Drug adherence in patient group with Parkinson's disease

Master Thesis in Pharmacy

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Abstract

Drug adherence in patient group with Parkinson disease

Background Patients with Parkinson's disease needs medicines administered frequently to manage their condition and maintain their quality of life. Poor medicine adherence may influence health negatively, and cause an unnecessary medicine wastage. It is therefore important that they are effectively supported to ensure that they adhere to their medicine regime.

The aim of the study is to identify barriers to medicine adherence in patients with Parkinson's disease or Parkinsonism and to identify interventions to improve medicine adherence.

Method A postal questionnaire containing 39 statements was sent to 430 patients. The statements were used to identify patient barriers to adherence. A focus group consisting of healthcare professionals discussed interventions to improve medicine adherence.

Results 229 (53,3%) patients responded to the questionnaire. The main barriers to adherence are; having enough time with doctor and pharmacist; being requested to attend to follow-up sessions; knowing where to get help if needed; having the ability to solve problems appearing when taking medicines; worry about side-effects; feeling that taking medicines is a burden and knowing enough about their medicines to decide whether to take them. Disease length did not relate to the responded barriers to non-adherence. Motivation- intention and ability to remember- to take medicines are important barriers to non-adherence.

Conclusion There are several barriers to medicine adherence in the study population, indicating there is a need for interventions from healthcare professionals to improve adherence and increase the health of this patient group.

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Contents

Abbreviations and explanations

PD: Parkinson’s disease

L-dopa: Levodopa.

DDC: Dopa Decarboxylase

DDCI: Dopa Decarbocylase Inhibitor

CNS: Central Nervous System

PNS: Peripheral Nervous System

COMT- Catechol-o-methyltransferase Inhibitors

BBB- Blood-Brain Barrier

MAO-B- Monoamine Oxidase B

D2-receptors- Dopamine 2- receptors

1. Introduction

1.1 Parkinson's disease

Pathology

Parkinson's disease (PD) is a neurodegenerative disease with an unknown underlying pathophysiology. The neurodegeneration consists of selective loss of dopaminergic neurons in the substantia nigra (1) which is responsible for co-ordinating the skeletal muscles (2). In many neurodegenerative diseases, like PD, there are findings of Lewy bodies and Lewy neurites (3). A generally believed hypothesis called the *"prion-like" hypothesis*, states that misfolded α-synucleins produces Lewy bodies and Lewy neurites which leads to neuronal death (1). The mechanism is described below.

The mechanism of the "prion-like" hypothesis

A-synuclein recruits other similar endogenous proteins (seeding) to self-aggregation like prions. These biological cascades (including secretion, uptake and protein seeding) lead to pathogenic protein strains that recruits endogenous soluble proteins like Lewy bodies and Lewy neurites. The pathogenic soluble proteins cause neuronal death. This cascade is an important role in the initiation of the progression of the neurodegenerative disorder. It is believed that new therapeutic targets involve slowing or stopping this progression (3).

Motoric symptoms

The neurodegeneration within the substantia nigra may lead to a series of symptoms like bradykinesia, rigidity, postural instability and tremor, which are the main symptoms indicated in diagnosing PD (4). The definition of the symptoms is summarised in the BMJ (4) and is listed below in table 1.1.

Table 1.1 Key diagnostic factors for Parkinson's disease

Motoric symptoms	Description
Resting tremor	A 4-6 Hz tremor at rest that disappears while moving. The onset is generally asymmetrical. It's most commonly located in the limbs, but may also appear in the chin.
Rigidity	Increased resistance within the range of passive movement about a joint.
Postural instability	Imbalance or falling. Either detected spontaneously or from a test.
Bradykinesia	Delay in initiation of movement, slower movement, freezing of gait.

Non-motoric symptoms

In addition to motoric symptoms, there are many non-motoric symptoms linked to PD. Dementia (5-7), depression (8-10) and dysphagia (11, 12) will be discussed further. Patients with PD may experience symptoms like cardiovascular complications, dopamine dysregulation syndrome (lack of self-control), urinary urge, sexual dysfunction, constipation, sweating, insomnia, pain, fatigue and visual disturbances (13) to mention some of them.

Prevalence

The prevalence of PD in the Norwegian population is about 1% for people between 50-70 years, and somewhat higher for people over 70 years. It's assumed that there are between 6000 and 8000 patients with Parkinson symptoms in Norway (14).

1.2 Treatment

The aim of the medical treatment of PD is a better life quality and a reduced mortality rate, not remission. Up to this date, no medicines stop the progression of the disease. The treatment will be initiated when it is considered necessary for the patients. In Norway, it is preferred that the treatment will be initiated by, and followed up by, a neurologist (14).

As the disease progresses, the patient will experience worsening symptoms and the treatment will have a shorter effect on the symptoms than before. Experienced symptoms may not be equally strong all the time, meaning they may change rapidly and unexpectedly. This is called an “on-off-phenomena” (14). Patients who feel fine, may suddenly experience tremors and have difficulties moving.

There are different groups of medicines used for PD where the main goal is to increase the dopamine level in the substantia nigra. The main treatments used in Norway will be discussed further.

Levodopa

Levodopa (L-dopa) is a dopamine precursor which is converted to dopamine by an enzyme called Dopa Decarboxylase (DDC). When L-dopa passes the blood-brain barrier (BBB), it can be converted into dopamine, replacing the lost dopamine and therefore treating the symptoms experienced by the patient. L-dopa is given together with a peripherally acting Dopa Decarboxylase Inhibitor (DDCI) like Carbidopa and Benserazide. The DDCIs cannot pass the blood-brain barrier like L-dopa, and will only inhibit the conversion to dopamine peripherally. The DDCI will increase the amount of L-dopa that reaches the central nervous system (CNS), thus allowing the prescriber to reduce the dose (14).

The bioavailability of L-dopa is 90% in combination with a DDCI, and is reduced to a certain degree when taken with food. L-dopa tablets should be administered several times a day (dependent on the individual dose required) because of the short half-life of 2 hours (14).

Catechol-o-methyltransferase Inhibitors (COMT-inhibitors)

COMT is an enzyme converting L-dopa and dopamine into inactive metabolites. It is located both in the Peripheral Nervous System (PNS) and the CNS. COMT-inhibitors inhibit the COMT enzyme and will therefore increase the dopamine level by inhibiting the decomposition of L-dopa into inactive metabolites. Patients needing high doses of L-dopa, can be given L-dopa together with a COMT-inhibitor and thereby reducing the necessary dose of L-dopa. COMT-inhibitors are not used alone. The inactive metabolites of L-dopa compete

with the active form to pass the BBB. Inhibiting the degeneration of L-dopa will therefore lead to a greater access of active L-dopa to the brain (14).

Monoamine Oxidase B Inhibitors (MAO-B inhibitors)

MAO-B is also an enzyme metabolising dopamine. MAO-B inhibitors will, like COMT-inhibitors, increase the level of dopamine. They should preferably be given together with L-dopa, and has no documented effect alone. Seligiline and Rasagiline are non-reversible MAO-B inhibitors, while Safinamide is reversible. Seligiline is metabolised to Amphetamine, and will sometimes cause excitement, anxiety and insomnia (14).

Dopamine agonists

Dopamine agonists stimulate the dopamine 2 (D2)-receptors in the striatum selectively. The different dopamine agonists may work differently on an individual. If a dopamine agonist works inadequately on the patient, it could be beneficial to try a different medicine within this medicine group (14).

Anticholinergics

Anticholinergics are the oldest anti-parkinson medicine used today, and works best for tremor, rigidity and slow movement. The use of anticholinergics in Norway is restrictive because of the limited effect and severe side-effects. They are most commonly used in Parkinsonism caused by other medicines (14).

Summary

The medicines used for PD treat the symptoms by raising dopamine levels in the Substantia Nigra through different mechanisms. Table 1.2 provides a summary of the different medicine groups, mechanisms and examples of medicines used in Norway.

Table 1.2 Summary of medicine treatment options for Parkinson's disease in Norway (14)

Medication group	Effect	Examples
Dopa/ dopaderivates	A dopamine precursor. Adding more dopamine.	Levodopa
COMT-inhibitors	Inhibits decomposition of dopamine, thus increasing the dopamine level.	Entekapon, Tolkapon
MAO-B inhibitors	Inhibits decomposition of dopamine, thus increasing the dopamine level.	Rasagiline, Selegiline, Safinamide
Dopamine agonists	Stimulates the D2 receptors in striatum	Bromokriptin, kabergolin, kvinagolid, pramipeksol, ropinirole, rotigotine, apomorphine
Anticholinergics	Inhibits muscarinic acetylcholine receptors	Benztropine, biperiden, orfenadrine

Side-effects

Side-effects in the medicine treatment of PD appear due to the increased dopamine level, and is similar in almost every treatment group. The side-effects, and their severity, will vary between individuals. As the neurodegeneration continues, side-effects will appear faster (14). Gastrointestinal-, motoric-, cardiac- and neuropsychological side-effects together with anticholinergic side-effects will be discussed further, as they are common in PD patients.

Gastrointenstinale side effects (like nausea and vomiting) is a known side-effect of L-dopa (14, 15), but can also be a symptom of the disease (16). Gastrointestinal afflictions can be taken care of by taking the medicine with a light meal and some water during the start of the treatment (14).

Hyperkinesia is also a known side-effect of anti-PD medication (14), and is mentioned in a case study where a young male diagnosed with juvenile Parkinsonism reported involuntary movements (17). He reacted to L-dopa 100 mg and Benserazide (DDCI) 25 mg. Later he experienced the same with L-dopa 500 mg. The immediate reactions were violent movements in all 4 extremities followed by lighter symptoms.

Treatment with L-dopa may cause lack of cardiovascular control. A study indicates that L-dopa treatment could explain low heartbeat and blood pressure (18). This is explained by a reduction in number of baroreflex sequences. L-dopa lowers the plasma level of adrenaline and noradrenaline which may be related to lowering sympathetic cardiac stimulation (18).

Neuropsychological side-effects are common when a patient uses anti-PD medication for a long period of time. Psychotic symptoms (hallucinations, delirium, delusions) appear in 20-30% of Parkinson patients receiving anti- PD medication, where hallucination is the most frequent symptom (19). These side-effects may lead to insomnia in some patients (14). Cognitive impairment in elderly patients is a common neuropsychological side-effect (19).

The side-effects of anticholinergic medication are different than the other groups. Dry mouth, disturbances in sight, nausea, obstipation and slower emptying of the bladder is common in patients using this group of medication. It is not ideal for elderly as they may easily experience altered confusion (14).

1.3 The medicine regimen of a PD patient

Some patients with PD needs medicines multiple times a day. The frequency of dosing and the number of medicines may increase with time as effectiveness wears off, which would result in a complicated medicine regimen. In these cases, it is important to identify medicine non-adherence. This will be discussed further. Comorbidity, the appearance of other diseases together with PD, could lead to a necessity of additional medicines which could complicate the medicine regimen even further.

According to a double-blinded study with 441 subjects (2013), PD patients prefer to use medication taken once daily instead of three times daily (20). However, decreasing the dosing frequency is hard to accomplish considering the treatment options used today. The short half-life (discussed in chapter 1.2- Treatment of Parkinson's disease) makes multiple intakes daily necessary (21). Patients with moderate- to- advanced stages of PD may need to take up to 5 different drugs up to about 8 times a day (21). In a study from 2004 using a medication questionnaire and a computerized medication event monitoring system (MEMS) to monitor medication use, almost 30% of the total 39 patients with PD reported missing at least one of their medications. 76,4% reported either missing or mistime doses (22). The main explanation why they missed their doses was "being too busy".

1.4 Adherence

WHO's definition of adherence:

> *"the extent to which a person's behaviour- taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."* (23).

Non-adherence influence the quality of the patient treatment, and may influence health (e.g. more intense relapses, increased risk of dependence or increased risk of abstinence- and rebound effect) (24). It can also lead to medicine wastage. Paying for wasted medicines and paying to treat severe illness due to non-adherence may cause economic wastage (25). Generally, non-adherence can be divided into two subdivisions, *unintentional non-adherence* where the patients involuntarily fails to take their medication as prescribed and *intentional non-adherence* where the patient, for some reason, chooses not to take their medications as prescribed.

There is a distinct difference between compliance and adherence. A compliant patient is expected to comply with instructions, whereas an adherent patient behaves as agreed with the prescriber i.e. they are a part of the decision-making progress (23). Today, most prescribers focus on adherence instead of compliance. Listening to the patient is essential to take their medication as prescribed (26, 27). This way, the provider can determine the patient's beliefs,

concerns, attitudes and expectations about their treatment. Identifying difficulties for the individual patient is essential to make tailored interventions.

Problems using the definition "adherence"

Measuring adherence does not sufficiently identify difficulties using his/her medicines (28). Low adherence does not explain what difficulties the patient experiences when taking medicines. Detailed questions would provide this information. Therefore, a dialogue with the patient would be more important than measuring adherence in other ways. Adherence unjustified the patients, and is not always within the control of the provider.

1.5 Unintentional medicinal non-adherence in Parkinson patients

Unintentional non-adherence describes patients who does not take their medication for reasons they cannot control themselves. A patient who forgets to take their medication is a common example of unintentional non-adherence. Other reasons can be poor eyesight, lack of prehensile power, lack of competence to take their medicine in the correct way (for example crushing a modified release tablet) etc.

Dementia

Dementia is a well- known problem in Parkinson patients. Approximately 29-40% of patients with PD also suffer from dementia (5, 6, 29, 30), and according to several studies, it seems to be a correlation between dementia and the severity of the symptoms of PD (6, 7, 29). Dementia in PD may lead to impairment in planning, abstract thinking, episodic memory and attention which may all decrease medicine adherence unintentionally (31). Short term memory loss, associated with dementia, diminishes the ability to remember instructions and may cause non-adherence. There are studies showing a correlation between PD and cognitive impairment (32, 33). This may affect the learning process that is essential in adapting the patient's health behaviour (26).

1.6 Intentional medicinal non-adherence in Parkinson patients

Intentional non-adherence is when the patient voluntarily does not take their medicines as prescribed. An example of intentional non-adherence is omitting medicines caused by the fear of side-effects. Other reasons may be having limited confidence in the treatment, disliking the medication or not trusting the prescriber.

Depression

Studies have shown that a relative big part (40-68%) of Parkinson patients suffer from depression (8, 9, 34). This manifests slightly different from other types of depression, with a greater degree of anxiety and a less self-punitive behaviour (9). There are several assumed reasons leading to depression amongst this patient group. Studies have suggested uncertainty, fatigue, perceived health status (8) and major life events (35). Depression may lead to intentional non-adherence in patients with Parkinson's disease mostly because of the lack of motivation or fatigue. It is therefore an important factor that should be screened for in clinical settings, though depression is considered maybe the greatest challenge recognising and treating in the clinic (10).

Dysphagia

It is common for patients with PD to experience dysphagia (swallowing problems) (11, 12, 36). Swallowing is complex and is affected by 25 different muscles and oropharyngeal sensory feedback (36). The pathology of dysphagia is poorly understood, but there are traditional ideas presented in several studies. A neuroimaging study shows that not only does the brainstem and basal ganglia circuits affect swallowing, but also the cortical areas in the brain (36). Within PD patients; the dysphagic patients are assumed to lack compensatory pathways compared to healthy controls (36).

Dysphagia makes it harder to take oral solid medicine which may influence adherence (37). Screening after dysphagia in patients may be important, because they may not report this problem to their prescriber. A cohort study comparing thoughts about oral medication in patients with and without dysphagia, found out that patients with dysphagia had more problems swallowing oral tablets or capsules than patients without dysphagia (38). Generally,

patients with dysphagia preferred formulations that are easier to swallow compared to the other patient group, where dispersible- or effervescent tablets were the most popular (38). Using these types of formulations may alter the adherence in Parkinson patients with dysphagia.

1.7 Identifying non-adherence in patients

Healthcare professionals should identify the cause(s) of non-adherence in individual patients to decrease medicine non-adherence. Awareness of existing tools could help healthcare professionals identifying non-adherence in the clinic.

Major predictors of non-adherence

- Psychological problems, particularly depression.
- Cognitive impairment
- Asymptomatic disease
- Inadequate follow-up or discharge planning
- Side-effects of medication
- Lack of belief in benefit of the treatment
- Lack of insight into their illness
- Poor relationship between patient and provider
- Presence of barriers to medicine adherence
- Missed appointments
- Complexity of treatment
- Cost of health-related factors (39)

There are many factors leading to non-adherence, and it is hard to mention all of them. WHO has come up with examples of these factors, which is divided into 5 subgroup A-E (40). The subgroups are presented in the table below (table 1.3). Suggestions for interventions to the factors within these subgroups can be found in table 1.4.

Table 1.3 WHO's statements of factors influencing adherence in patients (41)

	Subgroup	Examples
A	Social and economic factors	Poor socioeconomic status, poverty, illiteracy, long distance from treatment centre, lack of effective social support, family dysfunction, culture and belief about illness etc.
B	Health care team and system related factors	Lack of knowledge and training of adherence, patient-provider relationship, overworked health care providers, short consultations, lack of follow-up etc.
C	Condition related factors	Illness-related demands, severity of symptoms, level of disability (physical, psychological, social etc.), rate of progression etc.
D	Therapy-related factors	Complexity of medical regimen, changes in treatment, duration of treatment, beneficial- and side-effects.
E	Patient-related factors	Resources, knowledge, attitudes, beliefs, expectations, frustration, forgetfulness etc.

Table 1.4 WHO's statements of interventions influencing adherence in patients (42)

	Subgroup	Interventions
A	Social and economic interventions	The policy-makers managing the health care environment must find difficulties regarding the social and economic factors to find interventions that are relevant to them. Examples: reducing poverty by selling medicines with affordable prices or enhancing social support by introducing community-based organizations.
B	Health care team and system related interventions	Training in adherence-management for providers, making an adherence counselling toolkit adaptable for different patients, suggesting interventions and follow up adherence.
C	Condition related interventions	Healthcare professionals should identify disease-specific demands, symptoms and impairments and identify co-morbidities (like anxiety and depression).
D	Therapy-related interventions	Pharmaceutical companies managing medicines with too many side-effects.
E	Patient-related interventions	Development of self-management interventions (like an organisation group) to improve motivation and increase patient education about medicines and behavioural self-regulation strategies.

1.8 Measuring and analysing adherence

Measuring adherence can be done after screening for- and proposing interventions to the causes of non-adherence. A measure of non-adherence can be useful to identify the need of follow-up consultations. There are two main ways to measure adherence; *direct measures* and *indirect measures (43).* The direct measures consist of observation of medication intake and biological assay of drug levels in the blood or metabolites (in either blood or urine). Indirect measures include self-reports (from patient or relatives/clinicians), pill counts, fill frequency of prescriptions, electronic monitoring etc. Observation of medicine intake is the only measuring method that verifies adherence, and would be optimal to in the clinic (43). It is important to think about what type of measuring method we use to address non-adherence. There is no method without disadvantages, and therefore both advantages and disadvantages should be considered before choosing a method. A summary of the most common measuring methods is addressed in the table below.

Table 1.5 Advantages and disadvantages of different adherence measuring methods (43)

Measuring method	Advantage	Disadvantage
Observation of medication intake	Measures accurate adherence	Needs a direct patient-clinician contact (impractical). Patients can hide the pills in the mouth and discard them.
Measurement of levels of medication in the blood/ measurements of medication metabolites in blood/urine	Objective measurement	Need a direct patient-clinician contact. Variation in pharmacokinetics. Expensive.
Self-reporting	Inexpensive/ easy to accomplish	Recall/ social desirability response bias
Fill frequency of prescriptions	Objective measurement (can also be used in placebo controls).	Requires complete pharmacy records, which is hard to achieve after a large amount of time.
Pill counts (pills collected, remaining or prescribed)	Objective, inexpensive, quantifiable	Does not work if the patient is hoarding or discarding medicine.
Electronic monitoring	Detailed measures, easily quantified	Expensive. Requires a certain contact with the clinic. Patient may not take the medication or take the wrong number of tablets.

1.9 Health behaviour

As PD is a chronic disease, it requires a certain life style (health behaviour) to improve long term medicine adherence. Changing health behaviour is hard and takes a lot of work. When a patient is sick, working is hard and learning is harder (44). However, there are several ways to handle this issue. Healthcare professionals can influence the patient's behaviour using techniques based on the theory of health behaviour change (45).

The theory of health behaviour change, The HAPA model

The Health Action Process Approach (HAPA) is a model providing theory about health behaviour change (45). This section is based on the article written by Schwarzer, R., Lippke, S., & Luszczynska, A. (2011).

There are two different types of models that can be used to describe the theory of health behaviour change; the continuum model and the stage model. In the continuum model, patients are moved along a range where the likelihood of action increases. TPB (Theory of Planned Behaviour), SCT (Social-Cognitive Theory) and PMT (Protection Motivation Theory) are three theories based on a continuum model. In the stage model, patients need to go to the first stage before they can move to the next one. There are limitations using both models. The continuum model is useful to explain and predict a person's behaviour, while the stage model is useful to adapt interventions to the individual. The Health Action Process Approach (HAPA) includes both a continuum model and a stage model.

To change health behaviour, the patient needs to have the *intention* to perform a behaviour change (motivational phase), and the patient needs to perform, and maintain, the behaviour change (volitional phase). The volitional phase is the actual behaviour changing phase. People going through a health behaviour change has a changing mindset, and the model is therefore divided into three phases representing three different mindsets. The motivational phase includes *Preintenders*, while the volitional phase includes *Intenders* and *Actors*. This will be discussed further.

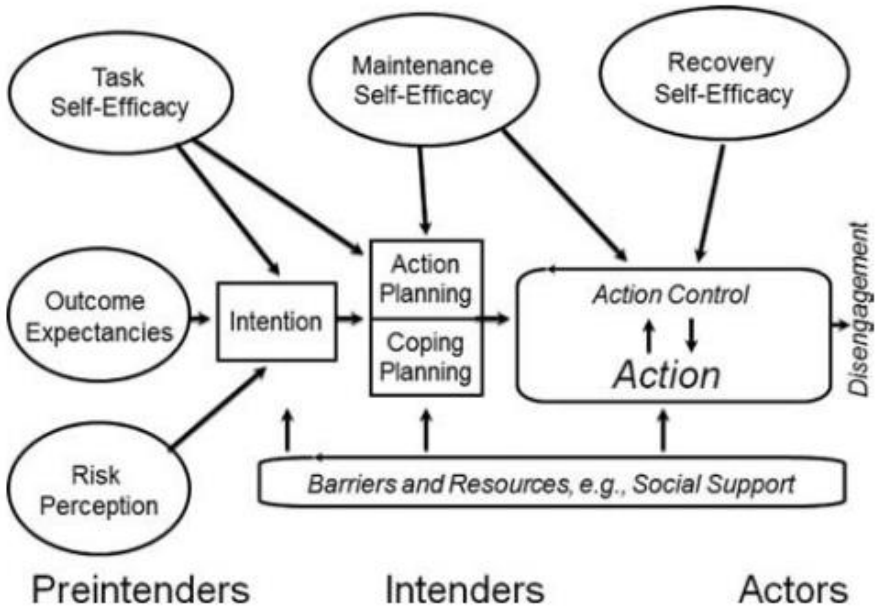

Figure 1.1 The theory of health behaviour changes in a chronic disease (45).

Motivational phase

Before a person can change their behaviour, they need the intention to do so. This is the greatest challenge in changing health behaviour. People in this phase are called *Preintenders* (see figure 1.1), and are influenced by three factors (shown in circles in figure 1.1); *Task self-efficacy*, o*utcome expectancies* and *risk perception*. Task self-efficacy means that the person believe that they can perform a specific behaviour change, outcome expectancies means the persons expectations of performing the behaviour change and risk perception means the understanding of the risks of not performing the behaviour change.

Volitional phase

When a person intends to change their behaviour, they need to perform it. In this phase, there are two different mindsets; the *Intenders* intend to change their behaviour, but does not actually perform. The *Actors* intend, and change their behaviour. It is important to separate people with different mindsets into different phases, as interventions are easier to adapt to the individual person. When a person has changed their behaviour, it needs to be maintained. *Planning* is important to Intenders, as they intend to change their behaviour but lacks the skills to do so. Planning can be divided into *action planning* (when, where and how to

perform) and *coping planning* (help to perform despite the restrains). *Action control* is important to Actors. Action control means that the behaviour change performed is compared to the standard behaviour, thus providing self-awareness. The belief that they can maintain (*maintenance self-efficacy)*, and recover (*recovery self-efficacy)* the behaviour change is important in this phase. *Social support* can act as a resource if provided or a barrier if not provided, and will influence the volitional phase. It can be divided into *instrumental*-, *emotional*- and *informational* support.

1.10 Previous studies regarding PD and adherence

The previous studies done on PD patients in relation with adherence has mainly been focusing on measuring adherence in patients. Additionally, patient demographics has been presented in more detail using scales. UPDRS (Unified Parkinson's disease rating scale), Mini-mental, geriatric depression scale etc. is commonly used.

Only a few studies have been searching for causes of non-adherence in PD patients. A qualitative study based on semi-structured interviews with PD patients is one of them (46). It was concluded in the study that memory failure mostly led to minor unintentional non-adherence. Examples of minor intentional non-adherence were also mentioned, like patients tailoring their medicines to support their lifestyle e.g. taking all of the medicines to let them go dancing. Patients were familiar with their treatment goals, but did not seem to understand the importance of taking their medication evenly throughout the day to achieve better symptom control.

1.11 IMAB-Q

IMAB-Q, The Identification of Medicine Adherence Barriers Questionnaire is a questionnaire designed by Dr Claire Easthall for her PhD project supervised by Dr Debi Bhattacharya, UEA, England, used for identifying barriers in medicine adherence.

There are two different versions of the questionnaire, IMAB-Q 10 with 10 statements and IMAB-Q 30 with 30 statements. The IMAB-Q 30 is used for research, while the IMAB-Q 10 is used in the clinic. This questionnaire is formulated in English in a patient-friendly way, to

enable patients to complete them on their own. Patients check off whether they agree or disagree. In total they have 5 choices (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree).

There are no gold standard on interventions to improve adherence today, and the aim of the IMAB-Q is to identify effective interventions (47). Each barrier is linked to the relevant domains of the Theoretical Domains Framework (TDF) which contains health behaviour changing techniques based on many different psychological theories. By using the IMAB-Q in the clinic, practitioners can identify and motivate patients to adhere to their medication.

1.12 Summary

PD is a neurodegenerative disease where medicine treatment is used to increase dopamine in Substantia Nigra and thereby decrease symptoms of the disease. Many side-effects may appear during the treatment due to the increased dopamine level. Patients need medicines administered frequently to manage their condition and maintain quality of life. Due to the necessity of frequent doses, the medicine regimen can be complicated. PD patients often experience co-morbidities like depression and dementia, which may increase the number of medicines needed and increase the complication of their medicine regime. Medicine adherence is achieved when the patient behaviour corresponds with the agreed treatment. Non-adherence can be subdivided into intentional (voluntary)- and unintentional (involuntary) medicine adherence. As PD is a chronic disease, adherence is important to identify and improve health and reduce medicine wastage. Health behaviour changing techniques can be used to improve non-adherence, which should be used by healthcare professionals in the clinic. Effective interventions to the barriers to adherence should be identified, and the IMAB-Q is a tool aiming to help practitioners identify this in the clinic.

1.13 The aim of the master thesis

The aim of this master thesis is;

- To identify barriers to medicine adherence in Norwegian patient group with Parkinson’s disease or Parkinsonism.
- To identify interventions to improve medicine adherence in a focus group consisting of healthcare professionals.

2. Method

2.1 Study method

The study consists of a retrospective survey of post-discharge patients with PD or Parkinsonism to identify barriers to non-adherence, and a focus group consisting of healthcare professionals to identify interventions to the barriers.

2.2 Questionnaire design and covering letter

The questionnaire is categorized into 3 major topics; barriers to adherence directly influenced by information and follow-up of health personnel, you and your medicines (IMAB-Q 30) and personal information. Personal information includes questions regarding gender, disease length and number of medicines.

The IMAB-Q 30 was translated from English to Norwegian by the main researcher with help from the Norwegian supervisor.

Statements based on the theory of health behaviour change in patients with a chronic disease (HAPA model, section 1.9), was added as this was considered important to the study. The statements are presented in the table below (table 2.1) explaining how they influence health behaviour.

Table 2.1 Statements added by the researcher

Number	Statements	Factors influencing health behaviour
1	I have a good relationship with my doctor(s) who prescribed my medication	Emotional support
2	I have enough time to talk to my doctor about my medication	Informational support
3	I have enough time to talk to the pharmacist at the pharmacy about my medication	Informational support
4	I made a plan with my doctor about my future medicine use	Action planning
5	I understand why I need my medicine(s)	Outcome expectancy
6	I expect my medicines to help me for my disease	Outcome expectancy
7	I know the risk of not taking my medication(s)	Risk perception
8	I have been requested to come to follow-up consultations to discuss my medicine use	Informational support
9	If problems appear with my medicine use (i.e. forget to take the, or get difficulties swallowing them) I know where to get help	Coping planning

The original statements are based on the behavioural domains from the TDF explained in section 1.11 (47).

Table 2.2 Original IMAB-Q statements

Number	Statements	Behavioural domain
1	I know how to take my medicines as prescribed	Knowledge
11	I know enough about my medicines to decide whether to take them	Knowledge
21	I have the information that I need to be able to easily order and collect my prescriptions	Knowledge
2	I am physically able to take my medicines as prescribed	Skills
12	I have a system in place to help me order, collect and take my medicines as prescribed	Skills
22	Telling my medicines apart from each other would not be a problem for me	Skills
3	I remember to take my medicines as prescribed	Memory, attention and decision making processes
13	I am easily distracted from taking my medicines	Memory, attention and decision making processes
23	I remember to order and collect my medicines on time	Memory, attention and decision making processes
4	I trust my doctor(s) with decisions about my healthcare	Social influences
14	If I needed support from others to take my medicines as prescribed, I could get it	Social influences

24	I worry about what other people would think of me if they know I took medicines	Social influences
5	I can easily get hold of my prescribed medicines from the pharmacy	Environmental constraints
15	Changes to my daily routine would not interfere with taking my medicines as prescribed	Environmental constraints
25	My pharmacy provides efficient service for ordering and collecting my medicines	Environmental constraints
6	I have negative emotions (e.g. frustration, embarrassment, anger) about taking my medicines as prescribed.	Emotions
16	Taking my medicines as prescribed is an unwelcome reminder of my condition	Emotions
26	Taking my medicines as prescribed is a burden to me	Emotions
7	I am motivated to take my medicines as prescribed	Motivation & goals
17	Taking my medicines as prescribed is high on my list of priorities	Motivation & goals
27	I intend to take my medicines as prescribed	Motivation & goals
8	I do not have to choose between paying for my prescriptions and paying for other things that are important to me	Goal conflicts
18	Taking my medicine as prescribed does not fit with my daily routine	Goal conflicts
28	Life gets in the way of me taking my medicines as prescribed	Goal conflicts

9	I feel confident about all aspects of managing (ordering, collecting and taking) my medicines	Beliefs about capabilities
19	I am confident that I could find ways to solve any difficulties that I have with taking my medicines as prescribed	Beliefs about capabilities
29	I don't think I could cope if my medication regime kept changing	Beliefs about capabilities
10	I worry about the unwanted effects (e.g. harmful effects or side effects) of taking my medicines	Beliefs about consequences
20	If I don't take my medicines as prescribed I think my condition will get worse	Beliefs about consequences
30	I have my reasons for not taking my medicines as prescribed	Beliefs about consequences

The translated questionnaire can be found in Appendix A.

The covering letter was designed to increase response rate with focus on short, specific information.

Some actions were done to increase the response rate further. These actions are based on evidence from a Cochrane review comparing different techniques (48):

- Ensured an interesting questionnaire topic
- Kept the questionnaire as short as possible
- Provided university logo on the envelope and at the start of the questionnaire
- Provided a stamped return envelope
- Assured confidentiality
- Use of coloured headings and a relevant image on the covering letter
- Providing short instructions on the front page of the questionnaire

2.3 Selection of participants

The inclusion criteria used in this study are; Patients treated at Haukeland hospital from January to July 2017 diagnosed with Parkinson's disease (Classified as ICD-10 G20 in Norway). From the neurological ward at Haukeland, the Norwegian supervisor accessed a list consisting of names and addresses to patients who met the inclusion criteria, in total 600 patients. The list was immediately erased after sending out the envelopes.

Sample size justification

A sample size of 400 patients would provide 95% Cis of ±4% around a proportion of 80%. For 200 patients this would be ±5.5%. We chose to include 400 patients to the study population.

2.4 Pilot

Face validity

To test if the translation was understandable, we asked 9 patients visiting the hospital pharmacy at Haukeland hospital to read through the questionnaire and give feedback whether they understood the questions. The patients focused on different sections rather than the whole questionnaire, and gave positive feedback in general.

The recommended changes were:

- Specify the language to avoid confusion.
- Changes in the structure of the sentences to make the statements easier to read
- Clarify small words that could mean different things
- Ensure that the headlines (totally agree, agree etc.) are on top of every section of the questionnaire

Recommendations and feedback was discussed with the supervisor and used to improve the language of the questionnaire.

From the list received from the neurological department, 30 patients with names starting with different letters was sampled into a pilot group. The aim of the pilot group was to check how, and how many, patients responded. A blank space allowing patients to comment on the questionnaire or give relevant feedback was included to enhance face validity. As the response rate was appropriate and patients generally responded to the different statements, we considered the questionnaire to be understandable for the patients.

Adjustments to increase quality of the questionnaire

Two patients in the pilot group stated that they did not have Parkinson's disease. We discussed this with the head neurologist at Haukeland, who confirmed that because of lack of time, neurologists usually use the diagnose code ICD-10 G20 for patients with Parkinsonism as well. As our inclusion criteria was G20, we changed the title from "Medicine use in patients with Parkinson's disease" to "Medicine use in patients with Parkinson's disease or Parkinsonism".

Content validity

To make sure we covered all relevant barriers to adherence, we used a validated tool. The IMAB-Q provides structural validity using Mokken analysis (47).

2.5 Main study

For the main study, the first 400 patients on the list were chosen. We excluded patients who participated in the pilot study, ensuring no patients would receive the questionnaire twice.

2.6 Coding quantitative data

SPSS was used to analyse the results. Statements with no response were coded 999. Responses that were impossible to analyse (for example both agree and disagree, or answers in text format) were coded 777. If the respondent checked off two boxes next to each other (i.e. both "strongly agree" and "agree"), the most negative response was chosen (in this case "agree"). The mean value was chosen in interval responses to "Duration of the disease" (Question 41). The highest number has been chosen in interval responses to "Number of medicines" (Question 42). Vitamin supplements was excluded from the data. Some new

variables were made; “Newly diagnosed patients” is defined as “Disease length” (Question 41) less than 2 years. Dichotomous statements were defined “Yes” if patients agreed and “No” if patients were unsure or disagreed.

Creation of dichotomous variables

The following barriers from the IMAB-Q has been dichotomised and included in figure 3.6-3.9

- I worry about the unwanted effects (e.g. harmful effects or side effects) of taking my medicines
- I am confident that I could find ways to solve any difficulties that I have with taking my medicines as prescribed
- If I needed support from others to take my medicines as prescribed, I could get it
- I trust my doctor(s) with decisions about my healthcare
- I know enough about my medicines to decide whether to take them
- I have a system in place to help me order, collect and take my medicines as prescribed
- Changes to my daily routine would not interfere with taking my medicines as prescribed

The following barriers from the IMAB-Q has been dichotomised and included in figure 3.10

- I have enough time to talk to my doctor about my medication
- I have enough time to talk to the pharmacist at the pharmacy about my medication
- I have been requested to come to follow-up consultations to discuss my medicine use
- I know the risk of not taking my medication(s)
- If problems appear with my medicine use (i.e. forget to take the, or get difficulties swallowing them) I know where to get help
- I am confident that I could find ways to solve any difficulties that I have with taking my medicines as prescribed
- I worry about the unwanted effects (e.g. harmful effects or side effects) of taking my medicines
- Taking my medicines as prescribed is a burden to me
- Taking my medicines as prescribed is an unwelcome reminder of my condition
- I remember to order and collect my medicines on time

- I trust my doctor(s) with decisions about my healthcare
- I know enough about my medicines to decide whether to take them
- Taking my medicine as prescribed does not fit with my daily routine
- I don't think I could cope if my medication regime kept changing

Table 2.1 Statistical tests performed

	Reference to results	**Statistical test used**
Comparison of potential barriers from the IMAB-Q and direct influence of health personnel (dichotomised variables)	Figure 3.6- 3.9	Fisher's exact test
Comparison of the most frequent barriers between newly diagnosed patients and patients diagnosed for a longer time (dichotomised variables)	Figure 3.10	Fisher's exact test
Comparison of motivation, intention and ability to remember medicines with potential barriers from the IMAB-Q	Table 3.2- 3.5	Spearman's rank correlation

2.7 Qualitative analysis of comments from the questionnaire

Textual comments regarding the healthcare system was transcribed into Excel verbatim. These were read carefully and the placed into common themes, in total 14 subgroups. The subgroups were put together into 4 main groups. Answers were shortened for readability. The quotes selected was considered representative by the researcher.

2.8 Qualitative analysis of focus group results

A focus group is a qualitative method where 4-12 people participate to a semi-structured discussion, where a facilitator follows a set of topics and asks broad questions to start the discussion (49). Even though the participants present their individual experiences and opinions, they are encouraged to interact with each other. Knowledge can therefore be seen from different perspectives (49, 50).

The aim of the focus group was to discuss interventions that could be taken by healthcare professionals to improve adherence in PD patients based on the identified barriers. As we wanted a discussion of their individual thoughts and ideas, a focus group was decided as a suited method. We wanted to gather 2-3 doctors, 1-2 nurses, 1 clinical pharmacist and 1 community pharmacist as this would represent a variety of healthcare professionals to discuss the different aspects of the treatment of PD patients.

The main researcher, the student, was the facilitator in the focus group while the supervisor was a moderator. The meeting was done in Norwegian, as all participants were Norwegian. None of the researchers participating in the focus group was experienced clinical researchers. The moderator provided a meeting location at her workplace with a projector and space for the participants to feel comfortable.

The head neurologist of the neurological department and the hospital pharmacist acted as gatekeepers to recruit participants to the focus group. The community pharmacist was recruited by the main researcher from a pharmacy known by the researcher prior to the study. Participants were recruited by e-mail, receiving a written invitation attached.

A handout was given 6 days ahead of the meeting with a short presentation of the themes we were going to discuss, allowing the participants to prepare themselves and come up with ideas before the focus group meeting.

The moderator took notes during the focus group, and the notes were discussed with the moderator after the meeting was done. Different themes derived after discussing the focus

group data. We validated the results by sending the notes back to the participants, asking them if the notes reflected the conversation or not, and giving an opportunity to add further comments. No changes were needed.

The topics presented to the focus group were based on figure 3.1-3.5:

- Information and follow-up of health personnel
- Patients' attitude and thoughts about medicines
- Handling medicines
- Patient routines

Data was classified into four different themes:

- Better information
- Use of time
- Conversation skills
- Practical actions

2.9 Summary

- A retrospective survey was used to identify barriers to non-adherence. The tool has been validated, thus providing content validity. Face validity is enhanced by piloting the survey.
- A focus group containing healthcare professionals was put together, where the head neurologist of the neurological department and the hospital pharmacist, acted as gatekeepers to recruit participants. The main researcher recruited the community pharmacist.
- The inclusion criteria are; Patients treated at Haukeland hospital from January to July 2017 diagnosed with Parkinson's disease or Parkinsonism (G20).
- Textual comments regarding the healthcare system was transcribed verbatim into Excel and sorted into 4 main groups.
- The facilitator and moderator discussed the notes derived from the focus group meeting, and the results were sorted into 4 main groups

2.10 Ethics

We applied to REK (Regional ethics committee) in Norway, as this project is considered a scientific study. It was approved 01.09.17.

3. Results

3.1 Quantitative results

Table 3.1 presents the demographics of the study population. 430 questionnaires in total were sent out. The response rate in both pilot group (16 responses) and main study (213 responses) was 53,3%. The results from the pilot group was included in the study.

Table 3.1 Patient demographics

	Measure	**Study population (n=229)**
How many replied in pilot group	n (%)	16 (53,3 %)
How many replied in main study	n (%)	213 (53,3%)
Gender: Male	%	64,4%
Length of disease	Median (IQ)	6 years (3,10)
Number of medicines	Median (IQ)	3 (2,5)

All statements from the questionnaire has been presented in figure 3.1-3.5, describing the frequency of the different barriers.

Figure 3.1 and 3.2 describes patient responses on information and follow-up of health personnel. Many patients have a good relationship with their doctor. Almost one third did not plan their further medicine use or have enough time to talk to their doctor about their medication. This is greater with respect to pharmacists.

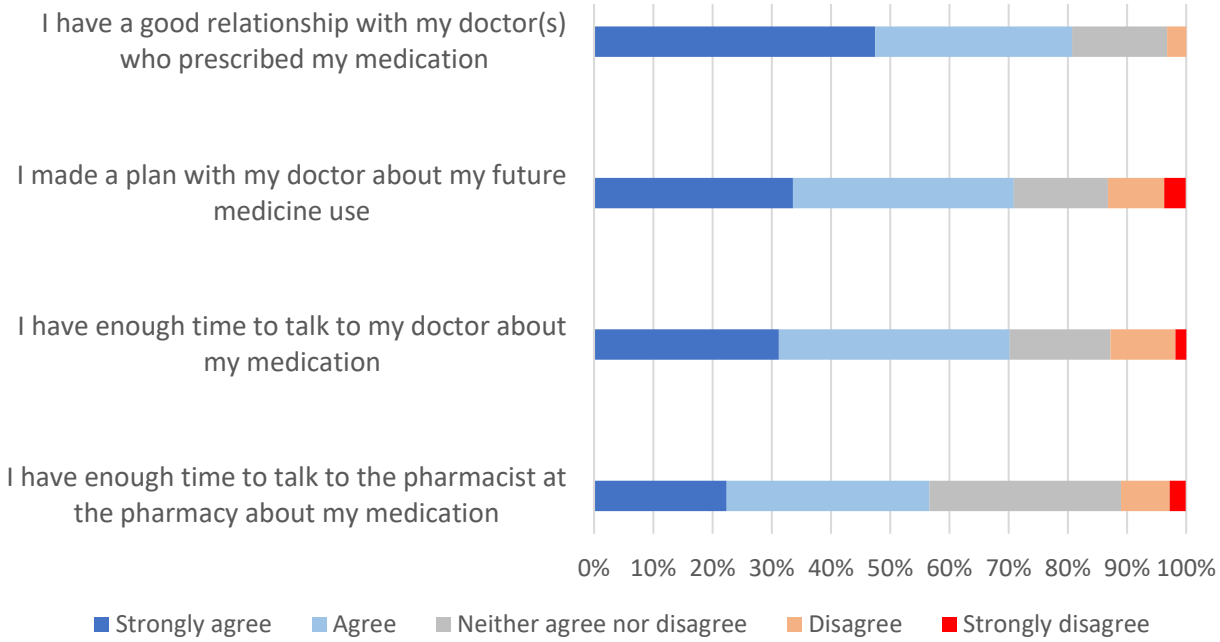

Figure 3.1 Information and follow-up of health personnel part 1

Patients generally understand why they need their medicines and expect them to work. Some patients do not know the risk of omitting their medicines. A significantly smaller proportion of the study population knows where to get help if needed and have been requested follow-up consultations.

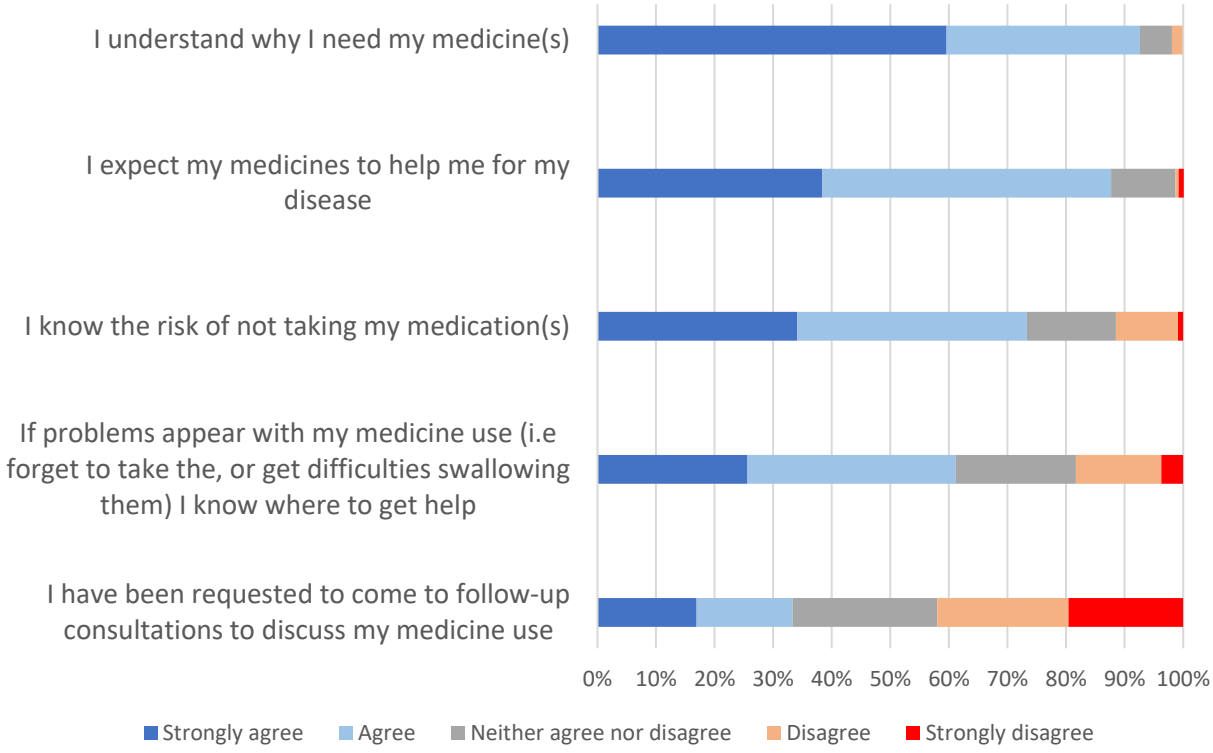

Figure 3.2 Information and follow-up of health personnel part 2

Figure 3.3 represents the medicine thoughts and attitudes of the study population. Their intentions to take medicines seems good, they seem motivated and they prioritise to take their medicines. Side-effects are a topic of concern for a big part of the study population. Taking medicines seems to be a burden and an unwelcome reminder of their disease in some patients.

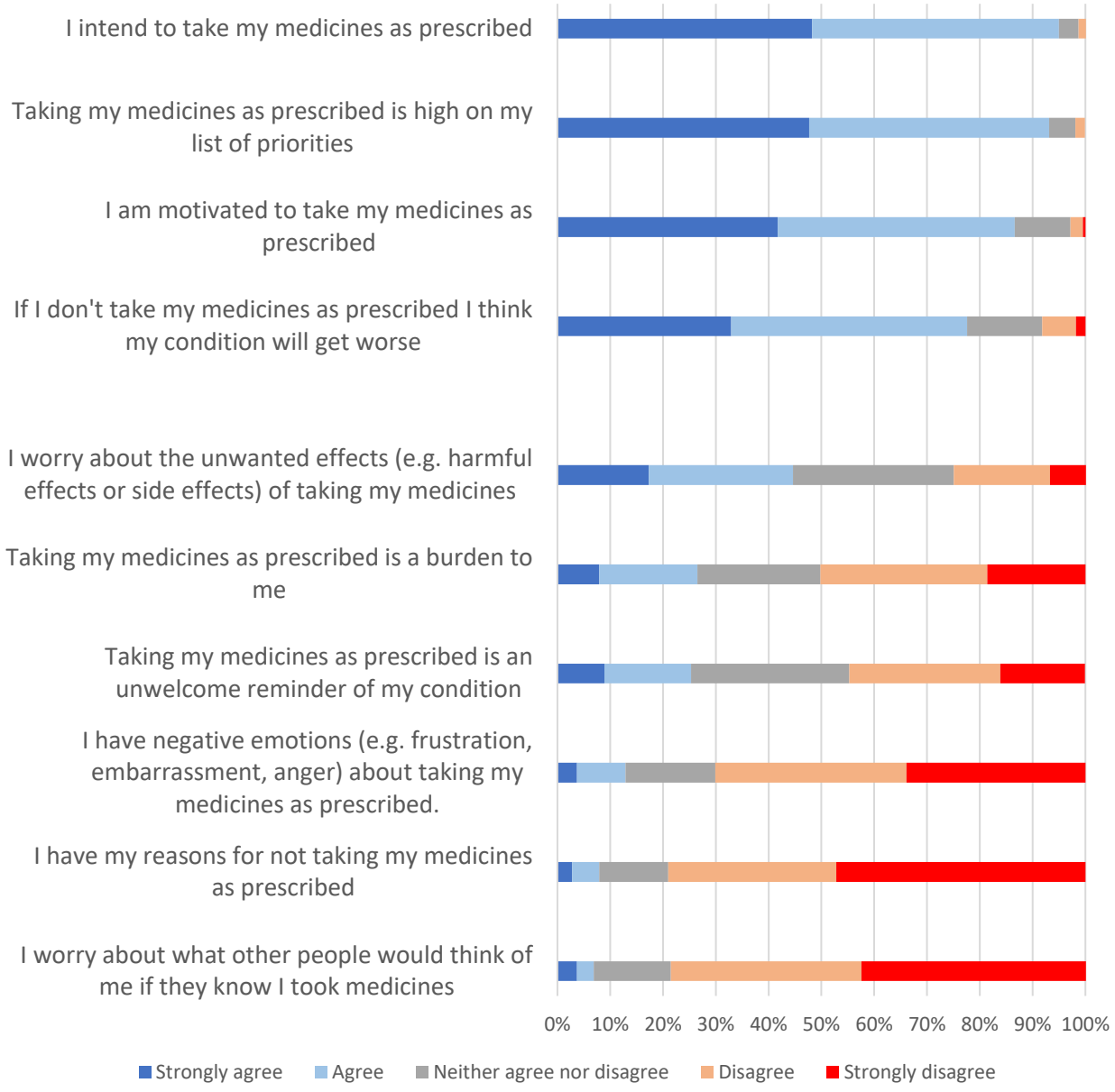

Figure 3.3 Patients' thoughts and attitudes about medicines

Figure 3.4 represents the responses regarding the handling of medicines. Most patients know how to take their medicines, and are physically able to take them. However, remembering to order and collect medicines in time seems to be a problem for some of the patients. A reasonably big part of the population does not trust their doctor's decisions about their healthcare, and have trouble finding help and solving difficulties that may arise. Few knows enough about their medicines to decide whether to take them.

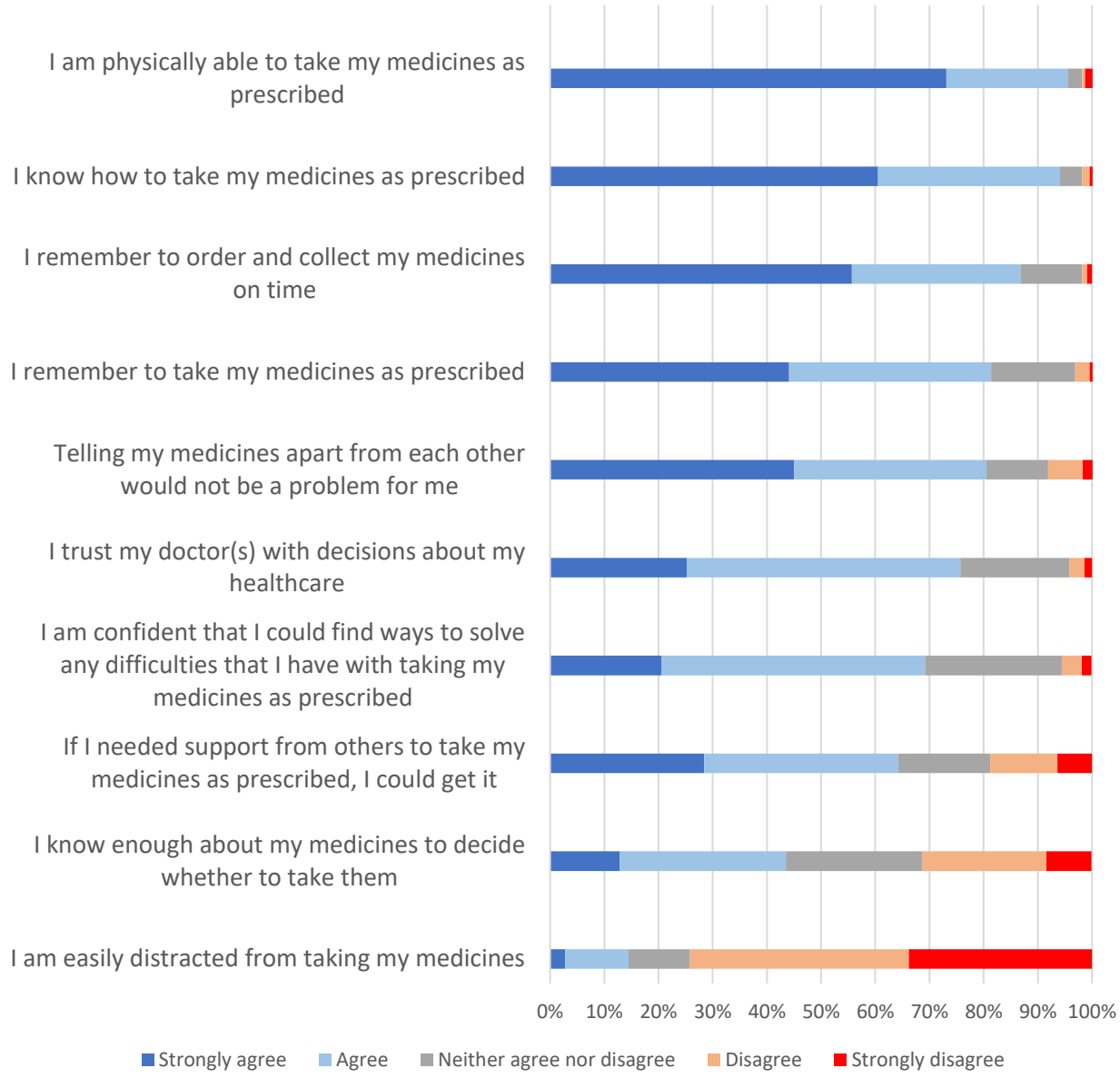

Figure 3.4 Handling medicines

Figure 3.5 represents the influence of the patients' routines on taking their medicines. The practical routines of ordering and collecting their medicines is manageable for the study population, even though few patients have a system to order, collect and take their medicines. It seems like they have been receiving sufficient information within this topic. Almost one third had to choose between paying for their prescriptions and paying for other important things. Their daily routines concerning their medicine use seems harder to manage, and a change in their daily routine would influence their medicine use in a lot of cases.

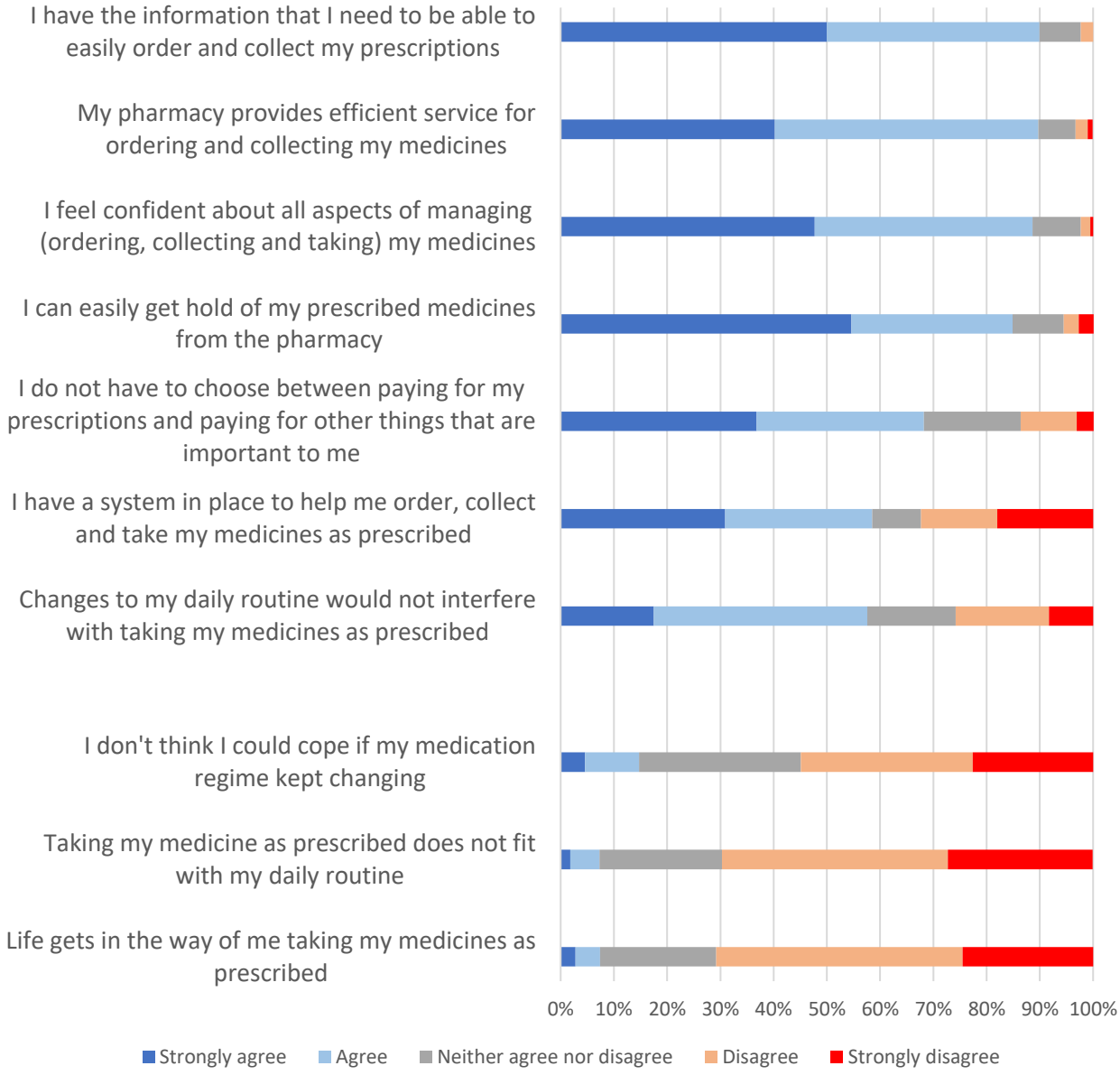

Figure 3.5 Patient routines

The barriers presented in figure 3.6- 3.9 has been dichotomised as explained in section 2.6. Fisher's exact test has been used to identify statistical differences between the groups.

Figure 3.6 provides a comparison between the responses to barriers from figure 3.1 and whether patients reported having a good relationship with their doctor or not. Those who reported a good relationship with their doctor were more likely to trust their doctor and less likely to worry about side effects.

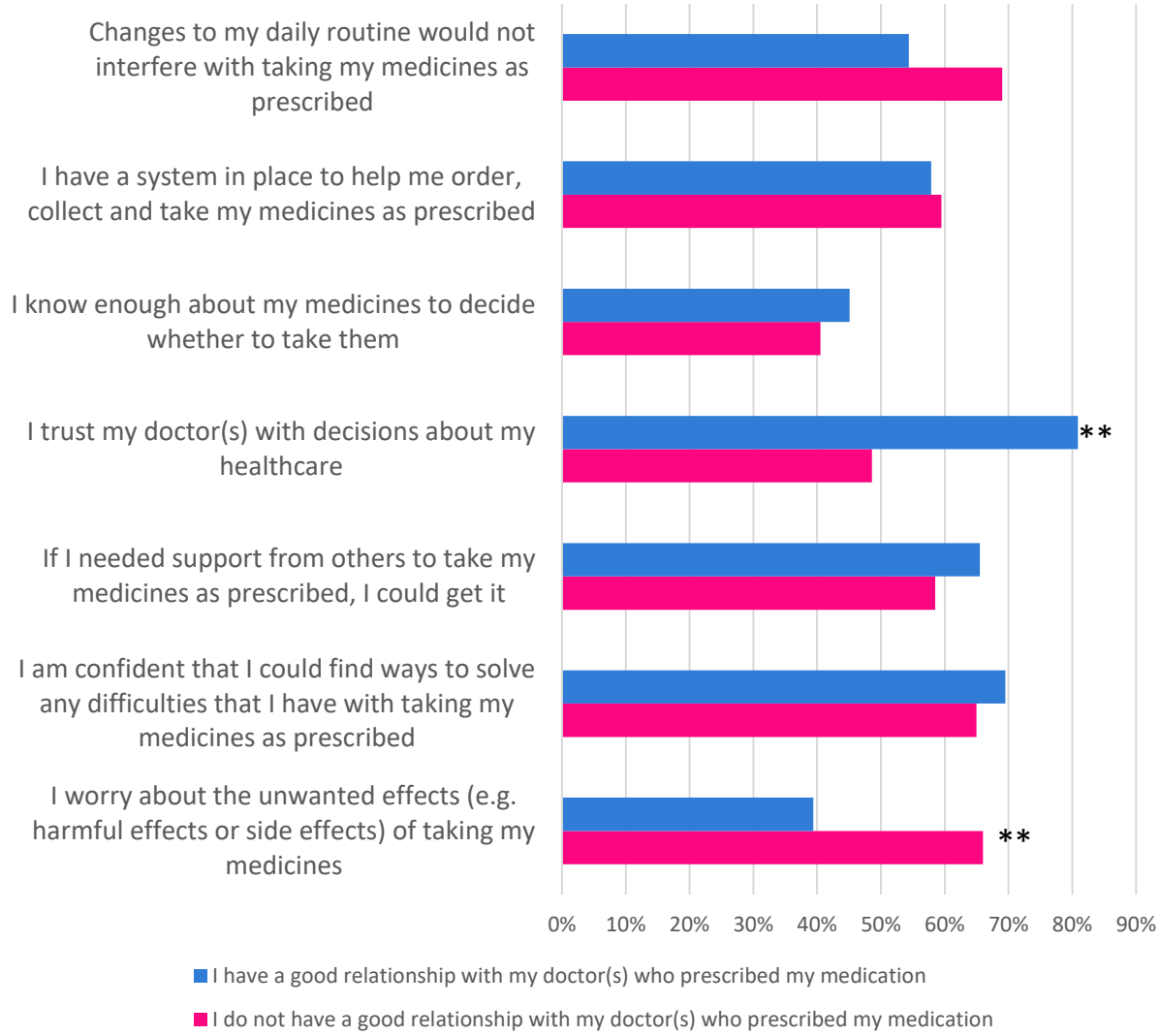

Figure 3.6 Comparison of patients with and without a good relationship with their doctor

* Significant at 0,05 level ** Significant at 0,01 level

Figure 3.7 provides a comparison between the responses to barriers from figure 3.1 and whether patients reported enough time with their doctor or not. Patients who reported having enough time with their doctor were more likely to trust their doctor, more likely to get support taking their medicines and less likely to worry about side effects.

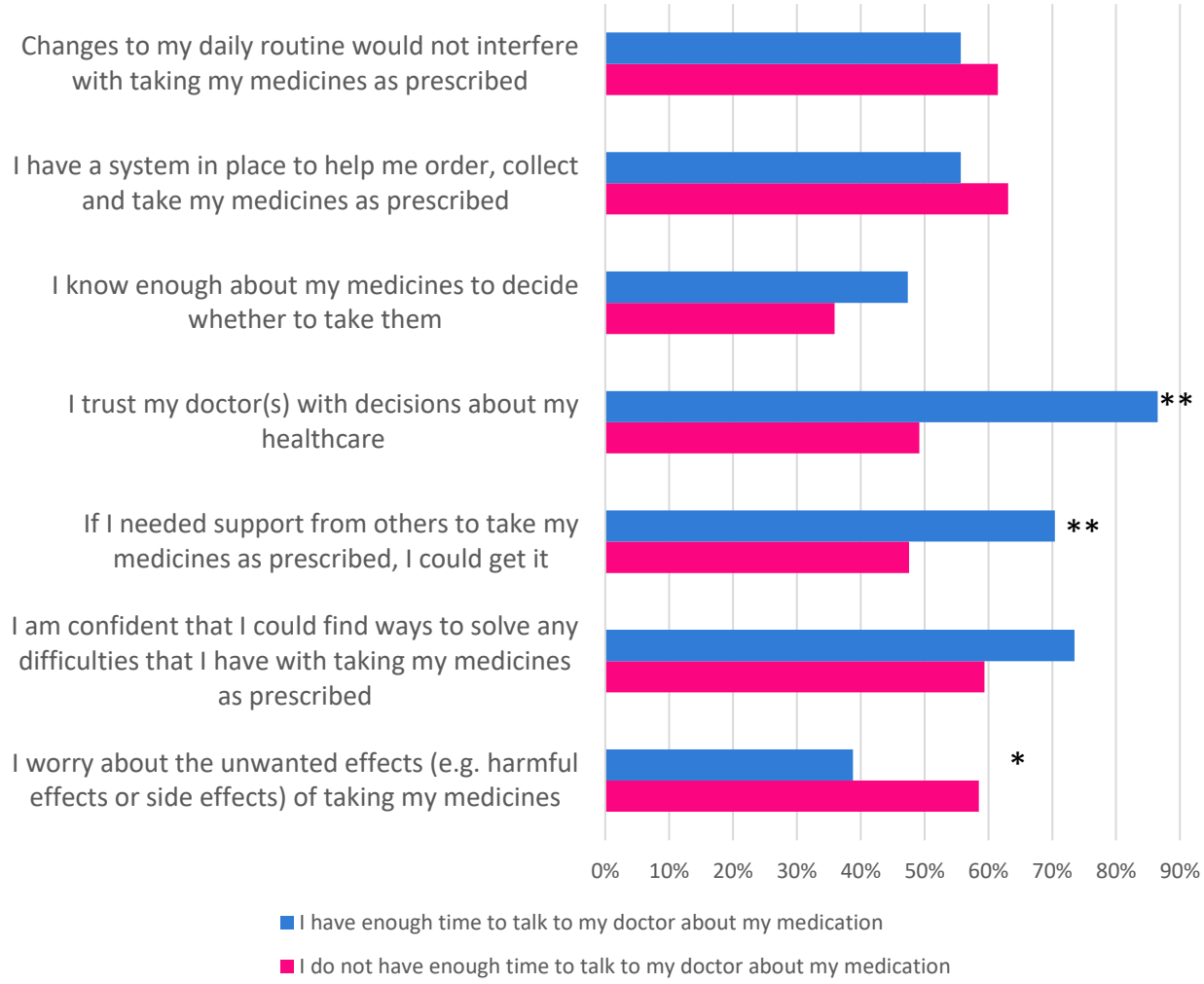

Figure 3.7 Comparison of patients with and without enough time with their doctor

* Significant at 0,05 level ** Significant at 0,01 level

Figure 3.8 provides a comparison between the responses to barriers from figure 3.1 and whether patients reported enough time with their pharmacist or not. Patients who reported having enough time with their pharmacist were more likely to trust their doctor, more likely to get support taking their medicines and more likely to be able to solve any difficulties regarding their medicine regime.

Table 3.8 Comparison of patients with and without enough time with the pharmacist

* Significant at 0,05 level ** Significant at 0,01 level

Figure 3.9 provides a comparison between the responses to barriers from figure 3.1 and whether patients reported planning their further medicine use. Patients who reported planning their further medicine use were more likely to trust their doctor, more likely to get support taking their medicines and more likely to be able to solve any difficulties regarding their medicine regime.

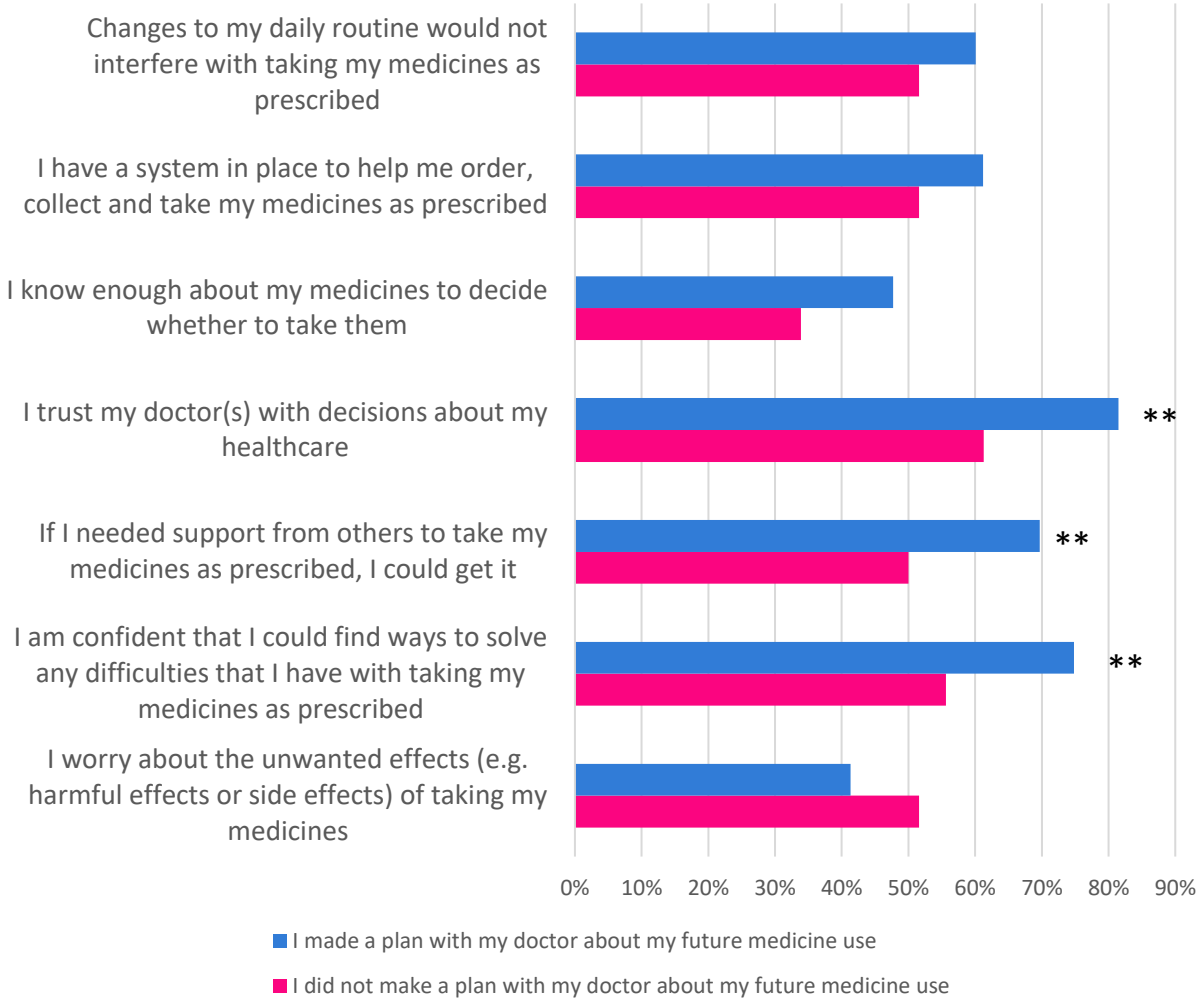

Figure 3.9 Comparison of patients who planned their further medicine use with patients who did not

* Significant at 0,05 level ** Significant at 0,01 level

Figure 3.10 provides a comparison between the most frequent barriers in newly diagnosed patients (less than two years) and patients diagnosed for a longer time (two years or more). Fisher's exact was used to test significant differences. Interestingly, there were no significant differences between the groups in any of the barriers tested.

Figure 3.10 Comparison of the most frequent barriers between newly diagnosed patients and patients diagnosed for a longer time

Table 3.2- 3.5 shows correlation between three statements; “I am motivated to take my medicines as prescribed”, “I intend to take my medicines as prescribed”, “I remember to take my medicines as prescribed” and the other barriers presented in this study. Correlations were tested to check if the three statements are important barriers to adherence. Spearman’s rank test was used to find correlations.

Table 3.2 addresses “Information and follow-up of health personnel”. These statements are strongly correlated with the patient’s intentions of taking medicine. From the observed data, it seems like pharmacists have less influence than doctors on motivation, but have an equally strong influence as the doctor on the patient’s intention of taking medicines and having the ability to remember to take medicines. Patients having a good relationship with their doctor, being provided sufficient time to talk to their doctor, understanding why they need their medicines, expecting their medicines to work and understanding the risk of omitting their medicines are more likely to be motivated to take their medicines as prescribed. Patients who planned their further medicine use and had been requested to come to follow-up sessions with their doctor are more likely to intend to take their medicines as prescribed. The ability to remember to take medicines as prescribed is not as strongly correlated with information and follow-up of health personnel.

Table 3.2 Identified barriers correlating with "Information and follow-up of health personnel"

	Measure #	I am motivated to take my medicines as prescribed	I intend to take my medicines as prescribed	I remember to take my medicines as prescribed
I have a good relationship with my doctor(s) who prescribed my medication	R P	0,341** 0,000	0,313** 0,000	0,186** 0,006
I made a plan with my doctor about my future medicine use	R P	0,258** 0,000	0,400** 0,000	0,192** 0,004
I have enough time to talk to my doctor about my medication	R P	0,406** 0,000	0,340** 0,000	0,230** 0,001
I have enough time to talk to the pharmacist at the pharmacy about my medication	R P	0,168* 0,014	0,230** 0,001	0,222** 0,001
I understand why I need my medicine(s)	R P	0,452** 0,000	0,379** 0,000	0,297** 0,000
I expect my medicines to help me for my disease	R P	0,361** 0,000	0,267** 0,000	0,100 0,141
I know the risk of not taking my medication(s)	R P	0,324** 0,000	0,285** 0,000	0,154* 0,024
If problems appear with my medicine use (i.e. forget to take the, or get difficulties swallowing them) I know where to get help	R P	0,365** 0,000	0,339** 0,000	0,263** 0,000
I have been requested to come to follow-up consultations to discuss my medicine use	R P	0,098 0,154	0,291** 0,000	0,062 0,361

#Spearman's rank correlation * Significant at 0,05 level ** Significant at 0,01 level

Table 3.3 addresses the patients' thoughts and attitudes about medicines. Motivation seems to be highly important regarding medicine thoughts and attitude. Patients motivated to take their medicines were more likely to intend to take their medicines as prescribed, and knowing the risk of omitting their medicines. Having negative emotions about taking medicines, feeling like medicines is a burden would less likely motivate the patients. Patients intending to take their medicines as prescribed were more likely to prioritise taking their medicines. Patients were not less likely to intend to take their medicines even though they were worrying about side-effects, thinking their medicines are a burden, thinking that their medicine is an unwelcome reminder of their condition and having negative emotions about taking their medicines.

Table 3.3 Identified barriers correlating with thoughts and attitudes about medicines

	Measure #	I am motivated to take my medicines as prescribed	I intend to take my medicines as prescribed	I remember to take my medicines as prescribed
I intend to take my medicines as prescribed	R P	0,380** 0,000	1 -	0,408** 0,000
Taking my medicines as prescribed is high on my list of priorities	R P	0,485** 0,000	0,569** 0,000	0,312** 0,000
I am motivated to take my medicines as prescribed	R P	1 -	0,380** 0,000	0,245** 0,000
If I don't take my medicines as prescribed I think my condition will get worse	R P	0,298** 0,000	0,317** 0,000	0,094 0,166
I worry about the unwanted effects (e.g. harmful effects or side effects) of taking my medicines	R P	-0,166* 0,015	-0,024 0,729	-0,047 0,488
Taking my medicines as prescribed is a burden to me	R P	-0,290** 0,000	-0,129 0,060	-0,181** 0,008
Taking my medicines as prescribed is an unwelcome reminder of my condition	R P	-0,164* 0,018	-0,031 0,657	-0,051 0,457
I have negative emotions (e.g. frustration, embarrassment, anger) about taking my medicines as prescribed.	R P	-0,283** 0,000	-0,057 0,402	-0,139* 0,041
I have my reasons for not taking my medicines as prescribed	R P	-0,236** 0,001	-0,315** 0,000	-0,276** 0,000
I worry about what other people would think of me if they know I took medicines	R P	-0,278** 0,000	-0,152* 0,026	-0,131 0,053

Spearman's rank correlation * Significant at 0,05 level ** Significant at 0,01 level

Table 3.4 addresses “Handling medicines”. Knowing how to take medicines as prescribed motivates the patients. Motivated patients may also have an increased chance of remembering to order and collect medicines on time. Patients intending to take their medicines as prescribed were more likely to know how- and remember to take medicines as prescribed and trust their doctor’s decisions. Medicine handling influenced the ability to remember to take medicines as prescribed more than the other topics, and the patients who reported being distracted from taking their medicines as prescribed were more likely to forget to take their medicines. Patients being physically able- and knowing how to- take medicines were more likely to remember to take their medicines as prescribed.

Table 3.4 Identified barriers correlating with "Handling medicines"

	Measure #	**I am motivated to take my medicines as prescribed**	**I intend to take my medicines as prescribed**	**I remember to take my medicines as prescribed**
I am physically able to take my medicines as prescribed	R P	0,288** 0,000	0,366** 0,000	0,467** 0,000
I know how to take my medicines as prescribed	R P	0,318** 0,000	0,418** 0,000	0,420** 0,000
I remember to order and collect my medicines on time	R P	0,303** 0,000	0,397** 0,000	0,343** 0,000
I remember to take my medicines as prescribed	R P	0,245** 0,000	0,408** 0,000	1 -
Telling my medicines apart from each other would not be a problem for me	R P	0,275** 0,000	0,296** 0,000	0,362** 0,000
I trust my doctor(s) with decisions about my healthcare	R P	0,353** 0,000	0,436** 0,000	0,322** 0,000
I am confident that I could find ways to solve any difficulties that I have with taking my medicines as prescribed	R P	0,218** 0,001	0,301** 0,000	0,205** 0,002
If I needed support from others to take my medicines as prescribed, I could get it	R P	0,204** 0,003	0,257** 0,000	0,131 0,053
I know enough about my medicines to decide whether to take them	R P	0,192** 0,005	0,086 0,209	0,104 0,128
I am easily distracted from taking my medicines	R P	-0,115 0,097	-0,304** 0,000	-0,493** 0,000

Spearman's rank correlation * Significant at 0,05 level ** Significant at 0,01 level

Table 3.5 addresses “Patient routines”. Within patient routines, motivation-, intention- and ability to remember- to take medicines as prescribed is influenced by the same barriers. These patients are more likely to have the information needed to easily order and collect prescriptions and feeling confident about managing medicines. The effectiveness at the pharmacy would more likely increase the patient’s intention to take medicines as prescribed than motivation and ability to remember to take medicines as prescribed.

Table 3.5 Identified barriers correlating with "Patient routines"

	Measure #	I am motivated to take my medicines as prescribed	I intend to take my medicines as prescribed	I remember to take my medicines as prescribed
I have the information that I need to be able to easily order and collect my prescriptions	R P	0,417** 0,000	0,463** 0,000	0,331** 0,000
My pharmacy provides efficient service for ordering and collecting my medicines	R P	0,289** 0,000	0,400** 0,000	0,319** 0,000
I feel confident about all aspects of managing (ordering, collecting and taking) my medicines	R P	0,389** 0,000	0,407** 0,000	0,427** 0,000
I can easily get hold of my prescribed medicines from the pharmacy	R P	0,274** 0,000	0,305** 0,000	0,307** 0,000
I do not have to choose between paying for my prescriptions and paying for other things that are important to me	R P	0,281** 0,000	0,266** 0,000	0,285** 0,000
I have a system in place to help me order, collect and take my medicines as prescribed	R P	0,033 0,63	0,093 0,175	-0,080 0,243
Changes to my daily routine would not interfere with taking my medicines as prescribed	R P	0,067 0,327	0,072 0,297	-0,016 0,815
I don't think I could cope if my medication regime kept changing	R P	-0,266** 0,000	-0,169* 0,013	-0,220** 0,001
Taking my medicine as prescribed does not fit with my daily routine	R P	-0,164* 0,016	-0,409** 0,000	-0,280** 0,000
Life gets in the way of me taking my medicines as prescribed	R P	-0,286** 0,000	-0,312** 0,000	-0,322** 0,000

Spearman's rank correlation * Significant at 0,05 level ** Significant at 0,01 level

3.2 Qualitative analysis of the comments from the questionnaire

Four themes were identified from the written comments within the returned questionnaires and these are explained in Table 3.6.

Table 3.6 Themes derived from written comments within returned questionnaires

Category	Description
Information	Comments on what type of information the patients got or what type of information they would want to have.
Thoughts about medicines	Patient attitudes and thoughts about taking medicines, either generally, concerning PD or side effects.
Experiences and impression	Patient experiences and impression of the health care system.
Everyday life and medicines	Comments about their medicine use in their daily lives.

Information

A major theme which arose from the written comments in the questionnaire was the need for better information, where side-effects was one important topic.

> *"It's important with information about side-effects (not just in a bisection)."* (Patient 93).

There has also been a focus on the lack of information about what medicines exist today and discussion with the patient about what treatment would be ideal for them.

> *"I know the medications I use, but have no idea what is on the market or how they work / interact with other types. I would like to get information about what exists on the market and what medicines I can take together."* (Patient 100).

Thoughts about medicines

It seems that the patients have different views when it comes to taking medicines (Appendix B). Side-effects has been discussed by several patients, and seems to be an important part of what the patients focus on considering their medicine treatment.

> *"I use medicines with a lot and dangerous side-effects."* (Patient 56).

Experiences and impression

As expected, patients have had several different experiences and impressions of the Norwegian health care system, where the topics; relationship with prescriber, having permanent neurologist or other health personnel, duration of consultation, contact with prescriber and follow-up have been mentioned.

Patients seem to have different opinions about their prescriber.

> ***"****I have been treated well by doctors and other health personnel in Haukeland hospital."* (Patient 34).
>
> *"Unlucky with prescribing doctor/neurologist every visit."* (Patient 35).

A permanent prescriber seems to be important as a part of their treatment, and may influence the patient's ability to discuss their medicines further after their consultation is over.

> *"At the half-yearly check at Haukeland, I never get the same neurologist. This makes the check difficult. If something happens to the medicines in the meantime (e.g. I was given too much medicine, became very ill 1 year ago) it is difficult for my doctor to contact a neurologist who knows me. There has also been given incorrect information about my medication back to the GP after visiting the polyclinic."* (Patient 73).

The duration of the consultation is important for the patients to ask questions that may influence their adherence. This issue has been brought up by several patients.

> ***"****It is frustrating to find that when one has met at the agreed consultation, they do not have time for me (…) I feel that there is a lot I should have asked for, but that there is never time for it. Nor do I feel that I'm being taken seriously. It's all about following up the patient and making it easier for you to encounter problems."* (Patient 225).

Patients have expressed different experiences regarding contact with their prescriber.

> ***"****I got an additional medicine 2 years ago. I couldn't use that because of stomach issues. But I never get to give feedback."* (Patient 77).

Patients have been requested follow-up consultations from their doctor on different levels.

> *"There's a problem that the hospital/ neurologist doesn't have good enough routines for follow-up/ monitoring considering side-effects. Today's lack of follow-up puts all risk on the patient."* (Patient 63).

> *"I am trying out new medicine. The doctor is going to follow up when the medicines have stabilised."* (Patient 40).

Everyday life and medicines

Within this topic, patients mostly commented on how their medicines affected their daily life, medicine administration difficulties and their thoughts about economy.

Patients have stated their different thoughts of taking medicine in their daily life.

> *"It can be hard to take Parkinson medication to meals, especially when I'm visiting my family that has different meal routines than we have at home."* (Patient 73).

> *"The tablets are in strips with daily doses (5 daily) so it's simple."* (Patient 153).

When it comes to administration of medicines, the preferences are individual.

> ***"****I take Medopar that is in a glass with cotton on top in a new container. The glass is hard to open, and it's hard to remove the cotton. It should have been a blister package."* (Patient 42).

> *"The new boards on "Sinemet" are difficult, easier tablet on glass. The tablets on the board are difficult to remove the entire tablet from the tray, they divide and crumble."* (Patient 85).

The economic part of the treatment is important to consider as the patients have commented on this.

> ***"****I use Duodopa. I get this covered 100%. If I had to pay it myself, I'd have to stop taking it."* (Patient 59).

> *"I think that customers/patients that use a lot of medicines every day should be given doset on blue prescription."* (Patient 109).

3.3 Qualitative analysis of focus group results

One hospital pharmacist and one community pharmacist participated in the focus group together with the two researchers. There was no one in the room not participating in the focus group. The hospital pharmacist knew the moderator and the community pharmacist knew the facilitator prior to the study. Unfortunately, the neurologist failed to recruit health personnel working at the neurological ward at Haukeland, resulting that doctors and nurses were not able to attend thus resulting in a pharmacist-directed point of view. The focus group meeting lasted for 60 minutes.

Table 3.7 Main interventions discussed

Theme	Suggested actions
Better information	Group education. Medicine start (A new service in Norwegian pharmacies with follow-up consultations for patients starting on a new medicine. Explained further in the discussion). Hand out short information leaflets More systematic follow-up on pharmacies concerning aids, offering different medicine containers if possible and practical handling of medicines. More active and focused information about side-effects Balanced amount of information about effect and side-effect Medicine review concerning side-effects Follow-up of side-effects in the hospital (by doctor, nurse or pharmacist).
Use of time	At hospitals: find out who can be used to give more patient-directed information in the most efficient way. Pharmacists can ease the work of both doctors and nurses by giving a larger quantity and more patient-directed information.
Conversation skills	Practice the consultation skills of pharmacists. Prioritise what information we want the patient to end up with. Find out what is important for the individual patient before starting the conversation.
Practical actions	Refer to appropriate websites. Use services to ease ordering medicines and use of multidose (medicines packed into daily doses).

4. Discussion

4.1 Identified frequent barriers

This is the first study to consider medication adherence post-discharge from hospital from the perspective of medication barriers and enablers. Generally, patients understood why they needed their medicines and expected them to work. The majority of the patients reported good relationships with their doctor.

One of the main messages to be taken away from this was the belief that patients reported that they did not get enough time to talk to health personnel about their medicines. Interestingly this was a greater problem with pharmacists than doctors. Not all patients knew the risk of omitting their medicines, some patients have also stated that they have not planned their further medicine use-, and few patients have been requested follow-up sessions- from their doctor. Furthermore, if problems occurred patients did not know where to get help from. All of these issues could be addressed through consultations with doctors or pharmacists.

Negative attitudes to medicines which are more difficult to address were perceptions of medicines being a burden, and an unwelcome reminder of their disease. Most patients are motivated to take medicines, but side-effects are a topic of concern and is supported by many of the comments from the questionnaire. Thankfully even with these views many patients stated that they intended to prioritise and take their medicines as prescribed.

Knowing how to take medicines seemed not to be problem for most patients. In general, they were physically able to take medicines. Patients would not get help or solve difficulties regarding their medicine use if needed, indicating too little information about this. Unfortunately, insufficient information about their medicines was provided for the patients themselves to decide whether to take their medicines. This is supported by their comments.

Healthcare professionals seem to provide enough information about ordering and collecting medicines and is therefore not a problem for most patients, even though few had a system to help manage their medicines. The economic aspect of their medicine regime scores low in the quantitative results. As commented, some patients struggle to fit their medicine regimen into their daily routine, and changing it (e.g. going on vacation), would influence their medicine adherence.

It would seem that where patients reported having enough time with their doctor, the worry about side-effects decreased. Where patients reported having enough time with their pharmacist, the patient’s ability to solve problems increased. Patients who were satisfied with

the provided time to talk to healthcare professionals in general seemed to report increased trust in their doctor's decisions about their healthcare and the ability to get support taking their medicines.

Disease length did was not seen to relate to the barriers to non-adherence in this study, indicating that addressing non-adherence in patients diagnosed for a long time is just as important as newly diagnosed patients.

Motivation-, intention- and ability to remember to take medicines are considered important as they relate to most of the barriers presented in this study. Patients who reported having enough time to talk to their doctor were more likely to be motivated than patients who reported having enough time with the pharmacist. Motivation correlated with many of the statements regarding medicine thoughts and attitude.

Interestingly, there was no relation seen between the patient's intention to take medicines as prescribed and the concern about side-effect or feeling that taking medicines is a burden or an unwelcome reminder. Nor did the patient's intention to take medicines seem to relate to the patient having negative emotions about taking medicines.

4.2 Strengths and limitations

The longer since the consultation at the hospital, the bigger the risk of forgetting their thoughts about their medicine regime. If the consultation took place just before the arrival of the questionnaire, there is a risk that the patient has not developed a health behaviour or identified any barriers yet. With this in mind, we chose to include patients treated at the hospital from January to July 2017.

Males are more likely to have PD than females because female genes and hormones have a neuroprotective effect (51, 52), and a higher proportion of males in the sample population is as anticipated. The response rate and gender distribution was reasonably similar to other studies using questionnaires of the same length, but the patients reported having the disease for a shorter period of time on average i.e. 6 years versus 8.6 (53-55). From these comparisons, the sample population seem to represent the general population of those with PD, therefore providing some confidence in the generalisability of the findings.

The response rate seems reasonable comparing to other literature, but a response rate below 60% does raise questions regarding response bias and whether the non-responders and responders are similar.

To improve response further we could have used several strategies (48):

- Monetary incentives or non-monetary incentives
- Unconditional incentives
- Recorded delivery
- A teaser on the envelope
- Pre-notification
- Follow-up contact
- Providing a second copy of the questionnaire at follow up
- Mentioning an obligation to respond
- Personalised questionnaires
- Use of hand-written addresses
- First class outward mailing

First class outward mailing is not relevant in the Norwegian mail system.

We put a deadline in the pilot group, but decided to remove it because the letter arrived only one week before Christmas, thus assuming the respondents needed extra time to reply. The Cochrane review did not mention deadline to limit response rate in postal questionnaires (48). Since the response rate did not change, we assume that removing the deadline did not affect the response rate.

The tool for this study is based on the Norwegian translation of the IMAB-Q, and is translated by the researchers (student and supervisor). The sample population responded well, suggesting the questionnaire was user friendly. However, we got several comments on the language while piloting the questionnaire, indicating that the translation was not ideal which affects face validity. There is a challenge translating and maintaining the original meaning and interpretation of the statement. The patients' answers are then translated back to English for the analysis. The analysed data may vary slightly due to different interpretation of the two languages. Further recommendations would be to spend more time with patients to determine whether their interpretation and that of the researchers were the same.

The focus group was small, giving a lot of time for each participant to speak. The atmosphere in the group was good, and there was good flow in the conversation between the participants. As the focus group consisted only of pharmacists, the actions discussed are mainly concerning their task. Therefore, we cannot assume that the interventions are suited for all kinds of healthcare professionals. Participation by different kinds of professionals could provide a greater insight into how services could be changed to address the problems identified. Further focus group meetings consisting of neurologists, nurses, hospital pharmacists and community pharmacists should be performed to discuss the different interventions further.

Some improvements of the questionnaire should be done in further studies. We should have specified what type of medicines we asked for in the questionnaire, as patients did not know whether to report all medicines or just medicines used for PD. We know this because some respondents commented on this question. These issues were not detected in the pilot study. Age could have been added along with disease length to the demographic questions of the questionnaire to help identifying the generalisability of the study population. Asking whether the patients got any help taking medicines would also be useful to know, as some of the questions would be irrelevant to them. As many patients misunderstood the question about economy “I do not have to choose between paying for my prescriptions and paying for other things that are important to me”, we should have clarified that patients getting medicines for free should not disagree with this statement.

4.3 Discussion of main barriers

There is a need for patients to provide enough information about where to get help if problems taking their medicines as prescribed appears, and where they can go to get help. Information about the risk of omitting their medicines also seems to be needed as this could increase non-adherence. Whilst doctors may not have time to provide all this information this provides an opportunity for pharmacists.

Interestingly patients reported that they did not have as much time with a pharmacist as they would like. This was corroborated within the focus group by the community pharmacist. An insufficient number of community pharmacists in each pharmacy within Norway may partially explain this (56). However, it was also discussed in the focus group that hospital

pharmacies had less problems with time limit than community pharmacies. When insufficient time limits the pharmacist to provide information, they should focus on the risks of not taking the medicine and what the patient should do if problems arise.

"Medicine start" is a new service in community pharmacies, where patients starting on a new medicines receives an opportunity of two follow-up consultations with a pharmacist (57). This is not established for all diseases yet, but this could be ideal for Parkinson patients where an optimal medicine routine could be established from the start. This service could attribute to the lack of follow-up the patients need, and could ease off the work of doctors.

As discussed in the focus group, leaflets, webpages and apps can be useful to provide information and support patients to take their medicines. When time is crucial, this could seem like an efficient solution. However, older patients who cannot read the leaflets provided or use a computer or a smartphone cannot use this offer. Younger people are not likely to read the leaflet, resulting that no information has been comprehended. This intervention is suboptimal standing alone.

It is reported from the patients in both the quantitative and qualitative results from the questionnaire that side-effects are a big concern. It is important that healthcare professionals identify patient concerns and address them. As discussed in the focus group, doctors, nurses or pharmacists at the hospital could provide follow-up sessions concerning side-effects. More active and focussed information about side-effects should be given in the pharmacies, as this is wanted by the patients (see appendix B).

Feeling that taking medicines is a burden may cause non-adherence. Doctors could influence this barrier by easing the medicine regimen. Further research should be done on the effects of easing medicine regimen in patients with PD. Pharmacists can reduce burden by helping the patient structure their medicine regime, for example by taking their medicines at the same time as specific events during their daily routine (e.g. after brushing their teeth or after breakfast).

Not all patients trust their doctor's decisions about their healthcare. This could be explained by the lack of knowledge about their own medicines, as many patients reported that they did not know enough about their medicines to decide whether to take them. Doctors could improve adherence by comparing the different medicines on the market focussing on effects and side-effects, giving the basis of making their own decisions when deciding the patient's treatment. Pharmacists can also increase the patient's trust in their doctor by confirming their choice of treatment and explaining why the treatment is important.

Planning further medicine use and providing follow-up consultations could be a solution when patients have problems getting help or solve difficulties regarding their medicine regimen. Healthcare professionals could improve adherence by addressing the problems the patient is having, and find out how to solve them together with the patient. Follow-up sessions can be useful to allow the patient to seek help after having used medicines for a while.

Almost two thirds of the study population stated that they did not have to choose between paying for medicines and paying for other important things. However, many patients commented their answers to this statement in the questionnaire. Due to the refund arrangement in Norway, many patients did not agree with the statement because they got their medicines for free. From the responses in the questionnaire, together with the comments, economy does not seem to be an essential barrier to non-adherence even though it is an important part of their medicine regimen.

Incorporating a medicine regimen into their daily routine has been reported to be difficult. Changing routines (e.g. visiting family or going on vacation) seemed especially hard, and was corroborated in the comments from the patients, saying it was hard to remember to take medicines while visiting family. Planning medicine use with their doctor discussing what to do when their daily routine changes, could be ideal to reduce this barrier. Patients who just started taking medicines may not be ready to receive this kind of information right away, and would probably fit better in a follow-up consultation. Healthcare professionals could ask the patient if they need to discuss this issue.

From the results observed, there seems to be a difference in the doctor's and pharmacist's influence on the patients, which is expected as they have different tasks in the Norwegian healthcare system. Communication between healthcare professionals about interventions to non-adherence could reduce the barriers effectively. Patients should be directed to the right healthcare professional to improve adherence in the most effective way.

Non-adherence seems to occur in patients regardless of the disease length. Healthcare professionals should address the necessity of identifying barriers to adherence in all patients, not just patients starting up on new medication.

Motivation-, intention-and ability to remember- to take medicines as prescribed were assumed to be important regarding non-adherence. The tests indicate this assumption to be correct, as they correlated with most of the barriers presented in the questionnaire. Doctors should look for these factors in all patients when screening for non-adherence. Healthcare professionals should find out what the patient expects from the treatment, and ask them what they think is important for them as this could be beneficial to motivate the patient.

5. Conclusion

5.1 Identified frequent barriers

This research has found that the patients intend to take their medicines as prescribed, and taking them is highly prioritised. Patients understand why they need their medicines, expect them to work, and know how to take them. From the observations provided, it seems like healthcare professionals influence the barriers to adherence in different ways. It is important to screen for motivation-, intention- and ability to remember- to take medicines as prescribed when addressing non-adherence in patients. Generally, screening for adherence seems to be important regardless of the disease length, as it seems to be unrelated to the barriers tested.

The general areas for improvement are providing sufficient information and providing enough time to talk to healthcare professionals, as patients reported this to be insufficient. Few patients have been requested follow-up consultations from their doctor. Patients did not seem to have enough information to decide whether to take their medicines. Supported by the comments from the patients, worry about side-effects and not knowing where to get help taking their medicines seemed to be a problem. Some patients think that taking their medicines is a burden.

5.2 Interventions to improve medicine non-adherence

Having a time limit at community pharmacies seems to be a problem. Therefore, focussing on important information is necessary. When there is a lack of time, pharmacists should focus on prioritising informing about the risks of omitting their medicines and what to do if problems arise as this information seems to be needed. Providing balanced and specific information about side-effects could also be beneficial as this information seems to be wanted. Healthcare professionals could reduce the concerns about side-effects by identifying and addressing them. Comparing the different medicines on the market and explaining the benefit of the chosen treatment could increase the patient's trust in their doctor. Easing- or structuring- the medicine regimen could contribute to reduce the burden taking medicines, and if other problems appear (e.g. taking medicines on vacation), it is important to address them, plan further medicine use to cope with them or address them in follow-up consultations. As different kinds of healthcare professionals perform different tasks, it is important to direct the patient to the right healthcare professional to improve non-adherence in the most effective

way. When necessary, healthcare professionals should address non-adherence in all patients, not just newly diagnosed patients. Asking them what they expect from the treatment and what they find important could be ideal to improve their motivation to take their medicines as prescribed.

5.3 Further research

More studies should be done identifying barriers to medicine non-adherence in PD patients, as there are few studies covering this topic. Providing in-depth studies regarding individual barriers discussed in this study would be ideal for discussing correlations with other barriers leading to non-adherence. More work is required to identify the most appropriate behaviour change techniques to address the barriers and test them.

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Appendix A: Translated questionnaire

Medisinbruk hos personer med Parkinsons eller Parkinsonisme

Hei!

Jeg er en mastergradsstudent i farmasi ved Universitetet i Bergen.

I forbindelse med masterprosjektet mitt vil jeg finne ut hvilke ting som hjelper personer med parkinson eller parkinsonisme å ta medisinene sine og hvilke ting som gjør det vanskeligere. Disse anonyme resultatene vil jeg dele med ansatte på Haukeland sykehus, slik at de kan hjelpe på best mulig måte med medisinene sine mens de er på sykehuset.

Svarene fra deltakere er nyttig for å hjelpe oss å forstå hvordan vi kan hjelpe deg til å ta medisinene dine hjemme. Informasjonen jeg får vite vil bli presentert i eventuelle publikasjoner som blir utgitt.

Dette studiet vil ikke direkte påvirke deg, men det kan hjelpe andre personer med disse sykdommene i fremtiden.

Bare spørreskjemaet sendes tilbake i vedlagte svarkonvolutt. Svarfrist: 20. desember 2017

- På hvert spørsmål skal du krysse av (x) i boksen som på best måte reflekterer hvor stor grad du er enig/uenig i påstandene. Det skal bare krysses av i én boks for hvert spørsmål. Noen av påstandene kan virke like, men det er viktig å svare på hver enkelt påstand.
- Spørreskjemaet vil hjelpe oss å forstå mer om eventuelle utfordringer du kan ha når du tar medisinene dine.
- Det er ingen riktige eller gale svar. Vi er interesserte i ditt ærlige syn på egen medisinbruk.
- Svarene du gir er helt anonyme og kan ikke spores tilbake til deg.
- Spørreskjemaet består av 43 spørsmål, og det tar ca. 10-15 minutter å fylle ut.

Denne studien er godkjent av REK (Regionale komiteer for medisinsk og helsefaglig forskningsetikk). 01.09.17- Etterlevelse av personer med Parkinson sykdom.

Tusen takk for hjelpen!

Med vennlig hilsen

Kine Sola Flagstad, student, Universitetet i Bergen (UiB)

Medisinbruk hos personer med Parkinsons sykdom eller parkinsonisme

Instruksjoner

- På hvert spørsmål skal du krysse av (x) i boksen som på best måte reflekterer hvor stor grad du er enig/uenig i påstandene.
- Det skal bare krysses av i én boks for hvert spørsmål.
- Noen av påstandene kan virke like, men det er viktig å svare på hver enkelt påstand.
- Bruk vedlagte svarkonvolutt ved retur.
- Spørsmål kan sendes til e-postadressene oppgitt i kontaktinformasjonen under.

Informasjon og oppfølging fra helsepersonell

	Utsagn	Helt enig	Enig	Verken enig eller uenig	Uenig	Helt uenig
1	Jeg har et godt forhold til legen(e) jeg har fått medisin fra					
2	Jeg føler jeg har god nok tid til å snakke med legen om medisinene mine					
3	Jeg føler jeg har god nok tid til å snakke med farmasøyten på apoteket om medisinene mine					
4	Jeg har blitt enig med legen om en plan om medisinbruken fremover					
5	Jeg forstår hvorfor jeg trenger medisinene mine					
6	Jeg forventer at medisinene mine vil hjelpe meg mot sykdommen min					
7	Jeg vet hvilken risiko jeg kan forvente dersom jeg ikke tar medisinene mine					
8	Jeg har blitt oppfordret til å komme til oppfølgingstimer for å diskutere medisinbruken min					
9	Hvis det oppstår problemer med å ta medisinene mine (f.eks. glemmer å ta dem eller får problemer med å svelge dem), vet jeg hvor jeg kan få hjelp.					

Du og medisinene dine

	Utsagn	Helt enig	Enig	Verken enig eller uenig	Uenig	Helt uenig
10	Jeg vet hvordan jeg skal ta medisinene mine som avtalt med lege					
11	Jeg er i fysisk stand til å ta medisinene mine					
12	Jeg husker å ta medisinene mine slik det står skrevet på bruksanvisningen på pakken					
13	Jeg stoler på at legemiddelbehandlingen er godt tilpasset meg					
14	Det er enkelt å hente medisinene mine fra apoteket					
15	Jeg blir frustrert, flau, lei, sint av å ta medisinene mine					
16	Jeg er motivert til å ta medisinene mine					
17	Jeg har råd til å betale for medisinene mine, og det går ikke utover andre ting som er viktig for meg					

	Utsagn	Helt enig	Enig	Verken enig eller uenig	Uenig	Helt uenig
18	Jeg synes det generelt går greit å fornye resepter, hente og ta medisinene mine					
19	Jeg bekymrer meg for uønskede virkninger (f.eks. bivirkninger, skadelige virkninger) av å ta medisinene mine					
20	Jeg kan tilstrekkelig mye om medisinene mine til å bestemme om jeg skal ta dem eller ikke					
21	Jeg bruker alarm, dosett, andre hjelpemidler eller får hjelp til å bestille, hente og ta medisinene mine					
22	Jeg glemmer ofte å ta medisinene mine					
23	Hvis jeg trenger hjelp for å ta medisinene mine på rett måte, vet jeg hvor jeg får det					
24	Mine daglige rutiner vil påvirke hvordan jeg tar medisinene mine					
25	Å ta medisinene mine er en uønsket påminnelse om sykdommen min					
26	Å ta medisinene mine er viktig for meg/er høyt prioritert					
27	Å ta medisinene mine slik det står på bruksanvisningen på medisinpakken passer ikke inn i hverdagen min					
28	Hvis det skulle oppstå problemer med å ta medisinene mine kan jeg finne en måte å løse det på					
29	Hvis jeg ikke tar medisinene mine som avtalt med legen, tror jeg helsetilstanden min vil bli verre					
30	Jeg har den informasjonen jeg trenger for enkelt å fornye resepter og hente medisinene mine					
31	Det er ikke et problem for meg å se forskjell på de ulike medisinene mine					
32	Jeg husker å bestille og hente medisinene mine tidsnok slik at jeg har de legemidlene jeg trenger					
33	Jeg bekymrer meg over hva andre måtte tenke hvis de visste at jeg tar medisiner					
34	Apoteket jeg bruker sørger for en god og rask ekspedering av medisinene mine					
35	Jeg synes det er en byrde å ta medisinene mine					
36	Jeg prøver alltid å ta medisinene mine som avtalt med legen					
37	Hverdagen min gjør det vanskelig å ta medisinene mine som avtalt med legen					
38	Jeg tror ikke jeg kunne greid å ta medisinene mine riktig dersom behandlingen min skulle endre seg					
39	Jeg har mine grunner for at jeg ikke tar medisinene mine som avtalt med legen					

Personlig informasjon

40) Kjønn Mann ❑ Kvinne ❑

41) Hvor lenge har du hatt sykdommen? _____ år

42) Hvor mange forskjellige typer medisiner bruker du? _____

43) Har du noen kommentarer utover svarene på spørsmålene på spørreskjema?

- Er det noe mer vi burde spurt om?
- Er det noen andre ting vi kunne ha gjort bedre på sykehuset eller apotek for å hjelpe deg å ta medisinene dine?
- Har du noen spesielle ting du vil si om medisinene dine eller spørreskjemaet?
- Var det noen spørsmål som ikke var relevante for deg?

Takk for hjelpen!

Appendix B: Patient comments translated from Norwegian

1. Information
2. Thoughts about medicines
3. Experiences and impression
4. Everyday life and medicines

1. Information

1.1 Information about side-effects

Patient 20

I wish I got more information about side-effects.

Patient 42

I have experienced a lot of side-effects from my medicines. Because of this, I've had to change my medicines. This is on my own initiative. I would like if the Pharmacy would inform me that if I experience unwanted side-effects, I should contact my doctor to change the dose or medicine.

Patient 93

It's important with information about side-effects (not just in a bisection).

Patient 191

I don't know what the combination of the side- effects can lead to.

1.2 Information about disease and medicines

Patient 28

I have done deep brain surgery (DBS) about 4 years ago. I would like information about how many medications I'd have to take, even though I was operated.

Patient 42

I think it's important that the pharmacy staff tell me what medicines I should take without food etc.

Patient 52

You must simply apply to the Parkinson's association to be updated (possibly new things).

Patient 55

They should hand out a floppy disk/ CD that could be downloaded on a computer that reminds/ alert which medicines I had taken for the day. I have 6 different Parkinson-, heart medicine/blood thinners. Sometimes I wonder what I have taken and what I have forgot (I assume a lot of patients feel the same).

Viagra in combination with Parkinsons/blood thinners.

Group seminars, light up/explains myths about the disease. NRK (Norwegian broadcasting corporation)/ media always tell us about "major improvements". If they invited 50-100 people multiple times a year, could help giving answers that we wouldn't get in half an hour in everyday life. As I have understood, there's a lot of competent specialists, send invitation!

Patient 100

I know the medications I use, but have no idea what is on the market or how they work / interact with other types. I would like to get information about what exists on the market and what medicines I can take together.

Patient 113

I think it there is one-sided information about my medicine in my treatment.

Patient 123

I haven't been given information, and guidance about the disease. Read about it myself.

Any good vision ahead? New medicines with less side-effects? Could one have extra medicine besides the ones dosed when needed.

Conversation with pharmacist?

Patient 134

The patient information leaflets are very similar. They could be shortened.

Patient 184

I miss that the doctor gives very little information about the disease, and information about things I can do myself. That it's important to exercise regularly, and that I have the right for physiotherapy. After a while I have been getting information (for instance the Parkinson association) has done a lot of work with this.

Patient 187

I don't know anything about medication, but I have to believe that the doctor does what's best for me.

Patient 213

Information and follow-up. Consequences and side effects of the medicine. Increased brain activity.

2. Thoughts about medicines

2.1 Attitudes for medicines

Patient 51

The medications I take seem to work well.

Patient 53

I have to take medicines for 3 different chronic diseases: glaucoma, angina and parkinson. I think that's a lot. I have always been restrictive trying out new medicines. I think a lot about side-effects.

Patient 62

Don't be afraid to take medicines. That's just something we need to do well.

Patient 76

I have an imbalance in my body, but there is nothing that helps.

Patient 81

My medicine use is going well.

Patient 117

I don't know how much my medicine is helping me, i.e. how my progression of my disease had been without my medicines.

Patient 225

I have no experience with pharmacists. I am fully aware that I need medicines and that it is important to take them. And what the consequences are if I don't take them. BUT, there are also side effects to take into account. And with bad follow-up and often diffuse information when one asks questions.

2.2 Thoughts about side-effects

Patient 17

I think a lot of people doesn't like the medicines, gas and pain, leading to little uptake. That varies in the day.

Patient 20

I'm tired, and fall asleep easily when we are out. Not fun.

Patient 45

I don't think I have Parkinson's disease. After the GP lowered the use of Sinemet, I have gotten a better sense of taste, men most things (except sweet things) still taste like "crispbread".

Patient 56

I use medicines with a lot and dangerous side-effects.

Patient 73

I can suddenly get very sleepy after intake of dopamine, something that, amongst other things, leads to that I can't drive a car anymore.

Patient 110

Side-effects of the medicines. A lot of bowel and stool problems.

Patient 155

I have stopped taking addition medicine (Elderyl) which gave me major side-effects like suicidal dreams. I stopped the medicine in consultation with my doctor. I am much better now.

Patient 163

My medicines give me bothering side-effects like dry mouth.

Patient 172

Side-effects creates uncertainty.

Patient 206

I am dizzy quite often. I think that's because of the pills, but I don't know if it comes from Sinemet, Neurontin or Panodil (or corresponding medicine).

Patient 213

Have experienced abstinence after reducing the dose of Sifrex. Medications affect sleep-pain-sex- impulse control.

Patient 214

1 medicine for hallucinations.

3. Experiences and impression

3.1 Thoughts and relationships with prescriber

Patient 34

I have been treated well by doctors and other health personnel in Haukeland hospital.

Patient 35

Unlucky with prescribing doctor/neurologist every visit.

Patient 50

I want to try out asthma medicine that is discussed in media, but both my GP and specialist tell me that there aren't enough trials yet. I can't be a "trial subject", even though I want to. My parkinson is by now tremor in my left hand, but often bothers me.

Patient 104

Do you get help/support every day?

Patient 224

It is a known matter that it is a big problem to get medications that work as desired.

3.2 Permanent healthcare professionals

Patient 12

The home nurse care should have regular people seeing them, so that they don't have to start all over again every time. Regular staff gives safety to patients. They need to see that treating Parkinson with medicines is important for other kind of healings also.

Patient 73

At the half-yearly check at Haukeland, I never get the same neurologist. This makes the check difficult. If something happens to the medicines in the meantime (e.g. I was given too much medicine, became very ill 1 year ago) it is difficult for my doctor to contact a neurologist who knows me. There has also been given incorrect information about my medication back to the GP after visiting the polyclinic.

Patient 77

A new doctor every control 1 consultation pr. Year. That makes it difficult.

Patient 86

It’s a dilemma that there are different doctors at neurology ward every time I’m there. I miss a permanent doctor.

Patient 184

What frustrates me is that I don’t have any permanent doctor. I have only met each doctor 2 times, then there’s a new doctor. Someone I’ve just met 1 time.

Patient 195

Now I have a permanent neurologist. At Haukeland there were constantly new ones (6-7 different) that had different “medicine politics”.

Patient 225

At Haukeland Hospital there are still new doctors to relate to, as far as I get consultation there.

3.3 Duration of consultation

Patient 19

It seems like the neurologists at the hospital are busy.

Patient 52

We, who live on the countryside, think it’s difficult to travel the whole day to have a 15 minute consultation. There’s no guarantee that the doctor contact after an mhi reference.

Patient 100

I have too little time at the doctor/ neurologist.

Patient 195

At St. Olav I get plenty of time at the consultation; in Haukeland I often get too short time. At Haukeland the doctors didn’t know my situation/ variant well enough.

Patient 225

It is frustrating to find that when one has met at the agreed consultation, they do not have time for me (…) I feel that there is a lot I should have asked for, but that there is never time for it. Nor do I feel that I'm being taken seriously. It's all about following up the patient and making it easier for you to encounter problems

3.4 Availability

Patient 39

Censurable that I haven't heard from St. Olavs hospital in a whole year.

Patient 52

I heard nothing after my visit in the neurological ward, Haukeland.

Patient 77

I got an additional medicine 2 years ago. I couldn't use that because of stomach issues. But I never get to give feedback.

Patient 79

I am a very new patient, so I haven't thought about my questions yet, but I have good contact with my GP.

Patient 133

The neurologic ward was going to make me another consultation after half a year. Now it's almost been a year since last time, but I still haven't gotten a consultation.

Patient 163

If I feel that I need to talk to the doctor (neurologist) it takes a bit long before I will get a consultation.

Patient 211

I wish for better contact with the neurological ward at the hospital.

3.5 Follow-up

Patient 40

I am trying out new medicine. The doctor is going to follow up when the medicines have stabilised.

Patient 46

The doctor took responsibility for my medicine plan/ doses.

Patient 63

There’s a problem that the hospital/ neurologist doesn’t have good enough routines for follow-up/ monitoring considering side-effects. Today’s lack of follow-up puts all risk on the patient.

Patient 123

Good follow-up by neurologist? – no

Good follow-up by GP- yes

Patient 195

I have been doing surgery (deep brain stimulation) at St. Olavs Hospital, and get followed up there 1 session pr. Year, including medicine use. This follow-up is substantially better than in Haukeland.

Patient 225

Usually have consultation half-yearly. When it's not a follow-up session, I think it's too bad. Have experienced being "forgotten" - when the time for new consultation was there and I heard nothing from there. Had to call and ask for a new consultation.

I have never been offered any follow-up hours either by a GP or a neurologist. This has to be done and I hope there are not many who have experienced this. When I have been with a neurologist, I get a new notice for a new consultation about half a year later. I do not call this follow-up especially if there was done was a change of medication. I should then expect the doctor / neurologist to contact to hear how the change worked. But no, I'll have to wait for the semi-annual consultation.

4. Everyday life and medicines

4.1 Handling medicines

Patient 62

If I forget to take a necessary medicine (in the morning), I can feel discomfort after. Then it's smart to have an extra medicine (pill) "in my pocket".

Patient 73

It can be hard to take Parkinson medication to meals, especially when I'm visiting my family that has different meal routines than we have at home.

Patient 93

"Intravenous" medicine would help me take the medicine at the right time.

Patient 153

The tablets are in strips with daily doses (5 daily) so it's simple.

Patient 186

The nursing home has the responsibility for my medicines. Sometimes errors still occurs.

Patient 206

The nursing home has taken a lot of the responsibility. They arrive with medicine bags, already dosed, and they come at inspections to check if I take the pills as agreed.

Patient 228

The Duodopa pump I have used since 2012 is far too big, heavy and inconvenient. Here must be a huge development potential! A book could be written about everything I've experienced and had to find a solution to the handling of the pump and its belongings!

4.2 Medicine access

Patient 195

Last summer I forgot my medicines, going to a cabin. I got Sinemet from the pharmacy in Geilo, but I didn't have any Oprymea left on my prescription. The pharmacist said that a break for 3-4 days was OK. It was not. I got, among other things, fever and depression: very uncomfortable.

Patient 214

Medicines are administrated by home nursing 6 times a day. Changes are hard to communicate into this service.

4.3 Physical ability to take medicines

Patient 42

I take Medopar that is in a glass with cotton on top in a new container. The glass is hard to open, and it’s hard to remove the cotton. It should have been a blister package.

Patient 85

The new boards on "Sinemet" are difficult, easier tablet on glass. The tablets on the board are difficult to remove the entire tablet from the tray, they divide and crumble.

Patient 168

Swallowing reflex, I have gotten small single-use juice bags that can be used to help people who have swallowing problems. Get access to help that will have an effect.

4.4 Economy

Patient 59

I use Duodopa. I get this covered 100%. If I had to pay it myself, I’d have to stop taking it.

Patient 71

Without a refund from the state, Duodopa medicine would be out of question.

Patient 100

I think the doctor/ neurologist has his/her commissions on some pills and prescribes these.

Patient 109

I think that customers/patients that use a lot of medicines every day should be given doset on blue prescription.

Patient 150

The packed daily doses should be available free.

4.5 Other

Patient 90

What about asthma medicine? When will that come?

Patient 206

The new system (multidose) is effective, but NO for plastic bags!