and the Faculty of Arts. Its research concentrates on public health, health psychology, epidemiology and medical sociology. The interdisciplinary research program focuses on **Youth and Health** and on **Chronic Disease.**

The Graduate School KISH is collaborating closely with the Department of Social Medicine, University Medical Center Groningen, University of Groningen, The Netherlands.

More information regarding the institute can be obtained from http://www.kish.upjs.sk.

Krokavcova M (2009) *Perceived Health Status in Multiple Sclerosis Patients*
SUPERVISOR: Prof. Dr. JW Groothoff
CO-SUPERVISORS: Ass. Prof. Dr. JP van Dijk, Dr. I Nagyova, Ass. Prof. Dr. Z Gdovinova, Dr. LJ Middel

Havlikova E (2008) *Fatigue, mood disorders and sleep problems in patients with Parkinson's disease*
SUPERVISOR: Prof. Dr. JW Groothoff
CO-SUPERVISORS: Ass. Prof. Dr. JP van Dijk, Dr. J Rosenberger, Ass. Prof. Dr. Z Gdovinova, Dr. LJ Middel

Zuzana Skodova (2008) *Coronary heart disease from a psychosocial perspective: socioeconomic and ethnic inequalities among Slovak patients*
SUPERVISOR: Prof. Dr. SA Reijneveld
CO-SUPERVISORS: Ass. Prof. Dr. JP van Dijk, Dr. I Nagyova, Dr. LJ Middel, Dr. M Studencan

Rosenberg J (2006) *Perceived health status after kidney transplantation*
SUPERVISORS: prof dr JW Groothoff, prof dr WJA van den Heuvel
CO-SUPERVISORS: dr JP van Dijk, dr R Roland

Sleskova M (2006) *Unemployment and the health of Slovak adolescents*
SUPERVISORS: prof dr SA Reijneveld, prof dr JW Groothoff
Co-SUPERVISORS: dr JP van Dijk, dr A Madarasova Geckova

Nagyova I (2005) *Self-rated health and quality of life in Slovak rheumatoid arthritis patients*
SUPERVISORS: prof dr WJA van den Heuvel
CO-SUPERVISOR: dr JP van Dijk

Geckova A (2002) *Inequality in health among Slovak adolescents.*
SUPERVISORS: prof dr D Post, prof dr JW Groothoff
CO-SUPERVISOR: dr JP van Dijk

ISBN 978 94 6070 026 2