Summary

The general aim of this thesis was to assess the effectiveness of a standardized psychosocial education program. The first studies of this thesis were aimed to assess the effectiveness of the Patient Education Program for Parkinson's disease (PEPP), as the original program was directed at Parkinson's disease. Thereafter, it was aimed to assess the program's feasibility in other diseases. A second step in the thesis was an evaluation of the feasibility of the program adapted to a new disease-specific form for Huntington's disease (PEP-HD). The third step was to evaluate a generic form of the program in a heterogeneous group of patients with chronic diseases and co-morbid psychiatric problems (PEP-CD).

Need for psychosocial help in Parkinson's disease

Parkinson's disease (PD) is one of the most common neurodegenerative diseases. The core features of the disease are a resting tremor, rigidity, bradykinesia/akinesia and postural disturbances. Also, non-motor symptoms such as cognitive deficits and psychiatric problems are common.[1-3] Often, PD has a substantial adverse impact on psychosocial wellbeing and quality of life (Qol).[4-6] In previous studies, increased psychosocial problems and depressive symptoms have been associated with more decline of Qol over time and are therefore often recommended to be addressed in PD treatment.[7-9] In order to explore psychosocial burden and need for psychosocial help in PD patients relative to their current use of psychosocial treatment and their actual request for help, we assessed data from 217 patients attending a multidisciplinairy outpatient assessment center in Nijmegen, the Netherlands (**chapter 2**). Ninety-seven percent of the patients reported psychosocial burden and need for help on the Belastungsfragebogen Parkinson-kurzversion (BELA-P-k) questionnaire.[10] Large differences were found in severity and type of problems. A higher score on the BELA-P-k, indicating more psychosocial burden, was found for women, and patients with a younger age and lower education, and patients with more depressive and anxiety symptoms (Hospital Anxiety and Depression Scale, HADS).[11] They also experienced a worse Qol (Parkinson's disease Quality of Life Questionnaire, PDQL).[12] Forty-three percent of the patients had scores indicative for a depression and/or anxiety disorder (HADS).[13] Of the patients, 70% reported an actual request for attention for their mood and 50% for social contacts. However, many patients seemed to doubt or seemed to feel insecure about their request. Less than 20% of the patients did receive current psychosocial or psychiatric treatment. These results indicated an unmet need for

psychosocial treatment in many PD patients. Patient education on psychosocial aspects may help patients to improve their quality of life.

The Patient Education Program for Parkinson's disease

The Patient Education Program for Parkinson's disease (PEPP) was developed between 2003 and 2005 by a European consortium called 'EduPark'. Participating countries were Germany, Spain, Finland, United Kingdom, Italy, Estonia, and the Netherlands. Patient education was defined as: 'A systematic and professional approach to support patients and caregivers by teaching them knowledge and skills in order to improve their Qol, complementing the medical treatment'.[14] The aim of the program is to empower them in dealing with psychosocial stressors caused by PD. The PEPP provides a parallel program for patients and caregivers, and consists of eight weekly sessions of ninety minutes. Each session has its own theme.

In the formative evaluation, the program was assessed on its feasibility by means of a pilot study in the seven participating countries. Macht et al,[15] described the results of the PD patients (n =151). We compared the results of the PD caregivers (n = 137) next to the data of the PD patients (**chapter 3**). Caregivers receive proportional treatment in the PEPP as they provide most of the care for patients with adverse effects on their own wellbeing.[16-18] The aim of the caregiver program is to provide caregivers with education and training about how to maintain or improve their wellbeing and to prevent them from caregiver overload. It was found that patients as well as caregivers from the seven countries evaluated the program favorably. Feedback from participants and trainers led to improvements of the program which were incorporated in the final manual.[14, 19-24] Self-report questionnaires were used to compare scores before and after participation. Psychosocial burden and need for help were assessed by the BELA-P-k. In the caregiver group, the Belastungsfragebogen Parkinson Angehörigen kurzversion (BELA-A-k)[25] was used. Quality of life was measured with the Parkinson's Disease Questionnaire (PDQ-39)[26] in the patients and with the EuroQol-5D (EQ-5D) in the caregiver group.[27] Depression was assessed with the Self-rating Depression Scale (SDS).[28] First results from the pilot study showed that caregivers as well as the PD patients were less bothered by psychosocial problems and had less need for help (BELA-P/A-k) after participation. Following individual sessions, participants' mood was elevated on a visual analogue scale measuring current mood (Mood-VAS).[29]

After the formative evaluation, a randomized controlled trial was performed in the Netherlands (**chapter 4**). Sixty-four PD patients and 46 caregivers were randomly allocated to either the intervention group which participated in the PEPP or to the control group which received usual care. Participants in the control group received the intervention after the study (waiting list group). Primary outcome measures were the same self-report questionnaires as used in the formative evaluation. A short neuropsychological assessment was used in addition. It was found that within one week after participation in the program, caregivers reported a significantly decreased psychosocial burden and need for help (BELA-A-k). In the patients group, a trend towards significant improvement of Qol was found, as measured with the PDQ-39. Patients' and caregivers' mood improved significantly after each session on the Mood-VAS.

The randomized controlled trial showed large variations in change scores, indicating variation in benefit. Information about treatment effect modifiers could be helpful to improve referring advices for participation in the program. The (cost) effectiveness of the intervention may increase if it can be selectively provided for those who benefit most.[30] Therefore, secondary analyses of data from the randomized controlled trial with 64 patients and 46 caregivers were performed by means of regression analyses with treatment group interaction terms (intervention versus control group) (**chapter 5**). Candidate treatment effect modifiers were participants' characteristics and baseline scores on psychological questionnaires and patients' neuropsychological test scores. In the caregiver group, a higher Mini Mental Status Examination (MMSE)[31] score, indicating better general cognitive functioning of the patient at baseline, was found to be a significant predictor of less psychosocial burden (BELA-A-k) of the caregiver after the program (corrected for baseline scores). Thus, better cognitive functioning of the patient was found to be a favorable treatment modifier for caregivers. This study did not find treatment effect modifiers for PD patients: demographics, disease stage and time of diagnosis, cognitive functioning, level of baseline psychosocial burden, participating with or without a caregiver, and caregiver changes did not influence treatment outcome. The PEPP seems suitable for the majority of the patients.

In the Netherlands, the PEPP manual[14] is freely available and training courses for health care professionals are being provided to ensure the quality of implementation of the PEPP.

Health care professionals from different health care settings across the Netherlands have followed this course and now provide the PEPP themselves. We assessed the effectiveness of the program in the uncontrolled 'real world' clinical practice (**chapter 6**). Fifty-five patients and fifty caregivers participated in the study at nine different sites across the Netherlands. When provided in clinical practice, the program showed significant short-term improvement of Qol (PDQ-39) for PD patients and psychosocial (BELA-A-k) improvement for caregivers. Compared to the RCT study, results were replicated and the effect on patients' Qol was now significant. Also, the effectiveness of the program in clinical practice at six-month follow-up was assessed. At six-month follow-up, scores returned to baseline levels. A booster session was suggested to be helpful in order to sustain enhanced Qol over a longer period of time. However, a temporary improvement of Qol may be beneficial because it may lead to a deceleration of Qol deterioration. Qol deterioration is expected in PD as, with the neurodegenerative character of the disorder, Qol is increasingly challenged as the disease progresses.[7]

The Patient Education Program for Huntington's disease

The program was adapted for use in Huntington's disease (HD) and named Patient Education Program for Huntington's disease (PEP-HD). This disease is an autosomal dominant inherited neurodegenerative disorder with mean age of onset in middle age. The disease is characterized by progressive motor, psychiatric and cognitive symptoms.[32] Psychosocial stressors may be comparable to those in PD.[33] However, additional challenges may be the cognitive problems, the hereditary aspect of the disease, and the possibility of genetic testing creating a premanifest stage. Despite many recommendations for future research about the need for studies on psychological interventions in HD,[34-37] no such study was performed thus far. Therefore, the PEP-HD was assessed on its feasibility in manifest as well as premanifest HD stages. Forty patients, 19 premanifest gene carriers and 42 partners participated. Four measurements were performed. Participants were assessed prior to participation twice to explore 'normal' changes without intervention (control period). First, the results found directly after participation were presented (**chapter 7**). A significant improvement was found for HD patients regarding behavioral symptoms (Unified Huntington's Disease Rating Scale (UHDRS), behavioral scale[38] and anxiety (HADS), and they used a less passive coping style and more seeking social support on the Utrecht Coping List (UCL).[39] The caregivers reported less psychosocial burden (BELA-A-k). Premanifest carriers and their partners improved their coping by seeking

social support more often (UCL). These changes were not found in the control period. Participants evaluated their participation in the PEP-HD positively. It was concluded that the results demonstrated the feasibility of the program in Huntington's disease, especially in manifest stages. An international multicenter study with a large sample is necessary to assess the program's effectiveness further.

The PEP-HD study was followed by a study on the effectiveness of the program at a six-month follow-up (**chapter 8**). We found that at six-month follow-up, patients with HD experienced significantly less psychosocial burden (BELA-P-k). The short-term effects regarding reduction of behavioral problems (UHDRS) and anxiety (HADS) in the HD patients, psychosocial burden (BELA-A-k) in the caregivers and the improvement of coping (UCL) in both the manifest and the premanifest group were no longer significant after six months. The program was evaluated as positive, most participants experienced benefit from participation and most of the copings strategies learned within the program were still used by the participants. Most participants reported a need for a follow-up session.

The Patient Education Program for Chronic disease

At last, we changed the program from disease-specific to generic: the Patient Education Program for Chronic Disease (PEP-CD). We conducted a pilot study to assess the feasibility of the program when patients with different chronic diseases participated in the same group. The study was performed at a medical psychiatric center where patients with a chronic disease are in treatment because of co-morbid psychiatric problems (**chapter 9**). Twenty-eight patients and 14 caregivers participated in the program. Patients were diagnosed with the following medical diseases: Multiple Sclerosis; Becker's Muscular Dystrophy; Complex Regional Pain Syndrome; Parkinson's disease; Myasthenia Gravis; Post-Whiplash Syndrome; Cerebrovascular Accident; Crohn's disease; Scoliosis; Diabetes Mellitus; Neurofibromatosis; Cerebral Ataxia; Fibromyalgia; Chronic Hepatitis C; Pituitary Adenoma; Kidney disease; and Myalgic Encephalomyelitis.

It was found that depression and anxiety (HADS) in the patients group significantly improved after participation and scores returned to normal (HADS < 8).[13] Furthermore, patients reported less burden by psychosocial problems and less psychosocial need for help (BELA-P-k), better mental quality of life (36-item Short Form health survey, SF-36),[40]

better health state (EQ-5D) and more use of ‘Seeking social support’ as a coping strategy (UCL). Caregivers reported less need for psychosocial help (BELA-A-k) and a better general quality of life (EQ-5D) after participation. We concluded that patients suffering from chronic disease with co-morbid psychiatric disease and their caregivers seem to benefit from participation in the PEP-CD. A randomized controlled trail should be the next step.

In conclusion, the program in its original form was found to be effective to improve quality of life of PD patients and to reduce psychosocial burden and need for help in PD caregivers at short term. Then, the program was found to be feasible in other diseases, in a disease-specific for Huntington’s disease as well as in a generic form for chronic diseases wilt co-morbid psychiatric problems. Notwithstanding that more research is needed to draw conclusions about their effectiveness, these findings do provide possibilities for a broader application of the program and for further research possibilities to assess the effectiveness in other chronic diseases. Important implications for future research comprise assessment of the working ingredients of the program and assessment of the cost-effectiveness. The conclusions of this thesis, the methodological limitations and considerations for future research are discussed in **chapter 10**.

References

1. Brown RG, Marsden CD. Cognitive function in Parkinson's disease: from description to theory. Trends Neurosci. 1990; 13:21-29
2. Foltynie T, Brayne CE, Robbins TW et al. The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study. Brain. 2004; 127:550-560
3. Nuti A, Ceravolo R, Piccinniet A et al. Psychiatric comorbidity in a population of Parkinson's disease patients. Eur J Neurol. 2004; 11:315-320
4. Macht M, Schwarz R, Ellgring H. Patterns of psychological problems in Parkinson's disease. Acta Neurol Scand. 2005; 111:95-101
5. Ellgring H. Seiler S, Perlethet B al. Psychosocial aspects of Parkinson's disease. Neurology. 1993; 43:S41-S44
6. Martinez-Martin P. An introduction to the concept of "quality of life in Parkinson's disease". J Neurol. 1998; 245:S2-S6
7. Visser M, Verbaan D, Van Rooden SM et al. A Longitudinal Evaluation of Health-Related Quality of Life of Patients with Parkinson's Disease. Value Health. 2008; 12:392-396
8. Forsaa EB, Larsen JP, Wentzel-Larsen T et al. Predictors and course of health-related quality of life in Parkinson's disease. Mov Disord 2008; 23:1420-1427
9. Visser M. Van Rooden SM, Verbaan D et al. A comprehensive model of health-related quality of life in Parkinson's disease. J Neurol. 2008; 255:1580-1587
10. Spliethoff-Kamminga NG, Zwinderman AH, Springer MP et al. Psychosocial problems in Parkinson's disease: evaluation of a disease-specific questionnaire. Mov Disord. 2003; 18:503-509
11. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983; 67:361-370
12. De Boer AG, Wijker W, Speelman JD et al. Quality of life in patients with Parkinson's disease: development of a questionnaire. J Neurol Neurosurg Psychiatry. 1996; 61:70-74
13. Bjelland I, Dahl AA, Haug TT et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002; 52:69-77

14. Spliethoff-Kamminga NGA. Patiënt Educatie Programma Parkinson. Harcourt Publishers, Amsterdam, 2006
15. A'Campo LE, Spliethoff-Kamminga NG, Macht M et al. Caregiver education in Parkinson's disease: formative evaluation of a standardized program in seven European countries. Qual Life Res. 2010; 19:55-64
16. Martinez-Martin P. Benito-Leon J, Alonso F et al. Quality of life of caregivers in Parkinson's disease. Qual Life Res. 2005; 14:463-472
17. Thommessen B, Aarsland D, Braekhus A et al. The psychosocial burden on spouses of the elderly with stroke, dementia and Parkinson's disease. Int J Geriatr Psychiatry. 2002; 17:78-84
18. Rolan KP, Jenkins ME, Johnson AM. An exploration of the burden experienced by spousal caregivers of individuals with Parkinson's disease. Mov Disord. 2010; 25:189-193
19. Smith Pasqualini MC & Simons G. Patient education for people with Parkinson's disease and their carers: a manual. John Wiley & Sons, Chichester, 2006
20. Ellgring H, Gerlich C, Macht M et al.Psychosoziales Training bei neurologischen Erkrangkungen-Schwerpunkt Parkinson. W. Kohlhammer, Stuttgart, 2006
21. Lankinen A, Viemero V, Lehtonen A et al. Psykososiaalinen valmennusohjelma Parkinsonin tautia sairastaville ja heidän Iäheisilleen, Suomen Parkinson-liitto ry, Turku, 2005
22. Ricci Bitti PE, Candini L, Carlini M et al. Intervento psicoeducativo nella malattia di Parkinson. Erickson, Gardolo, 2006
23. Taba P, Krikmann U, Kanarik E et al. Koolitusprogramm Parkinsoni tovega inimestele ja nende tugiisikutele. Tartu Parkinsoni Haiguise Selts, Tartu, 2005
24. Bayés A, De la Cruz Crespo M, Prats A. Psicoeducación para afectados de Parkinson y sus cuidadores. Elsevier, Barcelona, 2007
25. Spliethoff-Kamminga NG, Zwinderman AH, Springer MP et al. A disease-specific psychosocial questionnaire for Parkinson's disease caregivers. J Neurol. 2003; 250:1162-1168
26. Peto V, Jenkinson C, Fitzpatrick R et al. The development and validation of a short measure of functioning and wellbeing for individuals with Parkinson's disease. Qual Life Res. 1995; 4:241-248
27. EuroQol-a new facility for the measurement of health-related quality of life. The EuroQol Group. Health Policy. 1990; 16:199-208

28. Zung WW. A Self-Rating Depression Scale. Archives of General Psychiatry. 1965; 12:63-70
29. Luria RE. The validity and reliability of the visual analogue mood scale. J Psychiatr Res. 1975; 12:51-57
30. Newman S, Steed L, Mulligan K. Self-management interventions for chronic illness. Lancet. 2004; 364:1523-1537
31. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189-198
32. Bates G, Harper PS, Jones L. Huntington's disease. University Press, Oxford, 2002
33. Groves MS, Forrest DV. Parkinson's disease as a model for psychosocial issues in chronic neurodegenerative disease. Adv Neurol. 2005; 96:65-83
34. Paulsen JS, Nehl C, Hoth KF et al. Depression and stages of Huntington's disease. J. Neuropsychiatry Clin Neurosci. 2005; 17:496-502
35. Williams JK, Skirton H, Paulsen JS et al. The emotional experiences of family carers in Huntington disease. J Adv Nurs. 2009; 65:789-798
36. Skirton H, Glendinning N. Using research to develop care for patients with Huntington's disease. Br J Nurs. 1997; 6:83-90
37. Dawson S, Kristjanson LJ, Toye,C.M et al. Living with Huntington's disease: need for supportive care. Nurs Health Sci. 2004; 6:123-130.
38. Huntington Study Group. Unified Huntington's Diseases Rating Scale. Mov Disord. 1996; 11:136-142
39. Schreurs PJG, Teilegen B, Van de Willige G. Health, stress and coping: the development of the Utrecht Coping List. Tijdschrift voor Psychologie. 1984; 12:101-117
40. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): conceptual framework and item selection. Medical Care. 1992; 30:473-483