The influence of the disease and treatment on the life of patients with Parkinson's disease

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Abstract

Objective
As the Dutch society is ageing the prevalence of Parkinson's disease also will rise in the Netherlands. There is still no cure for Parkinson's disease and known treatments are focusing on suppressing the symptoms and improving the Health Related Quality of Life of the patient. The objective is to research the influence of the Parkinson's disease, symptoms and the treatment on the life of the patient from his or hers perspective. The focus will lie on the influence of the symptoms, the positive and negative treatment outcomes and treatment characteristic's on the patient's life.

Methods
Parkinson's disease patients were recruited from the area of Enschede and a total of seventeen were included in the research. Quantitative data is gathered with the use of (modified) HRQoL questionnaires and qualitative data with the use of semi-structured interviews.

Results
The quantitative results showed that relative the most respondents reported problems on the domains: cognitions, communication and bodily discomfort. Absolutely most problems were found with daily tasks, communication, and mobility. The qualitative results from the interviews showed that the greatest influence on their life were problems on the domains cognitions and communication. Problems caused by physical symptoms or disabilities had a smaller influence in contrast with what the quantitative data would suppose. The respondents diluted the influence of emotions, depression in particular, during the interviews. Fear of the future and disease progression was of influence of a substantial part of the respondents. This resulted in postponing adjustment of the treatment to the disease progression.

Conclusion
In daily life PD symptoms cause disabilities or problems performing normal tasks. However the respondents focus more on abilities as disabilities. The greatest influence on the life of the patient was the influence of the disease symptoms and adverse effects on the dimensions cognitions and communication and the fear of progression of the symptoms.

Preface

Before you find the results of almost a year of work into the influence of the disease and treatment of Parkinson's disease on the patient's life. During my study and bachelor thesis I missed the contact with the "patients". Quality of life, the impact of disease and treatment always interested me. From close I had seen that not only a disease can impact the life of a person but also the influence of the treatment and psychological effects should not be neglected.

Before starting my research my knowledge about Parkinson's disease was minimal. I knew Prince Clause had Parkinson's disease and my youth hero Michael J. Fox is a patient. I had knowledge of some of the primary motoric symptoms but I learned during my research that the non-motoric symptoms and side effects of medication could be of great influence on the patient's life too and should not be underestimated. During the research I interviewed a lot of patients, in a few hours you learned a lot of the influence of the disease and treatment but also about the persons themselves. The conversations were informative, sometimes funny and there were some emotional moments that had an impact on me.

While performing my research I learned a lot about carrying out research but also about my weaknesses, my strengths and myself. However finishing this research was mas made possible with the help of others. First of all I thank the respondents who were willing to cooperate with this research, without them this research was not possible. Also I want to thank the members of the research group for their help and input. Special thanks go to my father and brother who helped me during the difficult moments, my friends and roommates, and in particular Marten Lagemaat who reviewed my work.

And last but not least, my gratitude goes to my supervisors Janine van Til and Karin Groothuis-Oudshoorn. For their support, pointing me in the right direction at moments when I was lost, and above all the patience they had with me.

There are no Parkinson's patients; there are individuals with Parkinson's disease!

Raymond Kuipers

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1 Introduction

1.1 The history of Parkinson's disease

Around 1817 an apothecary and surgeon looked out of his window in London. He watched people who walked by and looked at their gesture and their movement. It was in that moment that a first clinical description was made of Parkinson's disease (PD) by Dr. James Parkinson ("Dr James Parkinson," 2011). It was until the sixties of the past century that an effective treatment for the symptoms was experimented and later used in treatment for PD (Jankovic, 2008).

1.2 Epidemiology of Parkinson's disease

The ageing society is an important fact for the importance of this study because PD is an associated with ageing. In the Netherlands in 2007 there were 26.300 persons diagnosed with PD, the so called point-prevalence (Gommer & Poos, 2011). The point prevalence only counts the persons diagnosed with the disease. That means that the number of persons with the disease can be and mostly is higher due the fact of the undiagnosed persons with PD. Estimates range from a factor 2 to 2,5 higher as diagnosed with the disease (Speelman & Poos, 2010). The estimated total number of persons with PD in the Netherlands, diagnosed and not diagnosed, lies around 18.600 men and 30.500 women, a total of nearly 50.000 persons (Den Oudsten, Van Heck, & De Vries, 2007). Technological development in healthcare and society in general led to the increase of life expectancy at birth. Due the fact of the aging Dutch society, the prognosis is that in the future the incidence and prevalence of PD rise enormously. From 2011 to the year 2039 the share of persons of the age 65 and above will increase from 2,6 million (16% of society) to 4,6 million (26% of society) in 2039. This goes along with an increase of the life expectancy (CBS, 2011). Not only people in society reach higher ages, their demands of a good life are increased as well. This has led to a greater focus on the quality of life and Health Related Quality of Life (HRQoL).

1.3 Problem description

This research will focus on the effect of the symptoms and treatment on the HRQoL of the patient. Parkinson's disease itself influences the HRQoL, but also the treatment and process characteristics influence the HRQoL. Science and professionals have neglected this for a long time. This is due the fact that their focus was mostly in the (recent) past on the disease and symptoms solely (Rumsfeld, 2002). Due the incurability of Parkinson's diseases the focus lies on maximizing the HRQoL.

For the patient the most important aspect of his treatment is to maximize the HRQoL until there is a cure for PD. In the treatment of Parkinson's disease (PD), the treatment itself can have a great impact on the HRQoL of the patient. Negative outcomes of the treatment can even influence the HRQoL more negatively than the relief from symptoms the treatment should treat.

1.4 Research goal

This study will look from the patient's point of view to the experiences with the treatment and process characteristics of the treatment of PD and how this influences the life of the patient. The goal is to establish a top list of elements of the health, non-health and process of the treatment of PD as experienced by the patients based on interviews with the patients. This exploration of positive and negative elements influencing the life can be used to gain insight in which aspects of a patient's life with the disease are affected most by the treatment. In the future this information can be used to establish a tool that selects the best possible treatment for individual patients with the best outcome for the HRQoL from a patient's perspective and their wants and needs.

1.5 Research question and sub questions

This research aims to explore the influence of PD medication; the positive and negative outcomes, side effects and process characteristics on the HRQoL of patients.

The main research question of this research is:

- ***What is the influence of the treatment and disease on the life of Parkinson's disease patients?***

To find a good answer to the research question the following sub questions were formulated:

- *Which HRQoL domains of the patient life are the most influenced by the Parkinson's disease Symptoms?*

For answering this sub question HRQoL instruments will be used to get an insight in which domains of life are the most influenced by the Parkinson's disease.

- *What are the patient experiences with the disease and the treatment of Parkinson's disease?*

This sub question will be answered with the data from the interviews with Parkinson's disease patients. The focus lies on the PD symptoms, the positive and negative effects of the treatment and the treatment characteristic's and how this influences his or hers life.

2 Theoretical background

2.1 Pathogenesis and treatment

Parkinson's disease is the degeneration of nerve cells in the brainstem that produce the substance dopamine (Speelman, 2007). The so-called nerve cells of the "substantia nigra", which produce dopamine, die or degenerate rapidly. Normal reduction rates in healthy human brain of the "substantia nigra" lay around 3% per 10 years. When around 80% of the cells have died the motoric symptoms of the Parkinson's disease will emerge (University of Maryland, 2010). The shortage of dopamine producing cells results in a shortage of dopamine. The role of dopamine is to activate processes in the basal ganglia (BG). The processes activated in the basal ganglia are involved with motoric processes, emotion, associative learning, planning, work and memory (Benitez-temino et al., 2008). A shortage of dopamine leads to an imbalance in the brain causing problems with the mentioned processes in the patient. There is no exclusive test to diagnose Parkinson's disease. The symptoms can be divided in motor and non-motor symptoms. The diagnosis of Parkinson's disease is based on medical history of the patient and for most on a neurological examination focusing on the motor functioning (Hughes, Daniel, Kilford, & Lees, 1992).

2.1.1 Symptoms

The symptoms of Parkinson are commonly grouped to four groups; the motoric-, autonomic-, sensory- and mental symptoms (Den Oudsten et al., 2007).

The four primary cardinal motor symptoms are tremor at rest, rigidity, bradykinesia and postural instability (Jankovic, 2008). The primary motor symptoms of PD normally start at the dominant side of the body (Weintraub, Cynthia, Cornella.L, Faan, & Horn, 2008). If a person is right-handed for example the resting tremor, 'counting money', starts with his right hand. When the disease progresses, both sides of the body can be affected.

Tremor at rest is trembling when the persons is not moving (at rest). This feature of PD is observed in 70 to 90% of the patients (Weintraub, Cynthia, Cornella, Faan, & Horn, n.d.). Other parts of the body can also have the rest tremor. Lips, chin, jaw and legs can be involved as well. The tremor at rest disappears when the patient sleeps or is moving (Jankovic, 2008).

Bradykinesia is the motor symptom of PD which is the greatest disabling burden for the patient and which occurs in 80% to 90% of the patients (Weintraub, Cynthia, Cornella.L, et al., 2008). Bradykinesia means slowness of movement and in extreme cases there is no initiation to movement at all which is known as akinesia (Jankovic, 2008; Weintraub, Cynthia, Cornella.L, et al., 2008). Bradykinesia can result in different associated motoric symptoms such as difficulties with planning, initiating and performing movements. Also

the sequential tasks, multitasking and the fine motoric can be affected (Shobha, Roa, Hoffmann, & Amer, 1997).

Rigidity is inflexibility or stiffness of the limbs. When a passive movement is performed the limbs resist as a result of not good working flexor and extensor muscles (Weintraub, Cynthia, Cornella.L, et al., 2008). Movements can be rigid, by a 'cogwheel phenomenon', which means that the passive movement is in steps and shocking (Jankovic, 2008). Rigidity as result of PD can cause patients pain and problems with movement.

The last main motoric symptom is postural instability. This manifests in the late stages of Parkinson when the other motoric symptoms increase in severity (Shobha et al., 1997). Postural instability is also a result of the treatment not working well anymore, leading to falls and injuries like broken hips (Weintraub, Cynthia, Cornella.L, et al., 2008).

Smaller motoric problems, or motoric related symptoms, are problems with eating and swallowing, writing, vision problems

2.1.2 Non-motor symptoms

There are also a lot of non-motoric symptoms, the most common (and disturbing) non motor symptoms will shortly be discussed. The symptoms are grouped into four categories:

- Neuropsychiatric;
- Autonomic dysfunction;
- Sleeping disorders;
- Sensory.

In the Table 1 on the next page the symptoms are listed for every group and additional information is given if that is needed to clarify the concepts. Not every patient develops these symptoms and not every symptom is a symptom of PD. A lot of the symptoms are also symptoms of ageing. However PD-symptoms differ from ageing symptoms on frequency and severity, PD patients have the symptoms more and more severe as persons with the same age (Krishnan, Sarma, Sarma, & Kishore, 2011).

Table 1 Non-motor symptoms of PD

Symptom group	symptoms	Additional information
Neuropsychiatric	-Anxiety	Also comes with stress, panic attacks and often comes with depression
	-Apathy	
	-Cognitive problems	Memory problems (STM), concentration and complex tasks
	-Confusion	
	-Dementia	
	-Depression	Higher risk with ageing
	-Hallucinations & delusions	High influence on HRQoL
	-Word finding	In communication problems finding right words/concepts
Autonomic dysfunction	-Gastrointestinal problems	Nausea, diarrhea and constipation are common
	-Bladder problems	Frequency (in night) and incontinence
	-Hyper salivation & Xerostomia	Over or under producing saliva which can cause communication problems
	-Orthostatic hypotension	Low blood pressure when standing up
	-Sexual dysfunctioning	Erection problems
	-Over transpiration	
Sleeping disorders	-Fatigue	Problems on the sleeping domain occur very often, between 60 to 90% of the patients have a sort of sleeping problem.
	-Insomnia	
	-Somnolence	Near falling asleep
	-Sleep attacks	Suddenly falling asleep
	-Dreams	Patients report vivid dreams
Sensory	-Pain	Can be caused by rigidity or muscle contractions, often result motor symptoms
	-Vision problems	
	-Parasthesias	Tickling or burning unpleasant feeling/sensation . Sometimes itchy or cold/warm feeling.
	-Restless legs	Form of inner restlessness of not being able to lie or sit still.
	-Akathisia	
	-Numbness	

Sources: (EPDA, 2012; Fahn, 2003; Frank, Pari, & Rossiter, 2006; Jankovic, 2008; Shobha et al., 1997; Weintraub, Cynthia, Cornella, Faan, & Horn, 2008; Weintraub, Cynthia, Cornella.L, et al., 2008)

2.1.3 Treatment

The treatment of Parkinson's disease is primary targeting the motoric symptoms to diminish the symptoms. Till this moment there is no cure for Parkinson's disease. There are different treatments to suppress the symptoms with different working principles. There is a wide range of medications and depending on the patient and his disease characteristic's (age, disease duration, treatment time, etc.) a regime is prescribed. Mostly starting with one drug in a young patient in an early stage to a complicated regime of several drugs with a tight schedule. In Table 2 the sort of drugs are grouped with their working principle and most common adverse effects.

Table 2 Most common used medication

Medication group	Working principle	Adverse effects
Antichloregics	Oldest treatment of PD. Blocking passage of signals/impulses by nerves as result of surplus acetylcholine. Restoring balance with shortage dopamine. Used to treat tremors in early stages by young patients with still good cognitive functioning.	Cognitive problems, constipation, dry eyes, bladder problems, dry mouth, hallucinations, Gastroinstenal problems, neuropsychiatric adverse effects.
Levodopa (carbidopa)	After converted in brain to dopamine L-dopa replenish natural dopamine. Carbidopa prevents dopamine being converted outside the brain (less adverse effects + more dopamine in brain). (Also available in controlled release). Mostly given in beginning and stays cornerstone treatment	Hallucinations, hypotension, nausea, somnolence, leg edema. Motor fluctuations & dyskinesia's after long usage.
COM-T inhibitors	Blocking enzyme that breaks down dopamine. Natural dopamine & levodopa stays longer active. Given as combination drug with levodopa. Improve wearing-off and commonly described in a later stage against degradation of levodopa and extend half-life of L-dopa.	Diarrhea, intensifying levodopa adverse effects, liver problems, color change urine.
Dopamine agonists	Almost same structure as dopamine. Used by the parts of the brain if as it is natural dopamine. Instant stimulation. Reduces off periods'. Begin (initial) young patients & late stage reduce off time and need L-dopa. Cause less dyskinesia as levodopa Improving motor impairment and disability	Nausea dizziness, headache, leg edema, hearth & lung problems, nausea, sleeping problems hallucinations, vivid dreams. Compulsive behavior (gambling, shopping, sex), vomiting, hypotension.
Dopaminergics	Similar structure as dopamine. Dopaminergics (Amantadine) works by increasing the dopamine by restoring balance between dopamine and glutamate.	Nausea, hypotension, hallucinations, confusion, edema, insomnia.
MAO-B Inhibitors	MAO-B is a natural enzyme in the brain breaking down dopamine. MAO-B inhibitors block this enzyme resulting in more and longer dopamine in the brain. Early stage, lower motor flux, reduce levodopa need, lower disability	Nausea, insomnia, weight loss, hypotension, dry mouth.

Sources: (EPDA, 2012; Lewitt, 2008; Samii & Ransom, 2005; Schrag, Quinn, & Quinn, 2000; Shobha et al., 1997; Weintraub et al., n.d.)

Non-drug based treatment

Duodopa is an form of internal levodopa (+ carbidopa) deliverance in the form of an gel with an continuous calculated stable flow of levodopa (Nyholm, Klangemo, & Johansson, 2012). This treatment is commonly prescribed for long term patients with motor fluctuations and on the maximum of treatment (Nilsson, Nyholm, & Aquilonius, 2001). Negative elements of this treatment are the need for an external port connected internally to the duodenum connected to an relative large and heavy external pump who has to be filled with duodopa every 24 hours (Hauser, 2011).
This treatment is still relative rare but could be a great improvement for patients suffering from motor fluctuations as 92% in a research indicated an improvement of their HRQoL (Hauser, 2011). Besides possible hardware problems the side effects are the same as those from levodopa that can be found in Table 2.

Deep Brain Stimulation (DBS) is a relative new treatment for PD. Due its invasive character, risks and costs it is not commonly used in the treatment of PD. In 1997 DBS was used for the first time to treat PD, and especially the symptom “tremors”. Electrodes are placed inside the brain and connected to a neuro-pacemaker placed in the chest of the patient. The neuro-pacemaker can be programmed and adjusted at every moment and even patients can control it to their needs (Benabid, 2003).

Today the treatment is being used for patients with severe motor fluctuations and levodopa induced dyskinesia’s when the drug regime is not sufficient anymore (Benabid, 2003). A large study in 2004 compared two almost identical patient groups divided on basis of the best medication treatment and DBS. The outcome was that patient’s receiving the DBS treatment scored on all tests better that the drug group. Also on quality of life items the improvement was greater as in the best drug treatment (Bötzel et al., 2006). Problems with DBS mostly concern hardware failures, maintenance (battery), brain hemorrhages, infarcts and seizures (Samii & Ransom, 2005).

2.1.4 Motor Fluctuations, dyskinesia and dystonia

As the disease progresses, substantia nigra cells diminish and their functioning. Also the medication loses its working effect and dose and treatment have to be adjusted. From research is known that within five years an estimate of 40% of the patients develop motor-fluctuations and dyskinesia (Shobha et al., 1997). After five years of levodopa based treatment this percentage is even 50% for motor fluctuations (Schrag, Jahanshahi, & Quinn, 2000a). After ten years of levodopa use percentages were even higher, 67% had motor fluctuations and 57% dyskinesia’s (Schrag, Jahanshahi, & Quinn, 2000b). A recent research even found that 33% of the patients between one and two year of levodopa use showed wearing off (De Rijk et al., 1997).

Wearing-off means that the effectiveness of a drug becomes less in time or as the PD progresses. When medication is taken the PD symptoms go away or diminish. As time passes by the symptoms return and a new intake of medicine is needed. The time the

medication works, is called “on”, and becomes shorter. A new dose or adjustment of the treatment is needed. The period that the symptoms are back is called the “off” period.

Subsequent to wearing-off and the off period is the so-called “end of dose akinesia”. This occurs mostly in the morning when the patient wakes up and the muscles are stiff And is seen as one of the most disabling effects of Parkinson (Jankovic, 2008)

As a result of wearing-off a patient can have the on-off effect. This means the suddenly, sometimes unpredictable, passage from medication working and no symptoms to the state off medication not working anymore and symptoms being back.

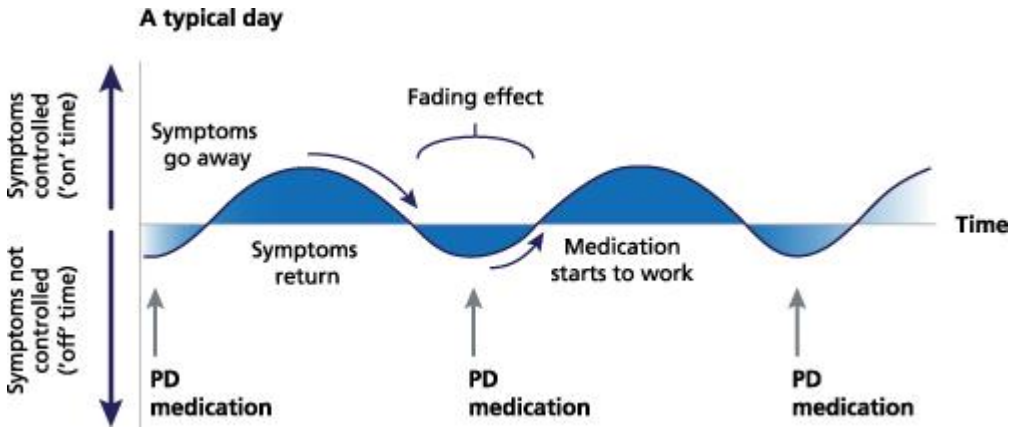

Figure 1 On-off effect (Source: Parkinsonpoly.com)

The Figure 1 above shows a “sine” function. As the disease progresses the tops (on-time) will get shorter and less high. At some point the treatment has to be adjusted or altered to sub stain a good control of the motoric symptoms.

Freezing is an suddenly moment of being unable to move, free zed or glued to the ground. The precise cause is still not known but it mostly happens in late stage patients and in the off period. Freezing can happen everywhere at any moment (Schrag, Quinn, et al., 2000).

Two other unwanted results of wearing-off are dyskinesia and dystonia. Dyskinesia is unwanted fast movements mostly as a result of a peak of dopamine in the brain. Dystonia are slow forced unwanted movements that mostly appear after or at the end of intake of levodopa (Rascol, Goetz, Koller, Poewe, & Sampaio, 2002). Dystonia is the effect of unwanted muscle contractions. As result of these contractions the limbs, body or face get abnormal expressions and positions.

Disease duration (progression), treatment duration and higher doses of levodopa was of significant influence on motor-fluctuations and dyskinesia (Schrag, Quinn, et al., 2000). From that research it was found that after 10 years of treatment all respondents developed motor fluctuations and or dyskinesia, 36% in the range from 6 to 9 years of treatment and 13% with 5 years or less of treatment.

2.2 Health status, Quality of Life and Health Related Quality of life

2.2.1 Health status and Health Related Quality of Life

Three concepts are widely used in health science and also misused. Health status, Health Related Quality of Life and Quality of Life are related but not the same.

Health status (HS) is the functioning of an individual on physical, mental and social abilities or disabilities (Curtis & Patrick, 2003). Health status refers to being able (or not able) to do tasks a healthy normal person could do.

Quality of Life (QoL) is a wider concept. It is the rating of a person of his life based on wide spectrum of aspects influencing his life. This involves his own health, of relatives, finance, social life, safety, leisure activities, etc. (Marinus, Visser, Jenkinson, & Stiggelbout, 2008). This is a very broad concept and involves all aspects of life of a human being.

Health Related Quality of Life (HRQoL) focuses just on the quality derived or compromised from health and influencing the quality of life. A good description for HRQoL can be defined as: "*Quality of Life in relation to the impact of disease and treatment on patients, the psychical, emotional and social well-being after diagnosis and treatment"* (Asadi-Lari, Tamburini, & Gray, 2004). HRQoL is important to healthcare and patients because it is able to measure the impact of a chronic disease from a more patient specific view (Guyatt & Feeny, 1993).
The main difference between HS and HRQoL is that HS does not measure the impact of a disability on the quality of life and HRQoL does. Person A and B can have a Spinal Cord injury giving them the same health status. However person B can still rate his HRQoL better as person A, this can be due personal characteristics or differences in treatment. Quality of Life involves everything influencing a person's quality of life.

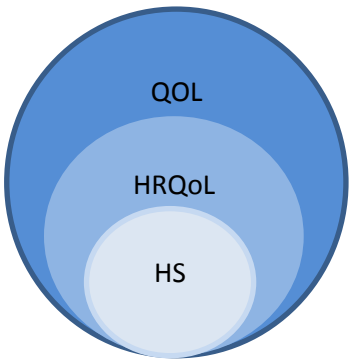

Figure 2 How HS, HRQoL and QoL are intervened

Figure 2 shows how the three concepts can be related with each other, clearly showing the differences in magnitude

As said before the terms HS and HRQoL are sometimes misused, measuring the HS instead of the HRQoL focusing on abilities and limitation (Den Oudsten et al., 2007).

HRQoL-instruments are not designed to measure HS solely but to measure the impact of the disease, limitations and treatment on the HRQoL of the patient. However this has lead in the past to the fact that patients and science/professionals have different point of views from what is quality, how to reach it and their approach to a disease and HRQoL.

Science and professionals have long focused on solely the disease and symptoms to cure or to improve the health status of the patient (Rumsfeld, 2002). In chronic diseases however the main focus of the patient is on the actual final outcome on his health related quality of life.

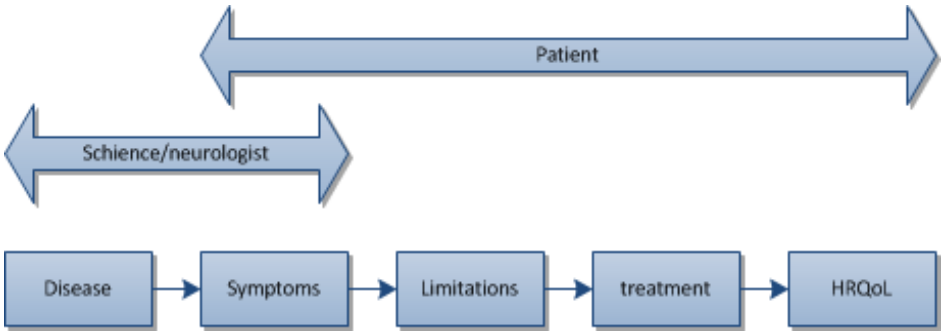

Figure 3 Health status viewed by patient and science/neurologist

Figure 3 above shows the scope and view of the patient and science/neurologist on HRQoL. The patient and professional have the symptoms in common. Science and health practitioners focus mainly on the disease and symptoms. The patient focuses on more aspects influencing his HRQoL; symptoms, limitations, treatment (characteristic's) and as outcome the HRQoL. Lately science and neurologist have shifted their focus more in line with the patient but still the impact of the treatment on HRQoL is not well researched and documented (Bridges & Jones, 2007). Focusing on the patient, a bottom-up approach means looking to the satisfaction of the patient with his treatment. Satisfaction means in this case that his experiences meet his expectations, if he is satisfied with his achieved HRQoL (Asadi-Lari et al., 2004). This leads to a better compliance to the treatment and influences the HRQoL (Guldvog, 1999).

It is important to make a distinction between health status and health related quality of life when treating a patient. The main difference between HS and HRQoL is that HRQoL is based on patient's perspective and evaluation of his situation where his disease influences all aspects of his quality of life. Health status is focusing more on the physical, mental, emotional and functioning and or limitations (Den Oudsten & De Vries, 2007).

2.3 Parkinson's disease, what influences the HRQoL

2.3.1 Treatment

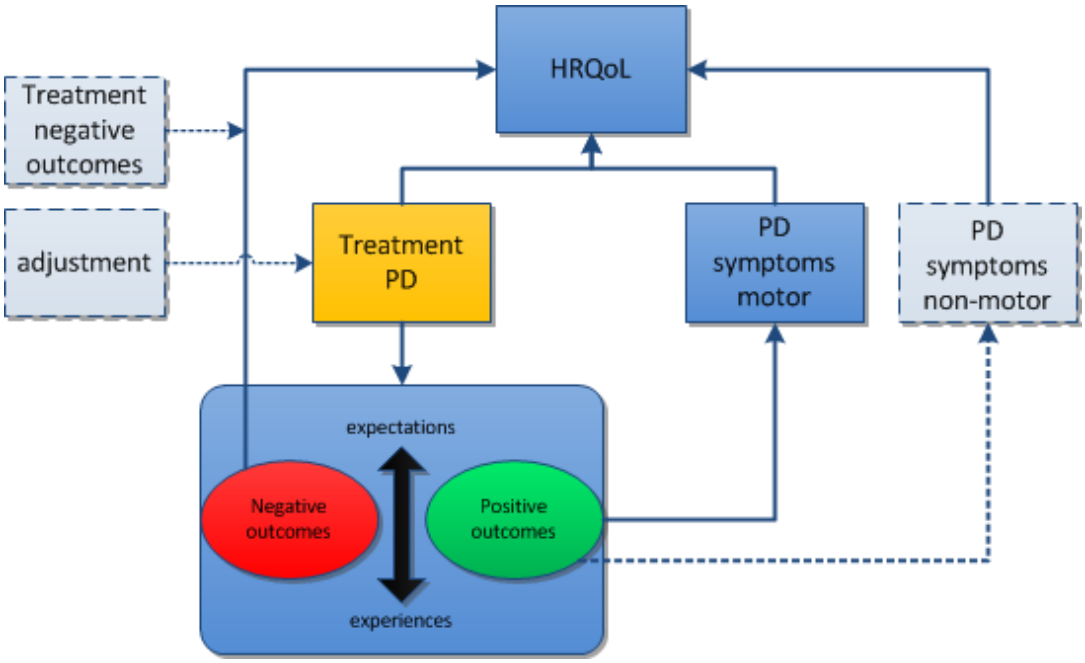

Figure 4 Visualization what contributes to the HRQoL

Figure 4 above shows what influences the HRQoL of a Parkinson's patient and what will be the focus of the research. The boxes with the dotted lines visualize the impact on the HRQoL but are not real part of the primary treatment and focus. However when a "being nauseas" is in the top of most negative outcomes the conclusion should be that treatment of this negative outcome will increase the HRQoL. Adjustment of the treatment is only of interest to this research when the reason can be found in the Treatment negative outcomes (adverse effects and treatment characteristic's). The focus lies on the box in the left corner. Improving or declining of the HRQoL is based on the negative and positive outcomes of the treatment. If the experiences meet or not the expectations of the patient influences the satisfaction and indirectly the HRQoL of the patient (Williams, 1994).

2.3.2 Medication adherence

Compliance to a medication/treatment regime for chronically ill patients is very import to the success of the disease treatment outcome. Compliance means that the patient follows the prescription rules given by the professional. Non-compliance means that the patients misses a doses, takes an extra dose, mistimed, underuses or overuses (Vermeire, Hearnshaw, Van Royen, & Denekens, 2001).

Non-compliance, poor compliance or sup-optimal compliance to the treatment regime in Parkinson's patients can result in motor fluctuations, side-effects or increased Parkinson symptoms (Leopold, Polansky, & Hurka, 2004). Overuse can result in worsening dyskinesia, confusion, visual hallucinations and obsessive behavior. Underuse is associated with under control of Parkinson symptoms with especially bradykinesia and rigidity (D. Grosset et al., 2009). The adherence to the treatment regime is of very important to the success of the treatment of the motoric symptoms and prevention of motor fluctuations of the PD patients.

Medication regime compliance in patients with Parkinson's disease is not optimal from the research that has been performed on this subject in the last decade.

To obtain data on regime compliance some research used an electronic pillbox to monitor when and how often it was opened to monitor the adherence to the treatment regime. After the research period the participants were asked about their compliance and this data has been compared to the electronic data. Only 10% had a complete adherence and up 53,8% had during the test non-adherence. With non-adherence it means missing, overuses, underuse or mistimed on one or more occasions. The respondents were a bit more positive about their adherence (Leopold et al., 2004). The most given explanation in the research was "too busy/forgotten".

In another research the focus was more on the causal relationships of non-adherence/sup-optimal adherence. The research found several causal relationships for adherence. The research divided satisfactory and non-satisfactory compliance on the 80% adherence threshold. This threshold was based on the total compliance during the entire test. The researchers found that a higher age and single dose medication contributed to a satisfactory medication adherence (K. a Grosset, Bone, & Grosset, 2005).

The research described above had a follow-up study. The population was bigger and additional causal relationships were found. From the research it was found that patients with a higher L-dopa dose had a lower adherence as patients with a lower dose of levodopa. The research also measured the stage of Parkinson and the HRQoL score of the participants.

The results indicated that worse scores on disability scale tools (UPDRS, Hoehn&Yahr, Swab&England) and PDQ-39, resulted in a greater risk of suboptimal adherence (D. Grosset et al., 2009). They also looked at the influence of having motor fluctuations (due

to disease progression/levodopa working less) or not on regime adherence. In the Table 3 below the differences between these two groups are listed.

Table 3 Adherence in patients with and without motor fluctuations

	With fluctuations	Without fluctuations
Total adherence	96%	98%
Day adherence	74%	93%
Timing adherence	25%	40%

Source: (D. Grosset et al., 2009)

The main differences can be found in day and timing adherence. Patients with less medication and/or no motor-fluctuations had a higher adherence (day and timing) as patients with a greater medication and or motor-fluctuations regime. A possible explanation could be due the fact that patients themselves adjust their regime to the motor fluctuations taking the medication not as prescribed adjusted to the occurrence of the motor fluctuations. This could be due to the reason that patients with earlier and severe motor fluctuations postpone drug intake to extend the time drugs keep working (D. Grosset et al., 2009).

Psychiatric disorders, duration of treatment, number of medications and frequency of intake also influence the compliance. The higher these factors the lower the compliance. High compliance was found with degree of disability which can be related to supervision (Vermeire et al., 2001).

Several reasons were found for non-compliance are listed in the Table 4 below.

Table 4 Reasons for Non-Compliance

Reason	Extra information
Side effects	Only 5-10% given as reason. Adjusting dose/lowest dose could be reason.
Complexity/large treatment & poor communication	Especially elderly persons or persons with memory disorders
Absence symptoms & delay effect drug	No (direct) symptoms or no direct results influence adherence
Wrong information	Beliefs and ideas about medication/healthcare. Information from relatives and friends. Experiences with medication (self and others).
No heterogeneity treatment/diagnostics	Specialists themselves not compliant to standards → heterogeneity prescribing
Emotional & social	Lack social support. Depression. Low QoL.

Source: (Vermeire et al., 2001) & (K. a Grosset et al., 2005)

The last important factor in medication adherence is the patient-doctor relationship. A sympatric understanding doctor who gives clear information to the patient and listens to his wishes and findings and co-operate to find the best regime were also important for a better adherence (Vermeire et al., 2001). In chronic diseases like PD patients themselves should have an important (leading) role in their treatment decision-making.

Due to the side effects of medication compliance to the (medical) care is becoming a big problem in health care, especially for chronic diseases in general. In the United States this results in 10% of the hospital admissions and 23% of the admissions in nursing homes (Vermeire et al., 2001). Suboptimal adherence in PD is widespread phenomenon in Europe that can lead to fluctuations. Better communication and understanding of their regime and importance could improve adherence and limit fluctuations and improve their HRQoL (D. Grosset et al., 2009).

2.4 Measurement of Health and related quality of life

To measure the supposed Health Related Quality of Life (HRQoL) there are different tools available. The addition of supposed is to point out that in the literature and health science many tools are marked as HRQoL tool even when they only or mostly measure HS.
The tools can be divided into generic and disease specific HRQoL tools. For this research the EQ-5D and the PDQ-39 will be used in an adjusted form to get an overall impression of the HRQoL of the interviewed patients.

PDQ-39

The PDQ-39 has been validated in many languages and some of the validating processes also tested for convergent validity with the generic HRQoL tools like the SF-36. Both scales have a range from 0 to 100 but in the SF-36 higher is better, where in the PDQ-39 it is opposite. In an extensive validation process of the US PDQ-39 it was compared with the SF-36 on relevant dimensions to test the correlation. Correlation between the two tools were high for most of the convergent dimensions except the social support (PDQ-39) and social functioning (SF-36) which can be the result of differences in culture between the united states and the UK and the translation (Bushnell & Martin, 1999). The UK validation of the PDQ-39, the original version, were also correlating for the relevant dimensions with the SF-36 (Viv Peto, Jenkinson, & Fitzpatrick, 1998).

The main advantage of the PDQ-39 is that it can be filled in by the patient self and the experiences of the disease from the patient's perspective. Also the PDQ-39 instead of generic HRQoL tools includes the disease relevant items for measurement (V Peto & Jenkinson, 2001). As the PDQ-39 is developed with the advice and input of PD patients itself it is able to address the most important dimensions. An advantage is that the PDQ-39 is sensitive to disease/patient progress and clinical changes (Bushnell & Martin, 1999). Changes in outcome between "identical" patients but with and a treatment plan could influence the outcome. In other words; the PDQ-39 could be used as an evaluation of treatment regimens and to monitor the onset of the disease (Jenkinson, Fitzpatrick, Peto, Greenhall, & Hyman, 1997).

EQ-5D

The EQ-5D is a generic instrument to measure the health related quality of life of a patient. It is widely used because of its short length and the ability for respondents to complete it themselves. The EQ-5D consist out of two parts, a questionnaire and a visual analogue scale (VAS)(euroqol, 2000).

The questionnaire is based on 5 dimensions that influence the health status and rating is based on “no problems”, “some problems” and “extreme problems”. The five dimensions are mobility, self-care, usual activities, “pain & discomfort” and “anxiety & depression”. This gives 243 possible health states with an range from 0 (dead) to a perfect health state (1) (Brazier, Roberts, Tsuchiya, & Busschbach, 2004). The main focus is on disabilities or abilities, to be able or not to be able. Only the dimensions pain/discomfort and emotions measure a more perceived health state.

The VAS asks the respondent to rate their own health state on a scale from 0 to 100; this rates more the perceived health status.

A research by Schrag in 2000 found significant correlations between the EQ-5D scores and the scores on disease severity and a significant relation with QoL. The outcome of this research makes the EQ-5D a good instrument to rate the HRQoL. The regression between the VAS and disease severity was still significant according to the same research but less strong (Schrag, Selai, Jahanshahi, & Quinn, 2000).

2.4.1 Patient preferences of endpoints

Important in a treatment is the satisfaction. Satisfaction is the degree in which expectations meet experiences. Expectations of the patient can be influenced by his own believes, what he knows from his own research or from what the physician told him. Patients can have low expectations but also overestimated expectations.

With chronic diseases the treatment itself and what the patients wants is important. Every treatment has it positive and negative sides and the individual patients have their own preferences. In past research evidence based medicine like RCT’s was based on preferred outcomes by the scientists and physicians such as diminishing symptoms and efficacy. Lately there can be seen a shift where research and treatment is more focused on patients’ needs and desires (Bridges & Jones, 2007).

There are many different kind of treatments and combinations possible for PD which have to be adjusted when the disease progresses. It is only a recent development that the HRQoL focus is a bottom-up. This means that research is focusing on patient relevant end-points in the treatment of mostly chronic diseases (Kinter, Schmeding, Rudolph, & Bridges, 2009).

Due to the fact that health care and social welfare results in a higher life expectancy also the prevalence of chronic diseases will raise. As for chronic diseases there is no cure, the point of interest is the HRQoL. We can measure the HRQoL, we can measure disability but we have not to this day a good tool to measure individual preferences of treatment and outcomes. The most important in the treatment of chronic diseases like PD is the individual preferences of endpoints instead of the general decrease of symptoms.

3 Research method

This research will be of qualitative, with quantitative elements, design with an explorative goal into the influence of the treatment on his life from the patient's perspective. A literature study was performed to understand the pathogenesis of the disease; the treatments, adverse effects and process characteristics and health related quality of life. To answer the research question interviews were held, and questionnaires were handed out before the interview, with the respondents with Parkinson's disease. In Figure 5 below the process of data collection is visually portrayed.

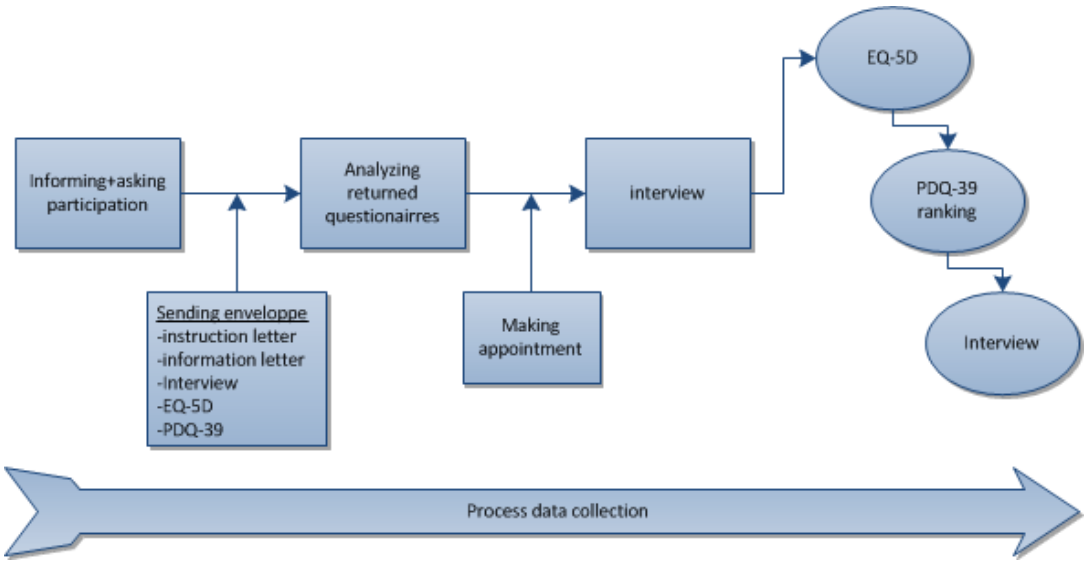

Figure 5 Process data collection

3.1 Informing and gathering respondents

The sampling took place at two locations in the Netherlands in Twente, The hospital MST and revalidation Centre “Roessingh”, both located in Enschede. At a patient information day at the MST, PD patients were informed about the research and the goal. From the database of the Roessingh respondents were selected and contacted by phone if they were willing to participate. When patients were willingly to take part in the research they were sent a envelop with the following content:

- Information letter
- Dutch translated and adjusted PDQ-39 questionnaire (Appendix 5)
- EQ-5D health status questionnaire (Appendix 6)
- Copy of the interview subjects and questions
- Addressed return envelope

A short period after this envelope had been sent the persons were called and asked to use the addressed envelope to return the EQ-5D, and the PDQ-39 and an appointment was made if they are still willingly to cooperate. A copy of the interview was included to get the respondent familiar with the subjects. At every moment the participant could stop their participation without justification. The data gained from the interviews was been handled with regard to their privacy and anonymity.

3.2 Interview method

The layout of the interview was a semi-structured interview, which means that a number of subjects were discussed and a few questions per subject were formulated. These questions had the purpose to gather basic data and to trigger the respondent’s experiences on subjects.

On the first page there is room for the personal information and contact information. In a text box the patient was informed about on-off effect of medication. After this box the patient was asked if he is in the on or off modus of his medication/treatment. The full interview subjects and questions can be found in Appendix 4.

The subjects that were discussed are:

1. Personal characteristics
2. Global health status
3. Positive treatment outcomes
4. Negative treatment outcomes (side effects treatment)
5. Negative treatment outcomes (motor-fluctuations)
6. Treatment characteristics and adherence

The design of the interview was based on the literature on HRQoL in relationship with the Parkinson’s disease and the input of the project group. Of essential input were the test-interviews with patient-experts and their remarks and input. A few essential flaws have been corrected and improvements could be made based on their experience and insight.

The essence of a semi-structured qualitative interview is that there is room for flexibility during the interview. A basic set of subjects and directional questions is made but during the interview there is room for the interviewed own input (Babbie, 2010). During the interviews a mining model will be used. This model supposes that the subject has the specific, for interviewer unknown, information that is wanted for the research (Kvale, 2007).

During and after the test-interviews it was found out that there could be a potential threat to the validity. When introducing a subject or question, the interviewed person not always directly could give his experience or answer. Even after the interview or at another subject the respondent came with an experience he forgot to tell before. This is the main reason why was chosen to handout the interview along with the questionnaires before the interview. The reason behind that is that respondents can get familiar to the subjects, overthink it and even make notes about what they want to share during the interview. The small research population is also a reason why was chosen for semi-structured interviews. In this research new insights are explored and longer, deepening qualitative interviews, are more preferable in this situation.

3.3 Sample population

A target of twenty complete interviews was set. A research protocol, Appendix 1, and a patient information letter, Appendix 2, was written and submitted to the METC (Medisch Ethische Tucht Commisie (Medical Ethical Commission)) for approval and clearance for conducting this research that was granted (Appendix 3). The global inclusion and exclusion criteria can be found in Table 5 below.

Table 5 Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Parkinson's disease	Parkinsonism
Undergoing a treatment	No treatment
Cognitive able	Cognitive disabled (severe)
(H&Y 1-2-3-4)	Bed ridden (H&Y5)

Patients were not excluded on base of sort treatment or how long they are diagnosed with PD. The sample size was also too small to select patients and make groups on base of treatment or the H&Y scale. The essences of this research are the experiences and outcomes influencing the patients HRQoL.

3.4 Questionnaires

Respondents were asked to return the EQ-5D and the PDQ-39 before the actual interview. The questionnaires were analyzed and it gave an indication on which domains the patient had problems concerning his HRQoL or what his health state was that day and could be compared with the health state at the day of the interview.

3.4.1 The PDQ-39 Questionnaire

The PDQ-39 exists out of eight dimensions and 39 questions that are involved with the supposed HRQoL. The number of questions per dimension and the scoring can be found in Table 6. The scoring possibilities are; never=0, occasionally=1, sometimes=2, often=3 and always or cannot do at all=4.

Table 6 PDQ-39 dimensions and characteristics

Dimensions	Number of questions	Which questions	Scoring
Mobility (Mob)	10	1-10	Score/40*100
Activities of daily living (ADL)	6	11-16	Score/24*100
Emotional well-being (Emo)	6	17-22	Score/24*100
Stigma (Stig)	4	23-26	Score/16*100
Social support (Soc)	3	27-29	Score/12*100
Cognitions (Cog)	4	30-33	Score/16*100
Communication (Com)	3	34-36	Score/12*100
Bodily discomfort (Bod)	3	37-39	Score/12*100
Total PDQ-39 score	39	1-39	Sum single index scores/8

Source: (Jenkinson et al., 1997)

Scores can be calculated for the single dimensions and as total score. Single dimensions as a measurement have been validated which means that differences in treatment can be found (Jenkinson et al., 1997). The range of the outcomes lies between 0 and 100, zero meaning excellent health and 100 meaning (near) death.

The PDQ-39 however focuses more on abilities and limitations instead of the related Quality of Life. This clinical/professional bottom-up approach is not always patient relevant when it comes HRQoL of a specific disease (Bridges & Jones, 2007). Being able or not being able does not tell how the impact is on the HRQoL from an individual patient. The PDQ-39 has been adjusted to see if the respondents personally rate the importance to their HRQoL different. After each set or dimension of questions the respondent is asked to rate the questions of the subject they just answered as shown in the next Figure 6.

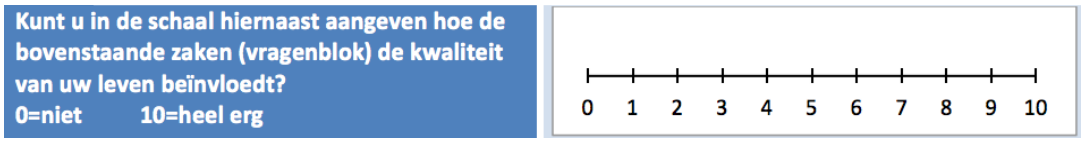

Figure 6 Rating scale dimension PDQ-39

This makes visible on which dimensions their limitations influences the HRQoL the most according to the respondent. However each dimension exists out of multiple questions and it has to be specified to see which “question” or limitation influences the HRQoL the most.

3.4.2 PDQ-39 ranking the items

Every question on the PDQ-39 can be rated from never to “always or cannot do at all”, the frequency of the problems occurring. The answer “never” indicates no problems and does not negatively influence the HRQoL. The other four answers influence the HRQoL but their relative perceived importance to the other questions is not known, it only tells the frequency of a limitation. When a person answers a question with always and another question with occasionally it still is not clear what has more impact on the HRQoL, it only tells which occurs more often.

The personal rating scale from Figure 6 indicates which domain influences the HRQoL relative the most. While conducting the test interviews with the patient experts a good example was given. *’Walking half a mile’* and *‘walking 100 yards’* are two questions from the PDQ-39. Both are weighted the same when it comes to impact on HRQoL. However the patient-experts said that the walking a 100 yards means walking around the house, to the neighbors or from the car to the shop. “Walking half a mile” is something that doesn’t occur that much in comparison to “walking 100 yards. Not being able to walk 100 yards has more consequences on HRQoL than not being able walking a half a mile.

The ranking of the items will tell which of the items contributes the most or is in the top influencing the HRQoL. The interviews will tell why and how frequency of the problems is related to the relative influence on the perceived HRQoL.

Every question was printed on cards and the questions sorted per dimensions. A question was placed in front of the respondent and the following question was read out and given with the task to place it above the previous, when it influences the HRQoL more or under when less. This was done with all the questions and every dimension if two or more items of a dimension were selected. This will tell from each dimension which item has the greatest influence when the results of the respondents are combined. Comparing the items between the dimensions would be difficult because there is not a direct comparison. The interviews should point out what the top of outcomes is that has the greatest impact on the HRQoL.

3.5 Statistical procedures

All quantitative data was processed with SPSS and Excel and first the relevant quantitative data has been tested for being normally distributed. The QQ-plots test was used to check if the data is normally distributed for the tails and the PP-plot for the means. Even when the population sample is small, the QQ-plots and PP-plots rendered by SPSS showed the variables are, or strongly approached a normal distribution.

For the PDQ-39 the average scores for the dimensions and total were calculated (original and weighted scores). The scores of the dimensions were compared with one sample t-test. The average score on a dimension were compared to the average score of the other seven dimensions. The same has been done with the weighted dimensions.

The original PDQ-39 scores were compared with the weighted scores on the dimensions with the Wilcoxon signed rank test. Correlations between the scores for the original and weighted scores were calculated with the Pearson's correlation.

The frequency of items of the PDQ-39 was measured by how many respondents reported the items as occurring/problem.

Rating of the items was based on a five-point scale used by the PDQ-39 to point out the occurrence of the items/problems. The average rating was based on every value possible including zero (never occurring).

Ranking of the items for the dimensions only and cannot be compared inter dimensional. The rankings were inverted when processed (a high rank has now a high score instead of low score). The items of each dimension have been tested with the student t-test to see if the mean of the item significantly differed from the average of the rest of the items in the dimension.

4 Results

In this chapter the quantitative results from the EQ-5D and the PDQ-39 questionnaires will be discussed.

4.1 Research population

The research population consists mainly out of respondents from the Parkinson information day at the MST, 16 respondents, of which 15 completed the questionnaires and 14 the interview. Five other persons were recruited from the database of the Roessingh, three returned filled in questionnaires and two of them participated in the interview.

A total of 16 interviews and 17 questionnaires were completely and correctly filled in, the details about distribution, age and treatment time can be found in Table 7. The sample consisted out of 12 male (71%) and 5 female (29%) respondents. The average age of the respondents is 66,2 years (*SD*=7,2). The average time being treated for PD was 8,3 years with a minimum of one year and a maximum of 20 years. The respondents have been divided into two groups based on treatment time. “Short” is zero to five years of treatment and “long” are six years or longer. Eight respondents were treated short and 8 respondents felt into the long treatment cohort. Only three of the respondents still were employed with or without adjustments to workload.

Table 7 Descriptives research population

	MST			Roessingh			Total		
	N	**M age years**	**M Treatment time years**	**N**	**M age years**	**M Treatment time years**	**N**	**M age years**	**M Treatment time years**
Male	10	65,1	7,1	2	75,5	13,5	12	58,5	8,2
Female	5	64,5	8,5	-	-	-	5	64,5	8,5
Total	15	64,9	64,9	2	75,5		17	66,2	8,3

4.2 Quantitative results

4.2.1 PDQ-39 results

In this section the results of the PDQ-39 questionnaires will be discussed. In the third column of Table 8, in the third column the original mean scores of the PDQ-39 can be found. The 4th column shows the dimension scores of the average weighting by the respondents. In column five the difference is tested between the original and weighted dimension scores

Original PDQ-39 results

Firstly the data form the original PDQ-39 score will be discussed. In Table 8, third column, for every dimension the average and SD is given.

The table shows that the highest mean scores in the population are for the dimensions Communication and Bodily discomfort. Short behind are ADL and "cognitions". The mean scores on "Stigma" and "Social Support" are lower as the score on the other dimension, giving the impression these dimensions do not influence. Most of the respondents did not report problems on these two dimensions as can be seen in Figure 7. Later the items within the dimensions will be compared.

PDQ-39 results after weighting

As part of the research the rating of the impact of a dimension on the HRQoL by the respondent was asked. The next step is to see how respondents rate the dimensions themselves. The results are shown below in the 4th column of Table 8.

The respondents rate the influence of the reported problems in the dimension of "Mobility" (*M*=42,77, *SD* 33,77) as the greatest. The dimension mobility has the most items and most of the problems were reported in this dimension. Due the fact that most reported problems are in this domain this could influence the weighting of the dimension. When it comes to rating, only the dimensions "stigma" and "social support" differ significant from the mean of the dimensions. This however is based on just a few observations. Communication, cognitions and bodily discomfort still are of great influence on the HRQoL as in the original results.

Table 8 Comparing the PDQ39 scores and the respondents' own rating on dimension level?

	N	Original PDQ-39 (SD)	Weighting pdq-39 (SD)	Wilcoxon test	*r*
Mobility	17	33,53 (26,3)	42,77 (33,8)	*z*=-2,55 *p*=0,01	,944*
Activities of Daily living	17	39,71 (23,8)	35,29 (22,2)	*z*=-0,95 *p*=0,34	,761*
Emotional well- being	17	23,78 (17,7)	30,06 (22,0)	*z*=-2,48 *p*=0,01	,925*
Stigma	17	9,56 (13,3)[1]	15,06 (21,6)[2]	*z*=-2.10 *p*=0,04	,918*
Social Support	17	13,24 (18,9) [1]	14,71 (22,1)[2]	*z*=-0,98 *p*=0,33	,952*
Cognitions	17	37,87 (15,9) [1]	35,24 (23,5)	*z*=-0,85 *p*=0,39	,793*
Communication	17	43,14 (22,9) [1]	39,65 (26,8)	*z*=-1,39 *p*=0,16	,935*
Bodily discomfort	17	43,14 (22,5) [1]	38,77 (25,3)	*z*=-1,61 *p*=0,11	,912*
Total PDQ-39	17	30,88 (15,9)	33,23 (21,2)	*z*=-1,18 *p*=0,24	,955*

[1] Means dimension significant different from mean Total PDQ-39 (t-test) p<0,05
[2] Mean dimension significant different from mean Total PDQ-39 (t-test) p<0,05
**P<0,01*

Comparing the original PDQ-39 results with the weighting

The means of the dimension have been compared for the original PDQ-39 score and weighting of the dimension by the respondent have been compared with the Wilcoxon signed rank test in column five. The outcome of the Wilcoxon test is for three dimensions significant. The outcome for mobility was that the respondents rate the influence on their HRQoL significant higher as the original test points out. The difference is 9,24 on a scale of hundred, which is a 27,6% difference with reference to the original PDQ-39 score.

Emotional well-being is from the personal rating also of more significant influence on the HRQoL, a difference of 24,6%. The last dimension which is being rated more influencing by the respondent is "stigma", a difference of 5,5 points (57,5%). Side note with stigma is that the number of respondents reporting problems is very low and is based on a few observations. That could indicate that when problems are experienced on these dimensions the impact on the HRQoL is great. The other dimensions also differ for the original and rating scores, but not significant. Some approach the significant level and with a larger population, significant differences could probably be found.

In the last column of the Table 8 the correlations are given. All correlations are significant on a p< 0,01 level and all but two have a correlation near 1. The correlation between original and weighting for the dimension "ADL" was weaker, $r(15)=0,76$, $p<0,01$. The correlation between original and rating for cognitions was also not as strong, $r(15)=0,793$, $p<0,01$. This can be an indication that the relation between having problems does not implicate that the impact of a problem is been experienced as of even great influence on the HRQoL and vice versa.

4.2.2 EQ-5D results

The respondents were asked to complete the EQ-5D on T=0 (before the interview), along with the PDQ-39, and during the interview (T=1).
Between the first and the second EQ5D questionnaire was between one and two months. The comparison of the results of the EQ5D on the two different moments can be found in the Table 9 below.

Table 9 EQ5D & VAS: Descriptives differences (T=0) Before and during interview (T=1)

	N	**Mean (*SD*)**	**Range (min-max)**
EQ5D T=0	16	0,73 (0,204)	0.87 (0,02-0,89)
EQ5D T=1	16	0,79 (0,199)	0,85 (0,15-1)
VAS T=0	16	0,686 (0,122)	0,48 (0,37-0,85)
VAS T=1	16	0,703 (0,091)	0,30 (0,5-0,8)

The Table 9 above shows that the mean score before the interview is lower than mean score during the interview. This implicates on the day of the interview the respondents rated their HRQoL better as before the interview. The rating of their health status by themselves also does not differ substantially.

It can be concluded that based on the EQ-5D, the health status of the respondents between completing the questionnaires and the actual interview, the health status did not change significantly as also did not the perceived health status by the respondents.

4.2.3 The outcomes of the tests compared

Tested is if the PDQ-39, PDQ-39-rating, the EQ-5D and the VAS at t=0 differ on outcome for the HRQoL measurement.

The outcome of the mean of the tests lies between 30.76 and 33,23 where the possible outcome range is between 0 and 100. This indicates that all four tests give a same average outcome. This is being tested with the "Friedman's test" and the outcome was that the test do not difference significantly from each other, $\chi(3, N=16)=2,1$, $p=0,552$). This however does not implicate that the perception of problems on the individual dimensions are equal also or measured well.

Table 10 Correlation PDQ-39 original, PDQ-rating, EQ-5D and VAS

	PDQ-original	PDQ-rating	EQ5D	VAS
PDQ-original	1			
PDQ-rating	,956**	1		
EQ5D	,690**	,595*	1	
VAS	,624**	,605*	0,398	1

**P<0,05*
***P<0,01*

The Table 10 above shows the correlations between the different instruments. The correlation is high and significant for the pdq-original and rating, $r(15)=0,956$, $p<0,01$). This means that the outcome of the PDQ-39 and the rating as whole is in coherence. The EQ-5D and VAS do not have a significant correlation. That can be an indication that health status as measured is not the same as been experienced by the respondents.

4.2.4 Ranking the PDQ-39 items and dimensions

Frequency

The analysis started with an inventory of the frequency of the items. For every item it is calculated how many of the respondents reported it. In Appendix 6 this data is grouped by dimension and sorted from high to low. The percentage of items reported as problem by the population has been grouped by dimension in the graph below.

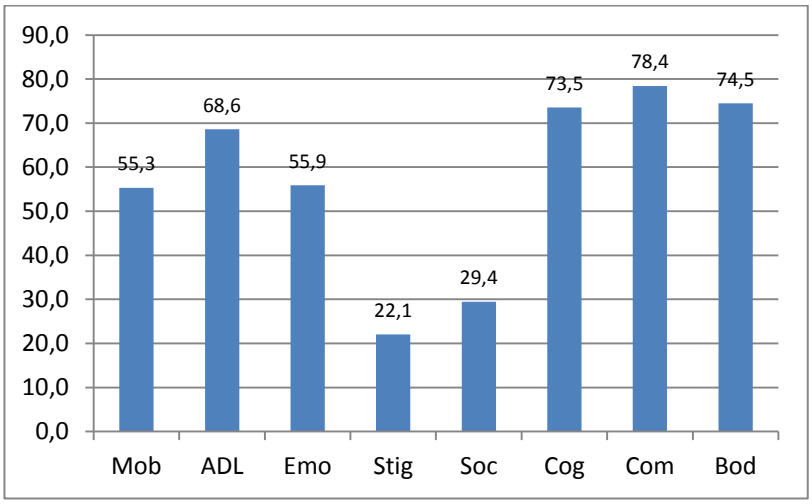

Figure 7 Frequency items reported per dimension by the respondents

Figure 7 shows that ”Stigma” and “Social support” are the less reported dimensions. Only 22,1% and 29,4% of the items in the dimensions Stigma and Social Support are being reported which does not directly implicate that they are not of great influence on the HRQoL. The dimensions on the right in the figure are the most reported by the respondents; around 75% of the all items concerning cognitions, communication and bodily discomfort occur in the respondent’s lives. This indicates that respondents relative have the most problems on these dimensions.

In Appendix 8 all the items are ranked on frequency from high to low. As Figure 7 already pointed out, stigma and social support items are reported minimal which can be an indication that problems on these dimensions almost do not exist, the acceptance and support of PD patients is well.

Table 11: Top ten items based on frequency of all items of the pdq39

Dimension	Item	N (percentage)
ADL	PDQ14) Had problems writing clearly?	16 (94,1)
COG	PDQ31) Had problems with your concentration, e.g. when reading or watching TV?	16 (94,1)
COG	PDQ32) Felt your memory was bad?	16 (94,1
COM	PDQ35) Felt unable to communicate with people properly?	15 (88,2)
BOD	PDQ38) Had aches and pains in your joints or body?	15 (88,2)
COM	PDQ34) Had difficulty with your speech?	14 (82,4)
MOB	PDQ1) Had difficulty doing the leisure activities which you would like to do?	13 (76,5%)
ADL	PDQ13) Had problems doing up your shoelaces?	13 (76,5%)
ADL	PDQ16) Had difficulty holding a drink without spilling it?	13 (76,5%)
EMO	PDQ22) Felt worried about your future?	13 (76,5%)

Table 11 shows that most of the problems found with the PDQ-39 are based on communication, ADL and cognitive functioning particular with concentration and memory. The items “PDQ-31 had problems with your concentration, e.g. when reading or watching TV” and “PDQ32) Felt your memory was bad?” could indirectly be of influence on communication. Interesting is that only one item of the dimensions mobility is in the top ten. This indicates that problems with items within this dimension are less frequently reported as being expected.

Rating

For every item the mean rating was calculated which can be found in Appendix 9. The ranking is from descending based on the mean per dimension. This gives a good overview which items are rated the most often and highest. The top 10 of highest rated items is listed in Table 12.

Table 12 top ten items based on rating of the pdq-39

Dimension	Item	mean
ADL	PDQ14) Had problems writing clearly?	2,4
BOD	PDQ38) Had aches and pains in your joints or body?	2,0
MOB	PDQ1) Had difficulty doing the leisure activities which you would like to do?	1,9
COM	PDQ35) Felt unable to communicate with people properly?	1,8
COM	PDQ34) Had difficulty with your speech?	1,8
MOB	PDQ2) Had difficulty looking after your home, e.g. DIY, housework, cooking?	1,8
COG	PDQ31) Had problems with your concentration, e.g. when reading or watching TV?	1,8
COG	PDQ32) Felt your memory was bad?	1,8
ADL	PDQ13) Had problems doing up your shoe laces?	1,8
COG	PDQ10) Been confined to the house more than you would like?	1,6

When we compare Table 11 and Table 12 it is obvious that the dimension cognitions cannot be found anymore in the top six when it comes to rating. This is due the fact that

problems of the dimension cognitions occur but not that often as other items. The mobility items moved up in the highest rated items. That is not unusual as being items of daily living, which can occur every day several times. The first listed mobility items are leisure activities and the second are household tasks.

Still three cognition items out of all four and two out of three communication items are in the top ten of highest rated items. This is a good indication that this has a relative great influence on the HRQoL especially when the mean ratings of most of the items only differ on hundredth decimal level.

Ranking

The outcome of the ranking is per dimension of the PDQ-39. For every item per dimension the mean rank is calculated and can be found in Appendix 11. In Table 13 below the items that were ranked significant higher by the respondents are listed.

Table 13 Rating x Ranking; the significant most influencing items on the HRQoL by dimension

Dimension	Item
Mobility	1) Had difficulty doing the leisure activities, which you would like to do?
	2) Had difficulty looking after you home, e.g. DIY, housework, cooking?
	5) Having problem with walking a 100 yards **
ADL	14) Had problems writing clearly?
EMO Well Being	22) Felt worried about your future
Cognitive	31) Had problems with your concentration, e.g., when reading or watching TV?
Communication	34) Had difficulty with your speech

**P<0,05 **p>0,05*

In the dimension mobility item 1 and item 2 were significant ranked higher by the respondents. Looking at the description of the items it are events that occur frequently on a daily base. The items describe daily routine activities in a “normal” daily life, both for leisure and self-reliance. Having problems walking 100 yards was not significant of more influence on the HRQoL as other items. However only six persons reported problems on this item but when they did it ranked high.

In the dimension ADL problems with writing was mentioned as most influencing the HRQoL of the patient. It can be seen as a daily activity but also as a form of communication, which is for elderly people more important as for younger people.

In the dimension emotional well-being the item worries about the future stands out. PD is a chronic disease where it progresses over time worsening the symptoms. For PD patients the future is unsure how the disease develops and how it affects their life. In the dimension cognitions all items were rated and selected often but the item problems with concentration was significant ranked higher as the others. The items of the dimension communication also were a problem for many respondents but difficulty with speech was standing out significantly.

4.3 Qualitative analysis

4.3.1 Global health and co-founding variables

Part of the interview concerned the global health of the respondents. Age, global health, other health problems and their treatment can influence the HRQoL as well. Ageing persons are more vulnerable for diseases, are stiffer and cognitive problems are more common. Some respondents have a history of severe diseases and some of them were still treated for those diseases like diabetes mellitus 2, CVA and cardiovascular diseases.

Respondents were asked if those co-founding variables were of influence on their HRQoL. Besides the PD most respondents (75%) were in good health and did not have uncommon problems for their age and gave the impression of a healthy lifestyle. If respondents had other diseases and treatments it never started chronology with PD, so in most cases differentiation between the different treatments, diseases and potential side effects was possible.

The role of age and associated limitations was a possible cofounding variable. Some respondents were themselves aware, and maybe overestimated age, and some underestimated age. One example regarding fatigue the respondents answered:

Quote 1: Respondent 12 → The influence age, pd or medication?

"For example, Friday night I had a party from the bicycle club, the tour before the party I cancelled because I cannot handle that anymore when I go on Saturdays to the TT (motor event, whole day). Sundays we held a party for my daughter who graduated. I cannot handle that all anymore."

This respondent is 57 years old and works almost fulltime. As the interview continued and afterwards he started to realize that he was not 30 years anymore and this could be of influence.

4.3.2 Positive treatment outcomes

Part of the interview was to make an inventory of the PD symptoms, their influence on the HRQoL and the success of their treatment. The essence of a treatment of PD is in the best case to totally suppress the symptoms with no side effects.

The respondents were asked which symptoms would be present if they would not take their medication. The respondents in the long-term cohort could not clarify that always because they mostly were adherent to the treatment. Besides new symptoms or the severity of the first diagnosed ones possibly were not experienced anymore due to effective treatment. In that case they were asked with which symptoms they were diagnosed or experienced when they forget their medication.

Thirteen out of sixteen respondents reported tremors. For almost every person (92,3%) the medication worked well to suppress his or her tremors. The tremors disappeared almost totally or were minimal in their "on" status. Depending on the severity of the tremor the medication could improve their HRQoL immense like the next respondent says:

Quote 2: Respondent 3 → Positive outcome tremor

"Interviewer: "which symptoms occur when you would not take your medication?"
"I would have tremors and not functioning"
What do you mean with not functioning?"
"I cannot accomplish anything; I could not even hold a cup of coffee"

All but one did not have emotional or social problems caused by the tremor and the tremor was only a practical limitation that in most cases was suppressed well by the medication to be of no not a great influence.

Ten persons said their PD started with postural instability, what was experienced as limiting and of great influence on their HRQoL. Walking and bicycling was getting harder or impossible and mend less social interactions. A walk to the supermarket, doing groceries, sometimes became impossible and disables not only ADL tasks but also impacts social contacts.

Medication worked well for most of the respondents for the physical problems. Most of them claimed symptoms were minimal and some respondents, mostly in the long cohort, claimed they were stable and or the progress of their disease and symptoms was slowed.

Four respondents said the treatment had a positive outcome on their memory and concentration. Three of them claimed improvement of their memory and concentration and one reported stability of memory and concentration. Six respondents claimed the treatment improved their fatigue (three persons) and slowness (three persons), it did not solve the problems but diminished them.

Main positive treatment, result as the respondents described, were results on motoric symptoms like the tremors and stability of the disease progression. This made them capable to do normal daily living activities and social participation. Four of them

benefitted when it comes to memory and concentration symptoms. Due to the adherence and adjustment of treatment it is difficult for the respondents to point out the exact positive treatment outcomes while some new developed symptoms are maybe suppressed due the good medication adherence.

4.3.3 Negative treatment outcomes

The negative treatment outcomes consist out of the possible side effects and motor-fluctuations and their effect on the HRQoL. First the side effects will be discussed and subsequently the Motor-fluctuations.

Sleeping problems, fatigue & slowness

The most reported sided effects were on the "sleeping" domain. Fifteen out of sixteen respondents had a form of sleeping problem. It was common to have problems to fall asleep, dreams, sudden sleep attacks, sleep through and waking up (to early). Most of the respondents however did not have "sleeping problems". The next Quote 3 explains that statement:

Quote 3: respondent → 4 sleeping problem

"No, the neurologist asked me if it troubled me. I said no, it does not bother me. The neurologist concluded that I did not have a sleeping disorder (laughing)"

Respondents also noticed having dreams, more frequent or abnormal, but still this was of no influence on the HRQoL for most respondents.

One respondent however reported it as a sleeping problem, his day and night rhythm was turned around. An important side note is that this respondent was extremely worried about the health of his second wife, because he already lost his former spouse.

Interesting is that most sleeping problems were reported by the partners of the respondent:

Quote 4: Respondent 7 → Sleeping problems

Interviewer: "Do those sleeping problems (waking up and dreams) influence your QoL?"
Respondent: "No, I just fall asleep again."
The respondent woman is starting to laugh and says:
"No, but I wake up and it influences my QoL"

A few were bothered due this, because they were afraid to accidently hurting their partner while sleeping (involuntary movements).

Sudden sleep attacks or falling asleep was reported by 50% of the respondents, only people still driving a car rated it as a severe problem and faired giving up driving. A respondent that was in a car accident and instantly gave up driving makes clear that this fear is not unfounded. This made him more immobile and caused loss of social contacts and activities.

This fear is been especially reported by two respondents young and employed and two persons living alone.

Quote 5: Respondent 9 →Impact fatigue driving

"I'm afraid to fall asleep while driving and to have my driving license taken away. I cannot without my driving license, it would be devastating"

A large part, 44%, of the respondents reported fatigue as side effect and two respondents complained about slowness. Depending on the severity of the problems on the sleeping domain a fatigue respondents had to schedule their daily activities and needed more time and or planning for tasks and activities.

Quote 6: Respondent 2 → Planning activities

" …. you have to take into account what you want to do on a day. Also on good days you have to plan your activities well otherwise you have to regret it the next day."

Quote 7: Respondent 6 Impact fatigue

…or gardening, physical activities, you get tired fast. In better days I mowed the lawn in the evening after a day's work, now it takes whole Saturday morning with 3 breaks"

The three respondents still employed however saw this as a big problem because it obstructed their work. They had to work fewer hours or take more breaks to get through the day. Their biggest fair was the moment to give up working due fatigue.

Psychiatric and mental disorders

Almost every respondent who reported depression and/or sadness on the PDQ-39 questionnaire relativized it during the interview. During the interviews most said it was normal being depressed/down sometimes just like other persons experience that. While ranking the items respondents were astonished these items showed up. A common response was that they felt sometimes depressed, angry of sad but said it was normal and relativized it the same way as the next respondent does:

Quote 8: Respondent 12 → about depression

"Someone without PD also has moments he feels terrible"

Only two out of the sixteen respondents showed severe problems on the emotional dimension. One respondent was in a late stage of PD and prisoned in his own home. This respondent did not explicitly tell he was depressed but his remarks during the interview were very cynical. The other respondent was not even a year diagnosed with PD and had a fast progression of the symptoms while they still had to find the best treatment.

The 14 others showed minor issues on these domains and accepted the fact that they were diagnosed with PD. Two of them had severe problems accepting the disease in the beginning but accepted it relative shortly later, with or without professional guidance or anti-depressive medication.

The respondents who accepted PD focused on abilities and not on disabilities. That can be a reason that HRQoL measurement is not always accurate as pointed out in the next two quotes.

Quote 9: Respondent 14 → Acceptance

"You have to use your energy in a good way and not thinking to much of your disease"
"A person gets that, another that and I got PD, so be it.

Quote 10: Respondent 2 → acceptance

I know that I can't do anything more, I accepted it as it is. I can think that I want to and more but I simply can't. You have to be happy with the things you still can. So you can do a lot of things, you have to give up a lot but there are still things left

Fifteen out of sixteen respondents were stable or progression of the disease was slow and stable, taking years or decades what can be a reason of acceptance and minor mental problems. The only person who had extreme difficulties with acceptance was, as mentioned earlier, the person who progressed fast at a relative young age.

The concept "depression" triggered a defensive attitude during the interviews and maybe worst case imaginations with only the word itself. This could mean that depression is still there in a mild form that is not being recognized by the respondents, or they don't want to recognize it or have a just accept is as part of life.

A substantial amount of respondents reported being more emotional (37,5%) and having some kind of restless feeling and/or ungrounded moments of fear (50%). During some interviews respondents started to cry and some reported being amazed they suddenly cried with for example drama movies as pointed out in Quote 11.

Quote 11: respondent 12 → Being emotional

When there is a sad movie on television I can start to cry out of nowhere. You asked me before if I was ashamed in public. Well when I'm watching with my daughters a dramatic movie I start crying sometimes.

The respondents reporting these incidents however expressively told that this did not influence their HRQoL a lot; they mostly were surprised by it.

Ten out of sixteen (63%) of the people feared the future and half of the respondents claimed they had a sense of fear that they did not had before. They feared new symptoms and worsening of symptoms that would affect their HRQoL. The intensity of the fear of the future different from a modest level to the level of making arrangements/collecting information for committing suicide when the HRQoL would worsen. Of importance to fear (of the future) was also the experience with other Parkinson patients. One person explained that he did not liked PD meetings because when he saw persons in a later stage he feared becoming that.

Quote 12: Respondent 12 → future comparing negative

"Sometimes I fear the future. When I think of him (older brother with PD, last stage, severe condition) I fear the future. But then I say to myself: he got it real early and I did not.

Other respondents said that meeting other patients who still were stable for many years gives them hope. And some looked at others assuring themselves they did fine because it could be worse:

Quote 13: Respondent 14→ Future comparing with others positive

At the meeting I watched the elderly persons. When you see how well they are doing with treatment I think: "mmm, my future looks fine"

The reason of the fear had in common to be not undependable anymore. Of importance to the level of the fear was also the age of the respondents and the time they were diagnosed with PD. Young newly diagnosed person feared the future while older patients who were stable for years did not fear the future so much.

Also some fears could be cause by other factors like age or character. Having PD puts everything under a magnifying glass and respondent's maybe to easily blame PD. One respondent talked that over with her neurologist:

Quote 14: Respondent 11→ cause and effect

*I was driving in the mountains in Spain **and** was extremely frightened. I contacted the neurologist and he asked: "what about your qualities of character?" I did not even thought of that before. I am easily frightened and not adventurous. That is the most annoying; you don't know what to attribute to PD and what to your qualities of character. Things that never stand out now become prominent and you ask yourself: "is it my character or PD?"*

Three respondents reported severe psychiatric disorders as result of side effects. They reported problems with confusion, hallucinations and paranoia. These problems were so severe that even one respondent was so convinced his spouse cheated that he wanted a divorce.

Quote 15: Respondent 10 → Disillusions

"…I lost my mind… all kind of delusions…seeing this that were not there en imagining things….You have to think of thinking your wife being unfaithful….it put a lot of pressure on the relationship …. But we survived that period "

All three respondents with severe mental side effects contacted the neurologist and quit the medication and the side effects disappeared. If the patients and partners did not notice these side effects as being side effects their HRQoL could be influenced enormous.

Short-term memory loss and concentration problems were reported as side effect by 50% of the respondents. During the interviews it was difficult for the patients to differentiate if memory and concentration problems were due side effects, as a result of the progression of Parkinson's disease or ageing. Depending on the personal characteristics and circumstances of respondents, it had influence on the HRQoL. Persons still employed, academic and/or literate reported it as a great problem and of great influence on their HRQoL. These problems also had as co-effect problems with communication.

Quote 16: Respondent 4 → Having a good conversation

"This is very annoying and also now during this interview when I have trouble formulating sentences and finding the right words. This happens on a daily base. …. I would love to be able to have a good conversation again"

One respondent even preferred incontinence and being less mobile to STM problems and clear thinking.

Quote 17: Respondent 9 → Preferring incontinence above mental problems

"….I only had problems keeping it dry. That was the reason I start using pampers, they absorb a lot you know"
"….I don't get gloomy about it, it is as it is"

However ageing and progression of the disease itself can be the cause of the (worsening) memory and concentration problems. To point out the exact cause or differentiating between the possible causes is difficult. Stress and large groups were mentioned as being a catalyst for these problems and respondents said they try to avoid stress and large groups.

Quote 18: Respondent 2 → Large groups worsen symptoms

Interviewer: "did it have consequences on social or personal level?"
Respondent: "I still have a social life, but less as before and in large groups I don't feel well."
Interviewer: "What do you mean with not feeling well?"
Respondent: It gets to demanding, a restless mind. In a crowd you are suddenly facing everything at once, I cannot handle that anymore"

Gastrointestinal disorders

Constipation, diarrhea and incontinence (or urge to pee) were a problem for seven out of the sixteen respondents interviewed. It was commonly unpredictable and sometimes painful. The respondents said this influenced their HRQoL because of the pain and limitations to social/work activities.

Quote 19: Respondent 4 → Diahrea fair social

"….When you go outside you have the fear you have to go to the toilet…..No real pain but is sensitive"

Quote 20: Respondent 9 → Constipation pain and incontinence

"….When I have obstipation it is really clogged and that really hurts…for example on the camping when I scream out of pain….I don't go to the theatre anymore because it is not done to stand up and go to the toilet…… But I have to say that I don't like going out in Twente (lived in Amsterdam before)."

Five respondents mentioned nausea and or vomiting and one of them quit the medication because of these side effects. Most of the respondents reported these problems in the morning (after taking their meds) or while having breakfast. The influence on the HRQoL however was limited due to the fact it was of short durance and with very limited pain or discomfort. Side effects like urine discolor and gain weight was reported but was rare and of negligible influence on the HRQoL.

4.3.4 Motor fluctuations

Respondents were asked about motor-fluctuations. The Table 14 below provides an overview the prevalence of the motor-symptoms for the two time cohorts of medication duration.

Table 14 Prevalence motor-fluctuations in population

	Dyskinesia		Wearing-Off		On- Effect Off		Freezing	
	Yes	No	Yes	No	Yes	No	Yes	No
Short Term (0-5 years)	2 (25%)	6 (75%)	3 (40%)	5 (60%)	1 (14,3%)	7 (85,6%)	5 (60%)	3 (40%)
Long Term (>5years)	6 (75%)	2 (25%)	5 (60%)	3 (40%)	4 (50%)	4 (50%)	3 (40%)	5 (40%)
Total	8 (50%)	8 (50%)	8 (50%)	8 (50%)	5 (45,5%)	11 (55,5%)	8 (50%)	8 (50%)

Eight out of sixteen respondents reported dyskinesia and six of them were in the long-term cohort. Of great influence was the moment it happened, the inability to foresee was the most annoying for the respondents.

Quote 21: Respondent 1 → Dyskinesia Unpredictable

"….it always happens on moments that come very inconvenient….mostly when I am at someone else"

Quote 22: Respondent 11 → Dyskinesia Unpredictable

"I'm doing something at home and suddenly I start to shuffle and I cannot get out. Then I become very bad tempered"

Of influence also was the time the respondents were diagnosed with PD, answers from the respondents showed that how longer PD how less difficult to cope and accept.

Wearing-off is a problem also reported in 50% of the cases and more common with long-term medication usage, five out eight of the cases. The greatest problem respondents have with wearing of is the fear of taking more medication. There were several reasons given by respondents to postpone a consult with the neurologist and increase or change the medication. The fear of a ceiling effect was mentioned often, reaching the maximum dose where it did not work anymore suppressing the symptoms. Additional to that fear was that they would get a new medication of which they feared side effects. Some said they already took a lot of medicine and more pills, more moments were not welcomed. Some respondents were aware of wearing-off, some postponed medication increase and some took, in consultation with, an extra dose on moments they needed it for some extra activities.

Quote 23: Respondent 11 → Wearing-off

"I don't, I struggle on, than I have more problems with walking. Till I have an appointment with the neurologist….And the medicine has to be increased. When the medication has been increased I notice that it goes better. But that point, you don't want more medicine. At a certain moment you reach the maximum you can take and you have to look for a new medication as I heard. That is the reason I postpone increasing my dose. That is something you have to learn, choosing between quality and guarding your medicine intake.

The on-off effect is not reported very often; one in the short-term cohort and three in the long-term medication usage cohort, the impact on the HRQoL was of no relevance.

Eight respondents are reporting freezing. For most, except one respondent, it occurs for a short duration. The respondents all reported that suddenly they could not move or turn; they realize it and developed a way to overcome the freezing. Every respondent developed his own method from starting to sing, turning over the other side, or to talk to themselves aloud giving themselves instructions to move. Respondents described it as "something that happens" to "a bit annoying but nothing more" and only one reported it as a great impact on the HRQoL. This respondent was the newly diagnosed and rapidly developing the disease and still very depressed by the diagnosis.

From all motor-fluctuations "dyskinesia" was mentioned as having the largest impact on the HRQoL. The duration and obstruction of daily tasks was mentioned as reasons. The unpredictable character of dyskinesia was of great influence. Wearing-off was reported in half of the cases and 6 respondents (80%) said it was their own choice to suffer from wearing-off symptoms because of the fear of an increase of the medication…

4.3.5 Treatment and treatment characteristics

The respondents were asked how they experienced their treatment and the characteristics and their influence on the HRQoL.

All but one were satisfied with their neurologist and PD nurse and were adherent to their prescription. Most of the respondents reported being stable or a stable slow progression of the disease and symptoms. Forgetting a dose happened a lot but when asking more details it mostly mend taking it a half hour or hour later. Really forgetting the dose occurred very rare according to the respondents. Most of the partners helped reminding the respondent taking their medicine. However in the past some respondents reported that they changed their regime where they only had to take medication in the morning instead of more moments during the day.

Some of the respondents complained that they had to take it on several moments where they were reminded of their disease but for most of them it was no problem. However most of the respondents would prefer taking medicine once a day in the morning and some arranged that:

Quote 24: Respondent 15 → Preferring meds once a day in morning

"…I had to take sifrol 3 times a day, especially in summer while camping or sailing I forgot them. I said that to my neurologist and he prescribed me the controlled-release version.

Taking medication in the morning with a controlled-release emission was preferable by the respondents. Reasons for that were that it would fit in their morning routine, they were not reminded during the day and the change of forgetting a dose was smaller. However when the disease progressed they had to take more medication and on different moments.

The dose in the afternoon was mentioned as being annoying and most problems remembering this dose was mentioned:

Quote 25: Respondent 17 → treatment

I find the medication regime a lot…The alarm goes every three hours…Then you have to stop what you are doing to turn of the alarm and you subsequently forget to take your pills. The best would be to have continuous supply so you don't face reality every three hours. Taking medication in the morning or two times on a day would be great!

Six respondents tried to postpone the moment were they should increase the medication to suppress the symptoms. Reasons where that they did not like medication, feared a ceiling effect or an increase of side effects.

Quote 26: Respondent 10 → fear of ceiling effect

"as you can see it is a huge amount of pills I have to take, I don't like the idea of higher doses and I'm afraid that I will reach the maximum dose to quickly"

Also interesting is that some patients use or used automatic dispensers (bagster) or pre-packed medication for a week. Respondents were not fond of these solutions because as they said they lost their control and independence over their treatment. Packaging in general caused some problems but not in a way it influenced the HRQoL a lot.

5 Conclusion, discussion & recommendations

5.1 Conclusion

Sub Question: Which HRQoL domains of the patient's life are the most influenced by the Parkinson's disease Symptoms?

The original results of the PDQ-39 showed that the most problems were reported on the domains "cognitions", "communication" and "Bodily discomfort. The respondents reported around 75% of the possible problems on these domains. The items of the dimensions "Mobility" (55,3%) "Activities of daily Living" 68,6%) and "emotional well-being" (55,9%) also were reported frequently by the respondents. In contrast to the first mentioned domains these domains have more items which means respondents experience more problems in these domains absolutely. These items also were reported probably more often (frequency) because they occur on a daily base. That could be the reason that when weighting by respondents of the dimensions, the dimension "Mobility" was of greatest influence on their perceived HRQoL and significantly differed from the original PDQ-39 rating for that dimension. The items of the domains stigma and social were only a problem for a newly diagnosed or severe and lonely respondents. Focusing on the level of the items it was found that problems with cognitions and communication still were a problem for most of the respondents on basis of the frequency, closely followed by mobility and ADL problems. Of interest is that the feeling depressed was not in the top ten, "only" mentioned by 10 respondents and occurring not often in the respondent's life. This could indicate that "depression" is not of great influence on the respondent's life. Being worried about the future however was something that was reported within the domain emotional well-being the most and occurred the most often. The worries about the future health state and quality of life are something that influences the life of the respondents according to this outcome.

Sub Question: What are the patient experiences with the disease and the treatment of Parkinson's disease?

Many respondents mention fatigue but the young employed have more difficulties with this because it limits their functioning at work and or still very active (social) life. The older respondent, mostly not employed anymore, solves this by taking a short break that does not interfere with his daily schedule.

Mental problems were reported as being of great influence and especially limiting the communication with other persons. This has been confirmed by both the outcomes of the PDQ-39 and the interviews. Problems on the "communication" and "cognition" dimension are the relative most reported and most influencing their HRQoL. Five persons reported quitting medication mostly due mental problems but other side effects were reported scares or of very little influence on the HRQoL.

Some respondents experienced problems with doing leisure activities and indirect social contacts. For some this became a great burden depending on the severity of limitations. On the dimensions “mobility” and “ADL”, tasks involving motoric, most “problems” of the total were reported. This is also, as mentioned before due the fact that they included items that can happen every day and more times a day.

Research Question: What is the influence of the treatment and disease on the life of Parkinson’s disease patients?
Most of the respondents said their treatment suppressed the motoric symptoms in a satisfying way. The focus of treatments is on suppressing the in particular motor symptoms. As discussed in the theory this is the result of health status view on the disease. The patients view is from a quality point of view. Suppressing motoric symptoms can cause side effects or limitations that can have influence on the HRQoL. Most of the symptoms are the same as adverse effects of medication, knowing the exact cause is sometimes difficult. However most mentioned and limiting to the HRQoL were problems with cognitions and communications as result of adverse effects according to the respondents.

Fear of the future and fear of more medication were of influence on the HRQoL and even led to postponing increasing the dose or adjustment of the treatment. Even when this would mean that their Parkinson’s symptoms were not suppressed well anymore. The frequency of intake was for some patients, especially with a large regime, annoying and efforts to make the process easier sometimes was experienced as losing independence.

Most of the respondents however focused on abilities and not on disabilities as for example the PDQ-39 measures.

5.2 Discussion

Research method
The PDQ-39 was used to gather information on which dimensions respondents had problems. However this was based on having a disability and not merely on how it influenced the HRQoL. Ranking of the items during the interview tackled this problem partly but comparing the items between the dimensions on how it influenced the HRQoL was not possible. This was due the fact that ranking was per dimension of the PDQ-39 and not based on all items of the total PDQ-39.

Research population
The research population included seventeen persons of which all completed the questionnaire and sixteen also the interview. This is for the quantitative part of the research not a large sample that can influence the significance of the outcomes; a larger population would give more robust results.
The recruitment of the respondents was based on two methods. At an information day for PD patients at the MST a presentation about the research was given and people were asked for co-operation. In the other method patients from the database of the Roessingh were selected and approached by telephone for participation. Most of the respondents in

the population were from the information day and 94% completed the interview while only 40% of the Roessingh respondents completed the interview. A thread to the validity of the research can be the positive attitude of the respondents who voluntary participated in contrast to the respondents who were actively approached to co-operate. The research can be biased by the positive attitude of the research population, their treatment works extremely good or experienced relative few and mild symptoms or progression of the disease.

Results

A few respondents in this research reported depression. During the actual interviews the respondents flattened the concept “depression” and it was for just a few respondents just after the diagnosis a problem. The impact of depression or a “negative” mood was marginal on the HRQoL. Several research however pointed out that depression had a great influence on the HRQoL (Schrag, Jahanshahi, et al., 2000b). The respondents in this research however indicated that depression or “bad mood” had little influence and was considered as normal for a human being. Several research pointed out that depression was found in approximately 40 to 50% of the patients with PD (Schrag, Jahanshahi, et al., 2000a; Sławek, Derejko, & Lass, 2005).

The PDQ-39 indicated that 10 respondents (58,8%) felt depressed. During the interviews only one person stated literally that he was depressed but due another reason as the Parkinson’s disease. In two persons signs of depression were observed and two persons claimed they were depressed shortly after the diagnosis for a brief period. Anxiety was reported as a problem, and influencing the HRQoL, often. When the respondents were questioned further their fear commonly was based on the fear of the future, how would their disease progress and would they stay independent. However research also points out that depression is not always recognized by the patients themselves (Parkinson, Survey, & Committee, 2002). According to the Dutch situation more screening and more sensitive tools have led to an increase of “depression” in the population in general (Volksgezondheid, 2012).

In this research most respondents claimed that the non-motor symptoms influenced their HRQoL the most. Communication and cognitions problems were reported often as limiting to the HRQoL. This is in contrast with research that indicates that only 28% of the respondents said the non-motor symptoms were of greater influence on the HRQoL (Sethi, 2010). That research also pointed out that motor-fluctuations and dyskinesia were associated with a lower HRQoL in long term patients. The results of this research pointed out that long term patients were more often confronted with motor-fluctuations and dyskinesia but that a relative large part of them choose that over increase of the dose or new medications. This was due the fact they feared a ceiling effect and possible (new) side effects of medication. This can be an indication that long-term patients out of fear postpone adjustment of their treatment.

Cognitive problems were reported often and for the employed respondents this had a greater influence on the HRQoL as older persons, which is in accordance with other research. An explanation given was that young and employed persons had more difficulties performing their tasks as employee (and their roles like a parent or spouse)

(Leroi et al., 2011). However in this research also newly diagnosed and older patients (unemployed and children already self-reliant) reported a higher influence of cognitive problems on their HRQoL. As reason was given they feared the progress of their disease and did not know the future. The older and long diagnosed respondents experienced this less because of the fact they were stable or progression was slow which made them less anxious about the future and their cognitive problems (and other symptoms).

A lot of research into the HRQoL of PD patients focused on HS instead of HRQoL (Den Oudsten et al., 2007). This can explain some differences and the relative different influence observations on the HRQoL between this research and other research (in the past).

Another explanation can be the difference in treatment of PD patients between the different counties (and health systems). A research by Fitzpatrick found that in-clinic patients rated their HRQoL higher as out-clinic patients and this was due to better care (Viv Peto et al., 1998). It is possible that the Dutch healthcare for PD patients is better which results in different outcomes in what influences the HRQoL. If for example the treatment is not well adjusted to suppress motor symptoms, this can result in motor symptoms having a greater influence on the HRQoL. When motor-symptoms are well treated, the patient's HRQoL mainly can be influenced by the non-motor symptoms and treatment characteristics.

In general the causal relationship was sometimes hard to determine. Medication side effects, ageing and PD symptoms can have the same effects. To attribute a certain effect to a cause can be difficult because the existence of another cause or confounding variable.

5.3 Recommendations

- A HRQoL measurement tool based on the PDQ-39 but with ranking within the rating. In the original PDQ-39 the respondent only reports the frequency of the problem. When a problem occurs often it does not automatically implicate that it influences the HRQoL/life of the respondent also severe. The opposite also can be the fact, a problem occurring not often having a great influence on the respondents HRQoL. Using ranking, with the use numbers the relative influence on the HRQoL can be measured for the individual. By doing this ranking and frequency of the items combined, the items can be compared mutual.

- Make side effects and treatment characteristic's part of the PDQ-39/HRQoL questionnaire. Not only the disease but also side effects and treatment characteristic's influence a patient's HRQoL and can be very limiting to a person's HRQoL and life.

- Making sure the sample includes all groups of patients based. A problem could be that only the Parkinson patients with a positive attitude volunteer. Recruiting patients by neurologists could lead to a more representative research population.

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7 APPENDIX

Appendix 1 Research protocol

Onderzoeksprotocol:

Korte titel: Invloed behandeling parkinson op HRQoL vanuit patiënt perspectief.
Versie: 22 april
Datum: 11-04-2012

Uitvoerder:

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06 288 861 10

Supervisie/hoofdonderzoekers:

1e supervisor: Dr. Janine van Til
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Titel:

Onderzoek naar de invloed van de behandeling van parkinson op de gezondheid gerelateerde kwaliteit van leven (HRQoL) van de patiënt.

Inleiding:

Voor de behandeling van de ziekte van parkinson bestaat er een breed scala aan verschillende behandelingsvormen. In de huidige wetenschap is de invloed van de behandeling zelf op de HRQoL nog relatief onbekend gebied.

Onder "behandeling" word verstaan; de positieve (symptoombestrijding) en negatieve gevolgen (medicatiebijwerkingen) en de invloed van de "last" van het opvolgen van de behandelings-/medicatievoorschriften.

Dit onderzoek wil de kennis omtrent de invloed van de behandeling zelf op de HRQoL in kaart brengen met als doel een patiëntvriendelijk keuze instrument te maken die de persoonlijke wensen van de patiënt behartigd.

Onderzoeksvraag:

"Hoe beïnvloedt de behandeling van parkinson de gezondheid gerelateerde kwaliteit van leven van de patiënt?"

Soort onderzoek:

Kwalitatief onderzoek door middel van open interviews om inzicht te verschaffen over de invloed van de behandeling van parkinson op de HRQoL van de patiënt vanuit diens perspectief en ervaringen. Hierbij is gekozen voor gedeeltelijk gestructureerde interviews. De onderwerpen liggen vast en per onderwerp zijn er enkele "introductievragen" waarop naar aanleiding van de respons van de respondent wordt doorgevraagd.

Studie populatie:

Alle wilsbekwame mensen ouder dan 18 jaar met de gediagnosticeerde ziekte van parkinson die een behandeling volgen. De grootte van de onderzoekspopulatie zal ongeveer 30 participanten zijn.

Exclusie criteria zijn patiënten die cognitief te grote problemen hebben waardoor ze niet kunnen deelnemen. Outliers op het gebied van leeftijd, dus buitengewoon jong en oud, vallen ook onder de exclusie criteria.

Inclusie criteria:

Alle patiënten onder behandeling in stadia 1, 2, 3 en 4 van de Hoehn & Yahr invaliditeit schaal die (cognitief) in staat zijn deel te nemen aan het onderzoek.

Deelnemers aan het onderzoek worden geworven op de volgende locaties:

- Neurologie afdeling Medisch Spectrum Twente
- Roessingh Revalidatie centrum
- Internet patiënten fora

Patiënt belasting:

De deelnemende patiënten wordt gevraagd om thuis twee vragenlijsten in te vullen, PDQ-39 en EQ-5D. Hiervoor zal ongeveer 20 tot 30 minuten nodig zijn maximaal.

Het interview zelf zal op de voor de participant gekozen tijdstip en locatie (thuissituatie). De duur van het interview zal 30 tot 60 minuten zijn tenzij de participant aangeeft dat hij voortijdig wil stoppen ongeacht de reden.

Werving en toestemming:

Participanten worden geworven in de periode eind april tot eind juni waarbij in dezelfde periode de interviews worden afgenomen.

Werving op locatie:

In samenwerking met het Medisch Spectrum Twente (MST) en het Roessingh Revalidatie centrum zullen de patiënten worden geworven in de wachtkamer/ontvangstruimte van beide instellingen.

- De behandelend arts attendeert de parkinson patiënt op dit onderzoek en vraagt of hij of zij belangstelling heeft in deelname. Vervolgens kan de patiënt in de wachtkamer aan ondergetekende of secretaresse haar contactgegevens achterlaten en een envelop met de vragenlijsten meenemen. Enkele dagen hierna zal de patiënt worden benaderd of hij of zij wil deelnemen aan het onderzoek en wordt er indien bevestigend geantwoord een afspraak gemaakt.

Werving via het internet:

Op internet zijn er diverse belangenorganisaties voor patiënten met de ziekte van parkinson. Enkelen daarvan hebben een fora waar leden informatie kunnen uitwisselen. Een optie is om daar, met goedkeuring van de beheerder, een oproep te plaatsen voor deelname aan het onderzoek. In de oproep zou de patiënten informatiebrief kunnen worden geplaatst met de contactinformatie. Wanneer gebruikers willen deelnemen zou per mail of via de post de formulieren kunnen worden toegestuurd en via mail of telefonisch contact een afspraak worden gemaakt.

De mogelijke participanten hebben steeds enkele dagen bedenktijd voor de genoemde methode van werving. Aan de potentiele participanten wordt meermaals en duidelijk aangegeven dat ze op elk moment zonder opgaaf van reden kunnen stoppen met deelname. De participanten wordt duidelijk gemaakt waarvoor het onderzoek dient, dat het interview uitsluitend wordt opgenomen met hun instemming en dat hun privacy ten alle tijden gewaarborgd is.

<u>Data verwerking:</u>

De interviews worden met toestemming van de participant opgenomen en tijdens het interview zullen aantekeningen worden gemaakt. De aard van het onderzoek is kwalitatief en er zal gebruik worden gemaakt van analoge content analyse.

Hierbij word achteraf de geluidsopname terug geluisterd en de relevante, met betrekking tot de onderzoeksvraag, antwoorden/passages verwerkt in het onderzoek.

Appendix 2 Patient information letter

Betreft: onderzoek naar de invloed van de behandeling van Parkinson op de gezondheid gerelateerde kwaliteit van leven.

April, 2012

Geachte heer/mevrouw,

Een projectgroep van Universiteit Twente, in samenwerking met het Roessingh en het MST, is bezig met een onderzoek naar de invloed van de behandeling van parkinson op de patiënt. Hierbij word gekeken hoe de voor en nadelen van de behandeling het leven van behandelde beïnvloedt.

Voor de behandeling van parkinson bestaan verschillende medicijnen in verschillende toedieningsvormen. Deze behandelingen kunnen gepaard gaan met bijwerkingen.

In het onderzoek waarvoor u wordt uitgenodigd wordt geprobeerd om een beter inzicht te krijgen in de voor en nadelen van de behandeling voor de ziekte van Parkinson en hoe belangrijk deze zijn voor de behandelde personen.

Doel van het onderzoek:

Het hoofddoel van het onderzoek is om een patiënt vriendelijke methode te ontwikkelen die kan meten wat mensen die onder behandeling staan voor de ziekte van Parkinson belangrijk vinden bij het beoordelen van de waarde van een behandeling (dus: wat is er goed, en wat is er slecht aan de behandeling, en hoe waardevol is deze behandeling voor u?)

In het eerste deel van het onderzoek worden interviews gehouden met mensen met de ziekte van Parkinson. In deze interviews wordt gevraagd naar de positieve en negatieve gevolgen u ondervindt van de behandeling en welke de meeste invloed hebben op uw leven.

Verloop van het onderzoek

Wanneer u interesse heeft en zou willen deelnemen aan het onderzoek kunt u dit aangeven bij Raymond Kuipers of de secretaresse. Uw gegevens worden genoteerd zodat er contact met u kan worden opgenomen voor een afspraak. U krijgt een envelop mee die twee korte vragenlijsten bevat over uw gezondheid en kwaliteit van leven en het interview. Deze kunt u op uw gemak voor aan het interview invullen en doornemen en eventueel het interview doornemen. Dit zal ongeveer 20 tot 30 minuten van uw tijd kosten.

Enkele dagen nadat u gegevens heeft achtergelaten zal ik u bellen voor het maken van een afspraak.

Met uw toestemming word het interview opgenomen. Natuurlijk zullen alle gegevens vertrouwelijk worden behandeld. De antwoorden zullen niet herleid kunnen worden tot uw naam. De duur van het interview is een half uur tot een uur

U kunt ten allen tijden het interview stoppen of aangeven wanneer u op bepaalde vragen niet in wilt gaan.

Voordelen:

Deelname aan dit onderzoek levert u geen persoonlijk voordeel op.

Door medewerking aan dit onderzoek draagt u bij aan de kennis over de invloed van de behandeling op de kwaliteit van leven van mensen met de ziekte van Parkinson. In de toekomst zou dit kunnen bijdragen aan een betere beoordeling van de voor en nadelen van behandeling. Dit zou kunnen leiden tot een instrument dat het mogelijk maakt de keuze voor behandeling beter te laten aansluiten bij de persoonlijke voorkeuren van de patiënt.

Deelname en vertrouwelijkheid:

Deelname aan dit onderzoek is op vrijwillige basis.

U bent niet verplicht deel te nemen en u kunt op elk gewenst moment uw medewerking stopzetten zonder opgaaf van reden.

De gegevens verkregen wanneer u deelneemt zullen vertrouwelijk worden behandeld en anoniem worden verwerkt.

Vragen en informatie:

Heeft u nog vragen of wenst u extra informatie dan kunt u contact met mij opnemen via de contactgegevens aan het eind van deze brief.

Bij voorbaat dank voor uw tijd,

Raymond Kuipers

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Appendix 3 METC Approval

Medisch Spectrum △Twente

MEDISCH ETHISCHE TOETSINGSCOMMISSIE (METC) TWENTE

Het Roessingh centrum voor revalidatie

Secretariaat METC, Medical School Twente, Instituut voor Toegepast Wetenschappelijk Onderzoek,
Postbus 50.000, 7500 KA Enschede Telefoon +31(0)53 487 30 11 Fax +31(0)53 487 2042 Email: metc@mst.nl
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Deurningerstraat 346
7522CP ENSCHEDE

Enschede, 08-05-2012

Kenmerk: METC/12186.kui

Titel: Onderzoek naar de invloed van de behandeling van Parkinson op de gezondheid gerelateerde kwaliteit van leven

K-nr.: K12-21

Geachte heer Kuipers,

Naar aanleiding van uw brief d.d. April 2012, waarin u bovenstaand onderzoek aanmeldt, berichten wij u het volgende.

In strikte zin, volgens de WMO, is het niet nodig dat de METC een oordeel velt over dit studieprotocol. De studie omvat het afnemen van enkel simpele vragenlijsten over de ervaringen met de behandeling van de ziekte van Parkinson en een kwaliteit van leven vragenlijst.

Wel is het goed dat METC Twente geïnformeerd is over het feit dat dit onderzoek in Medisch Spectrum Twente wordt uitgevoerd. De METC heeft kennisgenomen van uw voornemen dit onderzoek uit te voeren.

De proefpersoneninformatie wordt in dit geval dan ook niet door de METC beoordeeld.

U succes met uw studie toewensend,

Met vriendelijke groet,

namens de METC

dr. J.F.F. Lekkerkerker, voorzitter

Samenstelling METC Twente
Andriol, dhr. mr. G., jurist
Beuk, dhr. dr. R., arts
Boenink, mw. dr. M., ethicus
Colen, mw. dr. H.B.B., ziekenhuisapotheker
Duyts, MA, mw A.W., nurse practitioner
De Man, dhr. dr. F., arts
Groothuis-Oudshoorn, mw. dr. C.G.M., methodoloog
Haagsma, dhr. dr. C.J., klinisch farmacoloog
Hoogland, dhr. drs. J., ethicus
Huis in 't Veld, mw. dr. M.H.A., bewegingswetenschapper
Hummel, mw. drs. T.Z., arts, overig lid
Kamphuis, MANP, mw. M., nurse practitioner
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Renzenbrink, dhr. dr. G.J., arts
Schreuder-Hoenkamp, mw. mr. M.E.F., proefpersonenlid
Sikkema, mw. M.M., proefpersonenlid
Smeets-Schouten, mw. dr. J.S., klinisch psycholoog
Spijker, mw. drs. G.J.H., proefpersonenlid
Ten Vergert, dhr. mr. H.G.M., jurist
Van der Palen, dhr. prof. dr. J.A.M., epidemioloog
Van Putten, dhr. prof. dr. ir. M.J.A.M., arts
Venneman, dhr. dr. N.G., arts
Zweers, dhr. mr. A.E., jurist
Satink, mw. ir. S.E.A., ambtelijk secretaris

Appendix 4 Interview subjects and questions

	Subject		Question
1.	**Personal characteristics**	1.1.	What is your age?
		1.2.	Describe your family situation?
		1.3.	Are you employed (paid job, benevolence work, housekeeping)?
2.	**Global health status**	2.1.	When were you diagnosed with PD?
		2.2.	Do you know in which stage of PD you are right now?
		2.3.	When did the treatment for PD start?
		2.4.	Which medication are you using at the moment?
		2.5.	Are there besides Parkinson's disease other (sever) health problems for which you are treated?
		2.6.	Is medication taken for those health problems?
3.	**Positive outcomes treatment**	3.1.	Which symptoms would occur if you would not follow your treatment?
		3.2.	Does your treatment work well for these symptoms?
		3.3.	How does the treatment increase the QoL of your daily life?
4.	**Negative treatment outcomes (side effects)**	4.1.	Do you experience side effects of your treatment?
		4.2.	How often do these side effects occur?
		4.3.	What is the influence of these side effects on your daily life (the strain)?
		4.4.	(if applicable) You mentioned side effects, can you point out to me which causes the greatest impact and if so why?
		4.5.	Side effects can occur frequently differ on strain and or can be unpredictable. What has the most impact in your experience and why?
5.	**Negative treatment outcomes (motor-fluctuations)**	5.1.	Do you have experiences with involuntary movements (dyskinesia)?
		5.2.	Do you have experience with wearing-off from your medication?
		5.3.	Do you have experience with stiffness because the medication wears off faster (end-off-dose-akinesia)
		5.4.	Do you experience the on-off effect, one moment Parkinson symptoms and the other moment free of symptoms?
		5.5.	Did you have experience with the situation of suddenly not being able to move anymore (freezing)?
		5.6.	Which fluctuation has the biggest strain on your quality of life and why?
		5.7.	Is it the strain itself, the frequency or the unpredictability or a combination?
6.	**Treatment characteristics and adherence**	6.1.	Are you satisfied with your neurologist?
		6.2.	Can you describe your treatment regime?
		6.3.	What is your personal opinion about your regime (difficult, many, intense)?
		6.4.	Do you experience your treatment regime as straining to your daily life?
		6.5.	Are you satisfied with your treatment regime?
		6.6.	Are you adherent to your treatment regime?
		6.7.	What is the reason for that?
		6.8.	Did you ever quit a drug or has the dose changed?
		6.9.	What was the reason for that?

Appendix 5 The PDQ-39 Questionnaire items

Dimension		Item
Mobility (MOB)	1	Had difficulty doing the leisure activities which you would like to do?
	2	Had difficulty looking after your home, e.g. DIY, housework, cooking?
	3	Had difficulty carrying bags of shopping?
	4	Had problems walking half a mile?
	5	Had problems walking 100 yards?
	6	Had problems getting around the house as easily as you would like?
	7	Had difficulty getting around in public?
	8	Needed someone else to accompany you when you went out?
	9	Felt frightened or worried about falling over in public?
	10	Been confined to the house more than you would like?
Activities daily living (ADL)	11	Had difficulty washing yourself?
	12	Had difficulty dressing yourself?
	13	Had problems doing up your shoe laces?
	14	Had problems writing clearly?
	15	Had difficulty cutting up your food?
	16	Had difficulty holding a drink without spilling it?
Emotional Well Being (EMO)	17	Felt depressed?
	18	Felt isolated and lonely?
	19	Felt weepy or tearful?
	20	Felt angry or bitter?
	21	Felt anxious?
	22	Felt worried about your future?
Stigma (Stig)	23	Felt you had to conceal your Parkinson's from people?
	24	Avoided situations which involve eating or drinking in public?
	25	Felt embarrassed in public due to having Parkinson's disease?
	26	Felt worried by other people's reaction to you?
Social support (SOC)	27	Had problems with your close personal relationships?
	28	Lacked support in the ways you need from your spouse or partner? *If you do not have a spouse or partner tick here*
	29	Lacked support in the ways you need from your family or close friends?
Cognitions (COG)	30	Unexpectedly fallen asleep during the day?
	31	Had problems with your concentration, e.g. when reading or watching TV?
	32	Felt your memory was bad?
	33	Had distressing dreams or hallucinations?
Communication (COM)	34	Had difficulty with your speech?
	35	Felt unable to communicate with people properly?
	36	Felt ignored by people?
Bodily discomfort (BOD)	37	Had painful muscle cramps or spasms?
	38	Had aches and pains in your joints or body?
	39	Felt unpleasantly hot or cold?

Appendix 6 EQ-5D Questionnaire

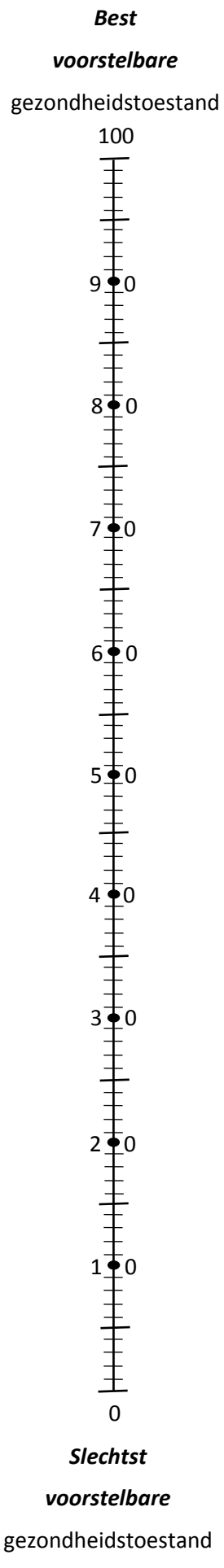
Zet bij iedere groep in de lijst hieronder een kruisje in het hokje achter de zin die het best past bij uw eigen gezondheidstoestand **vandaag**.

Mobiliteit	Ik heb geen problemen met lopen	☐
	Ik heb enige problemen met lopen	☐
	Ik ben bedlegerig	☐
Zelfzorg	Ik heb geen problemen om mijzelf te wassen of aan te kleden	☐
	Ik heb enige problemen om mijzelf te wassen of aan te kleden	☐
	Ik ben niet in staat om mijzelf te wassen of aan te kleden	☐
Dagelijkse activiteiten (bijv. werk, studie, huishouden, gezins- en vrijetijdsactiviteiten)	Ik heb geen problemen met mijn dagelijkse activiteiten	☐
	Ik heb enige problemen met mijn dagelijkse activiteiten	☐
	Ik ben niet in staat mijn dagelijkse activiteiten uit te voeren.	☐
Pijn/klachten	Ik heb geen pijn of andere klachten	☐
	Ik heb matige pijn of andere klachten	☐
	Ik heb zeer ernstige pijn of andere klachten	☐
Stemming	Ik ben niet angstig of somber	☐
	Ik ben matig angstig of somber	☐
	Ik ben erg angstig of somber	☐

Om mensen te helpen bij het aangeven hoe goed of hoe slecht een gezondheidstoestand is, hebben we een meetschaal (te vergelijken met een thermometer) gemaakt. Op de meetschaal hiernaast betekent “100” de beste gezondheidstoestand die u zich kunt voorstellen, en “0” de slechtste gezondheidstoestand die u zich kunt voorstellen.

We willen u vragen op deze meetschaal aan te geven hoe goed of hoe slecht volgens u uw eigen gezondheidstoestand vandaag is. Trek een lijn van het hokje hieronder naar het punt op de meetschaal dat volgens u aangeeft hoe goed of hoe slecht uw gezondheidstoestand vandaag is.

Uw
Gezondheidstoestand
Vandaag



Appendix 7 Frequency of items by dimension

		N	Percent of respondents	percentage	Mean	SD	p
Mob	PDQ1	13	76,5	13,8%	1,9	1,3	0,02
	PDQ2	12	70,6	12,8%	1,8	1,3	0,05
	PDQ3	11	64,7	11,7%	1,4	1,3	0,40
	PDQ7	11	64,7	11,7%	1,0	0,9	0,44
	PDQ6	10	58,8	10,6%	1,2	1,2	0,99
	PDQ10	10	58,8	10,6%	1,4	1,5	0,54
	PDQ4	9	52,9	9,6%	1,3	1,5	0,66
	PDQ9	7	41,2	7,4%	0,8	1,2	0,25
	PDQ5	6	35,3	6,4%	0,8	1,3	0,29
	PDQ8	5	29,4	5,3%	0,9	1,5	0,52
ADL	PDQ14	16	94,1	22,9%	2,4	1,1	0,00
	PDQ13	13	76,5	18,6%	1,8	1,3	0,28
	PDQ16	13	76,5	18,6%	1,2	0,8	0,29
	PDQ15	12	70,6	17,1%	1,5	1,2	0,80
	PDQ12	10	58,8	14,3%	1,3	1,4	0,77
	PDQ11	6	35,3	8,6%	0,7	1,2	0,02
EMO	PDQ22	13	76,5	22,8%	1,4	1,1	0,04
	PDQ17	10	58,8	17,5%	0,8	0,8	0,96
	PDQ19	10	58,8	17,5%	0,8	0,7	0,79
	PDQ21	10	58,8	17,5%	1,1	1,0	0,25
	PDQ18	7	41,2	12,3%	0,7	0,9	0,47
	PDQ20	7	41,2	12,3%	0,6	0,8	0,26
STIG	PDQ25	5	29,4	33,3%	0,5	0,8	0,28
	PDQ24	4	23,5	26,7%	0,4	0,9	0,47
	PDQ23	3	17,6	20,0%	0,2	0,4	0,49
	PDQ26	3	17,6	20,0%	0,3	0,6	0,91
SOC	PDQ27	6	35,3	40,0%	0,7	1,0	0,28
	PDQ28	5	29,4	33,3%	0,4	0,7	0,85
	PDQ29	4	23,5	26,7%	0,4	0,7	0,89
COG	PDQ31	16	94,1	32,0%	1,8	0,8	0,06
	PDQ32	16	94,1	32,0%	1,8	0,7	0,04
	PDQ30	13	76,5	26,0%	1,6	1,1	0,55
	PDQ33	5	29,4	10,0%	0,6	0,9	0,00
COM	PDQ35	15	88,2	37,5%	1,8	1,1	0,26
	PDQ34	14	82,4	35,0%	1,8	1,1	0,26
	PDQ36	11	64,7	27,5%	1,1	0,9	0,03
BOD	PDQ38	15	88,2	39,5%	2,0	1,1	0,07
	PDQ39	12	70,6	31,6%	1,3	1,1	0,50
	PDQ37	11	64,7	28,9%	1,4	1,2	0,67

Appendix 8 Frequency of items by total pdq-39

dimension	Item	N	Percent of respondents	Percent of total	Mean
ADL	PDQ14	16	94,1	4,2%	2,4
COG	PDQ31	16	94,1	4,2%	1,8
COG	PDQ32	16	94,1	4,2%	1,8
COM	PDQ35	15	88,2	4,0%	1,8
BOD	PDQ38	15	88,2	4,0%	2,0
COM	PDQ34	14	82,4	3,7%	1,8
Mob	PDQ1	13	76,5	3,4%	1,9
ADL	PDQ13	13	76,5	3,4%	1,8
ADL	PDQ16	13	76,5	3,4%	1,2
EMO	PDQ22	13	76,5	3,4%	1,4
COG	PDQ30	13	76,5	3,4%	1,6
Mob	PDQ2	12	70,6	3,2%	1,8
ADL	PDQ15	12	70,6	3,2%	1,5
BOD	PDQ39	12	70,6	3,2%	1,3
Mob	PDQ3	11	64,7	2,9%	1,4
Mob	PDQ7	11	64,7	2,9%	1,0
COM	PDQ36	11	64,7	2,9%	1,1
BOD	PDQ37	11	64,7	2,9%	1,4
Mob	PDQ6	10	58,8	2,6%	1,2
Mob	PDQ10	10	58,8	2,6%	1,4
ADL	PDQ12	10	58,8	2,6%	1,3
EMO	PDQ17	10	58,8	2,6%	0,8
EMO	PDQ19	10	58,8	2,6%	0,8
EMO	PDQ21	10	58,8	2,6%	1,1
Mob	PDQ4	9	52,9	2,4%	1,3
Mob	PDQ9	7	41,2	1,8%	0,8
EMO	PDQ18	7	41,2	1,8%	0,7
EMO	PDQ20	7	41,2	1,8%	0,6
Mob	PDQ5	6	35,3	1,6%	0,8
ADL	PDQ11	6	35,3	1,6%	0,7
SOC	PDQ27	6	35,3	1,6%	0,7
Mob	PDQ8	5	29,4	1,3%	0,9
STIG	PDQ25	5	29,4	1,3%	0,5
SOCS	PDQ28	5	29,4	1,3%	0,4
COG	PDQ33	5	29,4	1,3%	0,6
STIG	PDQ24	4	23,5	1,1%	0,4
SOC	PDQ29	4	23,5	1,1%	0,4
STIG	PDQ23	3	17,6	0,8%	0,2
STIG	PDQ26	3	17,6	0,8%	0,3
Total		379		100,0%	

Appendix 9 ranking of items per dimension based on rating

		N	percentage	Percent of respondents	Mean	SD	p
Mob	PDQ1	13	13,8%	76,5	1,9	1,3	0,02
	PDQ2	12	12,8%	70,6	1,8	1,3	0,05
	PDQ3	11	11,7%	64,7	1,4	1,3	0,40
	PDQ10	10	11,7%	58,8	1,4	1,5	0,54
	PDQ4	9	10,6%	52,9	1,3	1,5	0,66
	PDQ6	10	10,6%	58,8	1,2	1,2	0,99
	PDQ7	11	9,6%	64,7	1,0	0,9	0,44
	PDQ8	5	7,4%	29,4	0,9	1,5	0,52
	PDQ5	6	6,4%	35,3	0,8	1,3	0,29
	PDQ9	7	5,3%	41,2	0,8	1,2	0,25
ADL	PDQ14	16	22,9%	94,1	2,4	1,1	0,00
	PDQ13	13	18,6%	76,5	1,8	1,3	0,28
	PDQ15	12	18,6%	70,6	1,5	1,2	0,80
	PDQ12	10	17,1%	58,8	1,3	1,4	0,77
	PDQ16	13	14,3%	76,5	1,2	0,8	0,29
	PDQ11	6	8,6%	35,3	0,7	1,2	0,02
EMO	PDQ22	13	22,8%	76,5	1,4	1,1	0,04
	PDQ21	10	17,5%	58,8	1,1	1,0	0,25
	PDQ17	10	17,5%	58,8	0,8	0,8	0,96
	PDQ19	10	17,5%	58,8	0,8	0,7	0,79
	PDQ18	7	12,3%	41,2	0,7	0,9	0,47
	PDQ20	7	12,3%	41,2	0,6	0,8	0,26
STIG	PDQ25	5	33,3%	29,4	0,5	0,8	0,28
	PDQ24	4	26,7%	23,5	0,4	0,9	0,47
	PDQ26	3	20,0%	17,6	0,3	0,6	0,91
	PDQ23	3	20,0%	17,6	0,2	0,4	0,49
SOC	PDQ27	6	40,0%	35,3	0,7	1,0	0,28
	PDQ28	5	33,3%	29,4	0,4	0,7	0,85
	PDQ29	4	26,7%	23,5	0,4	0,7	0,89
COG	PDQ31	16	32,0%	94,1	1,8	0,8	0,06
	PDQ32	16	32,0%	94,1	1,8	0,7	0,04
	PDQ30	13	26,0%	76,5	1,6	1,1	0,55
	PDQ33	5	10,0%	29,4	0,6	0,9	0,00
COM	PDQ34	14	37,5%	82,4	1,8	1,1	0,26
	PDQ35	15	35,0%	88,2	1,8	1,1	0,26
	PDQ36	11	27,5%	64,7	1,1	0,9	0,03
BOD	PDQ38	15	39,5%	88,2	2,0	1,1	0,07
	PDQ37	11	31,6%	64,7	1,4	1,2	0,67
	PDQ39	12	28,9%	70,6	1,3	1,1	0,50

Appendix 10 ranking of items based on rating

Dimension	Item	N	Percent of respondents	Percent of total	Mean
ADL	PDQ14	16	94,1	4,2%	2,4
BOD	PDQ38	15	88,2	4,0%	2,0
Mob	PDQ1	13	76,5	3,4%	1,9
COM	PDQ35	15	88,2	4,0%	1,8
COM	PDQ34	14	82,4	3,7%	1,8
Mob	PDQ2	12	70,6	3,2%	1,8
COG	PDQ31	16	94,1	4,2%	1,8
COG	PDQ32	16	94,1	4,2%	1,8
ADL	PDQ13	13	76,5	3,4%	1,8
COG	PDQ30	13	76,5	3,4%	1,6
ADL	PDQ15	12	70,6	3,2%	1,5
Mob	PDQ3	11	64,7	2,9%	1,4
EMO	PDQ22	13	76,5	3,4%	1,4
BOD	PDQ37	11	64,7	2,9%	1,4
Mob	PDQ10	10	58,8	2,6%	1,4
BOD	PDQ39	12	70,6	3,2%	1,3
ADL	PDQ12	10	58,8	2,6%	1,3
Mob	PDQ4	9	52,9	2,4%	1,3
ADL	PDQ16	13	76,5	3,4%	1,2
Mob	PDQ6	10	58,8	2,6%	1,2
EMO	PDQ21	10	58,8	2,6%	1,1
COM	PDQ36	11	64,7	2,9%	1,1
Mob	PDQ7	11	64,7	2,9%	1,0
Mob	PDQ8	5	29,4	1,3%	0,9
EMO	PDQ17	10	58,8	2,6%	0,8
Mob	PDQ9	7	41,2	1,8%	0,8
Mob	PDQ5	6	35,3	1,6%	0,8
EMO	PDQ19	10	58,8	2,6%	0,8
ADL	PDQ11	6	35,3	1,6%	0,7
EMO	PDQ18	7	41,2	1,8%	0,7
SOC	PDQ27	6	35,3	1,6%	0,7
EMO	PDQ20	7	41,2	1,8%	0,6
COG	PDQ33	5	29,4	1,3%	0,6
STIG	PDQ25	5	29,4	1,3%	0,5
SOC	PDQ28	5	29,4	1,3%	0,4
STIG	PDQ24	4	23,5	1,1%	0,4
SOC	PDQ29	4	23,5	1,1%	0,4
STIG	PDQ26	3	17,6	0,8%	0,3
STIG	PDQ23	3	17,6	0,8%	0,2

Appendix 11 ranking of the items by respondents who influence the HRQoL the most per dimension

		N	mean inverted	p
Mob	PDQ2	12	7,1	0,01
	PDQ1	12	6,8	0,04
	PDQ5	6	6,5	0,92
	PDQ7	10	5,4	0,87
	PDQ10	10	5,4	0,72
	PDQ8	6	5,2	0,82
	PDQ6	9	4,9	0,57
	PDQ9	7	4,7	0,49
	PDQ3	9	4,7	0,41
	PDQ4	8	3,6	0,12
ADL	PDQ14	16	4,6	0,00
	PDQ13	14	3,2	0,34
	PDQ16	14	2,9	0,86
	PDQ12	11	2,5	0,36
	PDQ15	11	1,9	0,05
	PDQ11	7	1,4	0,01
EMO	PDQ22	12	4,3	0,01
	PDQ20	8	3,6	0,07
	PDQ21	10	2,8	0,75
	PDQ19	9	2,7	0,77
	PDQ18	7	2,3	0,38
	PDQ17	10	1,6	0,01
STIG	PDQ24	3	2,3	0,28
	PDQ25	4	1,8	0,85
	PDQ23	3	1,7	0,81
	PDQ26	3	1,7	0,86
SOC	PDQ29	4	1,8	0,06
	PDQ27	4	1,0	1,00
	PDQ28	4	0,3	0,06
COG	PDQ31	16	2,4	0,01
	PDQ30	14	2,1	0,32
	PDQ32	14	1,6	0,26
	PDQ33	6	0,3	0,01
COM	PDQ34	14	1,9	0,00
	PDQ35	14	0,9	0,15
	PDQ36	11	0,4	0,01
BOD	PDQ38	14	1,3	0,55
	PDQ37	11	1,2	0,95
	PDQ39	11	1,0	0,55