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**WHY PATIENTS DO NOT TAKE MEDICATION  
AS PRESCRIBED: THE COMPLEXITY OF  
MEDICATION ADHERENCE AS A  
PHENOMENON**

**Kirsi Kvarnström**

DOCTORAL DISSERTATION

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*Ei ole olemassa muureja  
on vain siltoja  
ei ole olemassa suljettuja ovia  
on vain portteja  
joiden läpi kuljetaan  
sähkövin silmin.*

*Tommy Tabermann*

# ABSTRACT

Poor medication adherence is a significant barrier to achieving the expected outcomes of a treatment. The prevalence of chronic diseases is increasing globally, and within ageing populations, both morbidity and use of medicines increase. Only about 50% of patients are estimated to treat their chronic diseases according to instructions in developed countries. Patients with multiple conditions and multiple medications are particularly challenging to healthcare professionals. A common feature of poor adherence is a tendency to stop taking the medication within a few months after the provider has prescribed it. In addition, the patients may not take the medicine as regularly as prescribed and skip doses or take lower or higher doses than prescribed.

This study aimed to enhance understanding of the complexity of medication adherence as a phenomenon by studying why patients do not take their medication as prescribed. The goal was to collect information on the factors influencing medication adherence by summarizing research evidence obtained using qualitative methods (Study I) and investigating primary care physicians' and patients' perspectives (Studies II and III).

Study I was a scoping review of qualitative studies (n=89). The literature search for eligible qualitative studies was conducted on September 23, 2019, and updated on June 9, 2021, using MEDLINE (Ovid), Scopus, and the Cochrane Library. The focus was on patients' experiences and attitudes towards medication adherence. The use of qualitative methods both for data collection and data analysis was mandatory. We used the PRISMA-ScR checklist to ensure the quality of the scoping review.

Study II applied the focus group discussions (n=4) for primary care physicians (GPs, n=16). The study was conducted in the Kirkkonummi Health Centre, Southern Finland. The qualitative design was chosen to understand GPs' perceptions of medication adherence and the problems GPs thought patients might have experienced following instructions for their medicine taking. An interview guide of semi-structured questions was used to allow the GPs to discuss the topic from a personal point of view.

Study III presents a study protocol of a new patient-oriented method to investigate reasons for non-adherence using pharmacist-conducted medication reconciliation in the primary care clinics as a data collection point. The study is based on pharmacist-patient communication during medication reconciliation. It will be carried out in the public primary care clinics in Vantaa, located in the capital region of Finland. By interviewing, the pharmacist will learn how the patient has been taking the prescribed medicines and whether any non-prescription medicines and food supplements have been used for self-medication. Patients aged 55 years or older will be included, as they most commonly have multiple medications and illnesses.

Medication reconciliation will occur upon admission to the public outpatient clinic, usually before a physician's appointment.

The search (Study I) revealed 4404 studies, of which 89 qualitative studies were included in the scoping review. The studies more often dealt with barriers than facilitators. The factors were classified as patient-specific, illness-specific, medication-related, healthcare and system-related, sociocultural, logistical, and financial. Information and knowledge of diseases and their treatment, communication, trust in patient-provider relationships, support, and adequate resources appeared to be the critical facilitators in medication adherence from the patient perspective. Patients were willing to discuss their concerns about medications. Better communication and better information on medicines appeared to be critical factors for patients.

The two main themes that emerged in the focus group discussions with the GPs (Study II) were non-adherence in chronic disease care and increased need for information about medicines. The GPs (n=16) were increasingly confronted with non-adherence in the care of chronic diseases. The medication management challenges identified were related to patient-specific factors, the healthcare system, characteristics of drug therapies and the function and role of healthcare professionals as a team. The GPs offered several solutions such as improved coordination of care, better patient education and IT systems, and enhanced interprofessional involvement in the follow-up of patients. To support medication adherence and self-management, the GPs appreciated pharmacists' assistance, especially with patients with polypharmacy and chronic diseases.

Study III will provide quantitative data for descriptive analysis to identify: 1) the number of discrepancies between the physician's prescription orders and the patient's self-reported use of the medicines, 2) what kind of discrepancies there are, 3) which are high-risk medicines in terms of non-adherence, and 4) why medicines were taken differently than prescribed. Based on the results, 5) a preliminary conceptual model of patient-reported reasons for non-adherence will be constructed.

There is a wide range of barriers and facilitators to medication adherence, but barriers seem to be better known than facilitators. Better communication and information appear to be the most crucial factors in enhancing medication adherence. Patients wish to discuss their worries about medications. Medication reconciliation could be used more effectively to monitor medication adherence and prevent the inappropriate use of medicines in routine clinical practice.

Based on the findings of this doctoral thesis, it is possible to continue developing a theoretical model related to adherence. The model could consider previous theories related to medication adherence, patient perspective and the research evidence constructed by qualitative methods. Developing new interventions should be based on an enhanced understanding of the patient's perspectives on medication adherence.

# TIIVISTELMÄ

Huono lääkehoitoihin sitoutuminen on maailmanlaajuinen ongelma. Väestön ikääntyessä sairastavuus ja lääkkeiden käyttö lisääntyvät. On arvioitu, että vain noin 50 % potilaista hoitaa pitkäaikaista sairauttaan ohjeiden mukaisesti. Erityisen haastavassa asemassa ovat potilaat, joilla on useita sairauksia ja useita lääkehoitoja.

Tämän tutkimuksen tavoitteena oli lisätä ymmärrystä lääkehoitoihin sitoutumisesta ilmiönä järjestelmällisen kartoittavan katsauksen avulla (osatyö I) sekä tutkimalla lääkkeiden ohjeidenmukaista käyttöä perusterveydenhuollon lääkäreiden ja potilaiden näkökulmasta (osatyöt II ja III).

Osatyössä I kartoitettiin potilaiden lääkehoitoon sitoutumiseen vaikuttavia tekijöitä laadullisten tutkimusten perusteella (n=89). Tutkimuksista tunnistettiin potilaisiin, sairauteen, lääkkeisiin, terveydenhuoltoon ja järjestelmään liittyviä tekijöitä sekä sosiokulttuurisia ja logistisia ja taloudellisia tekijöitä. Tutkimuksista tunnistettiin enemmän hoitoon sitoutumista estäviä kuin edistäviä tekijöitä. Osa tutkimuksista (n=17) oli käyttäytymisteorioihin perustuvia. Sairauteen ja sen hoitoon liittyvät tiedot ja taidot, kommunikaatio, potilaan ja terveydenhuollon ammattilaisen välinen luottamus, tuki ja riittävät resurssit näyttäisivät olevan potilaan näkökulmasta avaintekijöitä. Tärkeiksi tekijöiksi tiivistyivät potilaan ja ammattilaisen välinen kommunikaatio sekä lääkeneuvonta.

Huono lääkehoitoihin sitoutuminen ja lääkeneuvonnan tarve nousivat pääteemoiksi terveyskeskuslääkäreiden ryhmäkeskusteluissa (n=4) (osatyö II). Lääkärit (n=16) havaitsivat hoitoon sitoutumiseen liittyviä haasteita hoitaessaan pitkäaikaissairauksia. Haasteet liittyivät potilaaseen, terveydenhuoltojärjestelmään, lääkehoitoihin, terveydenhuollon ammattilaisten yhteistyöhön ja rooliin. Lääkärit ehdottivat ratkaisuiksi parempaa hoidon koordinointia, potilaiden kouluttamista, parempia tietojärjestelmiä sekä moniammatillisuutta potilaiden lääkehoitojen seurannassa. Lääkärit toivoivat farmasian ammattilaisten osallistumista erityisesti monilääkitysten ja monisairaiden potilaiden lääkehoitoon sitoutumisen ja omahoidon tukemiseen.

Osatyö III on tutkimussuunnitelma lääkärin määräämien ja potilaan todellisuudessa käyttämien lääkkeiden välisten erojen tutkimiseksi. Kotilääkitysten selvittämisen yhteydessä käydyn keskustelun perusteella halutaan tutkia, minkälaisia eroavaisuudet ovat, mitkä ovat hoitoon sitoutumisen kannalta suuren riskin lääkkeitä ja miksi potilaat käyttävät lääkkeitä toisin kuin lääkäri on määrännyt. Tutkimuksen tarkoituksena on luoda toimintamalli, jonka avulla voidaan edistää parempaa lääkehoitoon sitoutumista kroonisten sairauksien hoidossa.

Lääkehoitoon sitoutuminen on monimutkainen ilmiö, johon liittyy monia estäviä ja edistäviä tekijöitä. Tämä väitöskirjatutkimus auttaa ymmärtämään hoitoon sitoutumisen monimutkaisuutta laadullista ja potilaslähtöistä tutkimusnäkökulmaa hyödyntäen. Potilaat haluavat keskustella lääkkeisiin liittyvistä huolistaan. Tilanteen korjaamiseksi tarvitsemme parempaa potilaan ja terveydenhuollon ammattilaisten välistä kommunikaatiota ja informaatiota.

Tämän väitöskirjatutkimuksen tulosten perusteella on mahdollista jatkaa hoitoon sitoutumiseen liittyvän teoreettisen mallin kehittämistä. Mallissa voitaisiin ottaa huomioon aikaisemmat lääkehoitoon sitoutumiseen liittyvät teorit, potilasnäkökulma ja laadullisin menetelmin koottu tutkimusnäyttö. Potilaan näkemysten ja tilanteen huomioiminen on avainasemassa, kun lääkehoitoon sitoutumiseen tähtäviä toimintamalleja kehitetään.



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# LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications, referred to in the text by their Roman numerals (I-III):

- I            **Kvarnström K**, Westerholm A, Airaksinen M, Liira H: Factors contributing to medication adherence in patients with a chronic condition: A scoping review of qualitative research. *Pharmaceutics* 2021; 13: 1100. doi: 10.3390/pharmaceutics13071100 (Open Access)
  
- II           **Kvarnström K**, Airaksinen M, Liira H: Barriers and facilitators to medication adherence: a qualitative study with general practitioners. *BMJ Open* 2018;8: e015332. doi:10.1136/bmjopen-2016-015332 (Open Access)
  
- III          **Kvarnström K**, Westerholm A, Airaksinen M, Liira H: Why medicines are used differently than prescribed: a protocol for a prospective patient-oriented observational case study to investigate reasons for non-adherence in primary care (submitted manuscript).

The publications are referred to in the text by their Roman numerals.

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# DEFINITION OF THE KEY CONCEPTS

## **Adherence**

Adherence is 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 (World Health Organization, 2003).

## **Adverse drug reaction (ADR)**

A response to a medical product that is noxious and unintended, resulting not only from the authorized use of a medical product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse, off-label use, and abuse of the medicinal product (EU Directive 2010/84EU1).

## **Collaborative medication review (CMR)**

A structured process in which a patient's medication regimen and medication use are critically examined (National Institute for Health and Care Excellence, 2015). The examination is aimed to be conducted in interprofessional collaboration between pharmacists and physicians, and other healthcare professionals involved in patient's medication use (Kiiski et al., 2019; Leikola, 2012; National Institute for Health and Care Excellence, 2015).

## **Compliance**

The patient's willingness to readily follow the healthcare professionals' instructions (Marinker & Royal Pharmaceutical Society of Great Britain, 1997; World Health Organization, 2003).

## **Concordance**

An agreement reached after negotiation between a patient and a health care professional that respects the beliefs and wishes of the patient in determining whether, when and how medicines are to be taken (Horne et al., 2005). The healthcare professional and the patient are interacting as equals and forming a therapeutic alliance (Airaksinen et al., 2012; Routasalo et al., 2009).

## **Drug-related problem (also medication-related problem)**

An undesirable patient experience that involves drug therapy and that actually or potentially interferes with a desired patient outcome (Hepler & Strand, 1990; Pharmaceutical Care Network Europe Foundation PCNE, 2017).

## **Empowerment**

A process through which people gain greater control over decisions and actions affecting their health by developing skills, having access to information and resources, and opportunities to have a voice and influence

the factors affecting their health and well-being (World Health Organization, 2013).

### **Inter-professional collaboration (IPE)**

When multiple healthcare workers from different professional backgrounds work together with patients, families, carers, and communities to deliver the highest quality of care across settings (World Health Organization, 2010).

### **Medication reconciliation**

Medication reconciliation is a process in which all of the patient's medications are confirmed to match the medications the provider has prescribed (Institute for Healthcare Improvement IHI, 2011; National Institute for Health and Care Excellence, 2015; World Health Organization, 2014).

### **Medication review**

Medication review is a structured evaluation of a patient's medication regimen with the aim of optimizing medicine use and improving health outcomes. This entails detecting drug-related problems and recommending interventions (Griese-Mammen et al., 2018; Hepler & Strand, 1990).

### **Pharmaceutical care**

A patient-centred care and the responsible provision of drug therapy for the purpose of achieving definite outcomes to improve patients' quality of life in collaboration with other healthcare professionals (American Society of Hospital Pharmacists, 1993; Council of Europe, 2020; Hepler & Strand, 1990).

### **Primary care (PC)**

Primary care is a key process in the health system (World Health Organization, 2022). It is the first level of contact for the population with the health care system, bringing health care as close as possible to where people live and work (Organisation for Economic Co-operation and Development OECD), 2022). It addresses the main health problems in the community, providing preventive, curative, and rehabilitative services. Primary care goes beyond services provided by primary care physicians to encompass other health professionals such as nurses, pharmacists, auxiliaries, and community health workers.

### **Primary health care (PHC)**

Primary health care is a whole-of-society approach to health that aims at ensuring the highest possible level of health and well-being and their equitable distribution by focusing on people's needs as early as possible along the continuum from health promotion and disease prevention to treatment, rehabilitation and palliative care, and as close as feasible to people's everyday environment (World Health Organization & Unicef, 2018).

### **Rational use of medicines/Rational pharmacotherapy**

Patients use medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and

at the lowest cost to them and their community (WHO, 1985). Rational pharmacotherapy is effective, safe, high quality, economical and equal (Ministry of Social Affairs and Health, 2018).

**Shared decision making (SDM)**

An approach in which clinicians and patients share the best available evidence when faced with the task of making decisions, and patients are supported to consider options, to achieve informed preferences (Elwyn et al., 2010).

# ABBREVIATIONS

ADR	Adverse drug reaction
ATC	Anatomical Therapeutic Chemical categorization (WHO)
CMR	Collaborative medication review (Finland)
DRP	Drug-related problem
GP	General practitioner
HBM	The Health Belief Model
HUSeCRF	HUS electronic case report form
IMB	Information-Motivation-Behavioural Skills Model
KELA	Social Insurance Institution of Finland
MI	Medicines information
MRB	Medication-related burden
NCCSCH	The National Co-ordinating Centre for NHS Service Delivery and Organisation R&D (United Kingdom)
NHS	National Health Service (United Kingdom)
NICE	National Institute for Health and Care Excellence (United Kingdom)
OTC	Over-the-counter
PC	Primary care
PHC	Primary health care
PCNE	Pharmaceutical Care Network Europe
PLEM	Patients' Lived Experience with Medicines
RCT	Randomized controlled trial
RPAP	The Pharmacotherapy Action Plan (Finland)
SCT	Social Cognitive Theory
SDM	Shared decision making
TPB	Theory of Planned Behaviour
TRA	Theory of Reasoned Action
TTM	Transtheoretical Model
UK	United Kingdom
USA	United States of America
USP	United States Pharmacopeia
WHO	World Health Organization
e.g.	exempli gratia



# 1 INTRODUCTION

Despite decades of intensive research, poor adherence to medication remains an unexplained phenomenon. One milestone in understanding the phenomenon has been the finding that health care has to move from compliance to concordance in thinking (Bell et al., 2007; Horne et al., 2005; Marinker & Royal Pharmaceutical Society of Great Britain, 1997; National Institute for Health and Care Excellence, 2009; Routasalo et al., 2009). Although this finding dates to the 1990s, the situation has not essentially changed, and effective interventions to improve medication adherence are still intensively sought (National Institute for Health and Care Excellence, 2009; Nieuwlaat et al., 2014). Why so many patients do not use their medications as prescribed is still an unanswered question.

Low medication adherence is a significant barrier to the expected outcomes of the treatment (National Institute for Health and Care Excellence, 2009; World Health Organization, 2003). The prevalence of chronic diseases is increasing globally, and within ageing populations, both morbidity and use of medicines increase. Only about 50% of patients are estimated to treat their chronic diseases according to the instructions in developed countries (National Institute for Health and Care Excellence, 2009; World Health Organization, 2003). Patients with multiple diseases and multiple medications are particularly challenging to health care. Common features related to poor adherence include a tendency to stop taking the medication within a few months after the provider has prescribed it (Nieuwlaat et al., 2014). In addition, the patients may not take their medication as regularly as prescribed and skip doses, or they may take lower or higher doses than prescribed.

These examples of medication-taking behaviour indicate that medication adherence means whether a patient chooses to follow the instructions they are given concerning the use of medications (World Health Organization, 2003). However, patients may have valid reasons for their non-adherent behaviour. Unfortunately, these reasons are not very well understood. There may be a lack of communication and partnership, as patients do not always talk to health professionals about their concerns or experiences, which leads to adjusting medications (National Institute for Care and Health Excellence NICE, 2021). The health professionals may lack an understanding about the patient's journey with the chronic disease and its management, including medicine taking and the common phenomenon of self-regulating their medication regimens (Kekäle, 2016; Pagès-Puigdemont et al., 2016). Adverse effects, lack of expected therapeutic effects, or other drug-related problems may be the reasons for adjusting or not taking the medicine. Poor adherence can cause readmission to the hospital when expected treatment outcomes are not realized (Ravn-Nielsen et al., 2018).

According to the Cochrane review by Nieuwlaat et al. 2014 (Nieuwlaat et al., 2014), although there are numerous controlled trials on interventions to improve adherence, current methods of improving medication adherence for chronic health problems are mostly complex and not remarkably effective. Also, the effects are inconsistent from study to study. Simple interventions, such as written instructions to the patient or a brief discussion with a health care professional, may improve medication adherence in the short term (Haynes et al., 2008). Longer-term improvements have only been achieved through very complex interventions involving training of patients, treatment monitoring and follow-up visits (Nieuwlaat et al., 2014). Such interventions are challenging and expensive to implement in routine clinical practice.

There have been attempts to use technologies to strengthen medication adherence, e.g., sending text messages to remind the patient to take the medication in time (Amankwaa et al., 2018; Lester et al., 2010; Simoni et al., 2009). The interventions have not been remarkably effective. The Cochrane review concluded that the interventions may not be effective since we do not understand in sufficient detail what the adherence problems are (Nieuwlaat et al., 2014).

One reason may be the quantitative research approach, in which the patients' experiences of the medication treatment in everyday life have been lacking. Structured questionnaires are commonly used to measure medication adherence as they are an easy way to collect data from patients (Herrera et al., 2017). However, the ability of questionnaires to measure the underlying factors contributing to medication adherence is limited (Herrera et al., 2017). Indicators and methods are required to go deeper into the everyday life experiences of the patients than is possible with a series of questions.

Qualitative methods bring an approach to explore adherence as a phenomenon and complete the picture of the effect of the medication on the patient's daily life burden. This doctoral thesis seeks new insights to understand medication adherence as a complex phenomenon by using qualitative research evidence and examining the evolution of theories on medication taking behaviours and adherence.

## **2 REVIEW OF THE LITERATURE**

### **2.1 DEFINITIONS OF MEDICINE TAKING BEHAVIOUR**

Medication adherence can be seen as a reflection of patients' medication-taking behaviour. There have been many different terms to explain medication-taking behaviour, and the terms have changed over time.

A remarkable breakthrough in the definition of terms and conceptualizing medication-taking behaviour has been the evolution of concepts from compliance to concordance (Airaksinen et al., 2012; Bell et al., 2007; Horne et al., 2005; Marinker & Royal Pharmaceutical Society of Great Britain, 1997; National Institute for Health and Care Excellence, 2009; Routasalo et al., 2009). Concordance means a patient's and provider's equal relationship and shared decision-making to promote optimal self-management (Bell et al., 2007; Dickinson et al., 1999; National Institute for Health and Care Excellence, 2009; Royal Pharmaceutical Society & Merck Sharp and Dome Ltd, 1997). This evolution started in the UK with extensive research that aimed at identifying the root causes of poor compliance (Marinker & Royal Pharmaceutical Society of Great Britain, 1997). The research came up with the finding that we need to forget compliance and shift towards concordance (Dickinson et al., 1999; Marinker & Royal Pharmaceutical Society of Great Britain, 1997). This finding pointed to the need to evolve thinking of the content of the concept of compliance and shift towards a new concept that reflects better an increased understanding of medication-taking behaviours from a patient perspective (Horne et al., 2005; Marinker & Royal Pharmaceutical Society of Great Britain, 1997; National Institute for Health and Care Excellence, 2009; Routasalo et al., 2009).

Compliance describes the patient's willingness to readily follow the healthcare professionals' instructions (Bissell et al., 2004; Cushing & Metcalfe, 2007; Dickinson et al., 1999; Marinker & Royal Pharmaceutical Society of Great Britain, 1997; McGivney et al., 2007; World Health Organization, 2003). The idea of compliance is that every prescribed medication is suitable for the patient, and the patient must agree and change the behaviour to follow the medication regimen. According to Horne et al., compliance is "the extent to which the patient's behaviour matches the prescriber's recommendations" (Horne et al., 2005). Compliance may be seen as a negative and paternalistic term where the patient is a passive recipient whose responsibility is to follow the prescriber's order.

Another landmark in understanding medication taking behaviours is the report "Adherence to long-term therapies – evidence for action" by World Health Organization (WHO) (World Health Organization, 2003). The WHO report summarized research evidence published by 2003 to describe key concepts in medicine-taking behaviours. The WHO's definition of medication



adherence has become a widely recognized key definition to this phenomenon (World Health Organization, 2003). The WHO's report has been a pathfinder in understanding medication adherence as a concept to be considered in clinical practice, policymaking, and research, even in research and development of new medical innovations, e.g., pharmaceuticals.

The WHO report describes adherence to long-term therapies as a phenomenon from a theoretical perspective and a clinical practice perspective in selected common diseases, such as diabetes, asthma and hypertension (World Health Organization, 2003). According to the WHO's report, only 28% of patients with diabetes reach reasonable glycaemic control, and despite diabetes, they often have co-morbidities (World Health Organization, 2003). Hypertension increases the risk of a cardiovascular event and causes approximately 40% of acute myocardial infarctions or strokes. Nevertheless, only about 25% of patients reach optimal blood pressure. Likewise, adherence to asthma medication seems to be poor, and in general, non-adherence of asthma patients found to vary between 30% to 70% (World Health Organization, 2003).

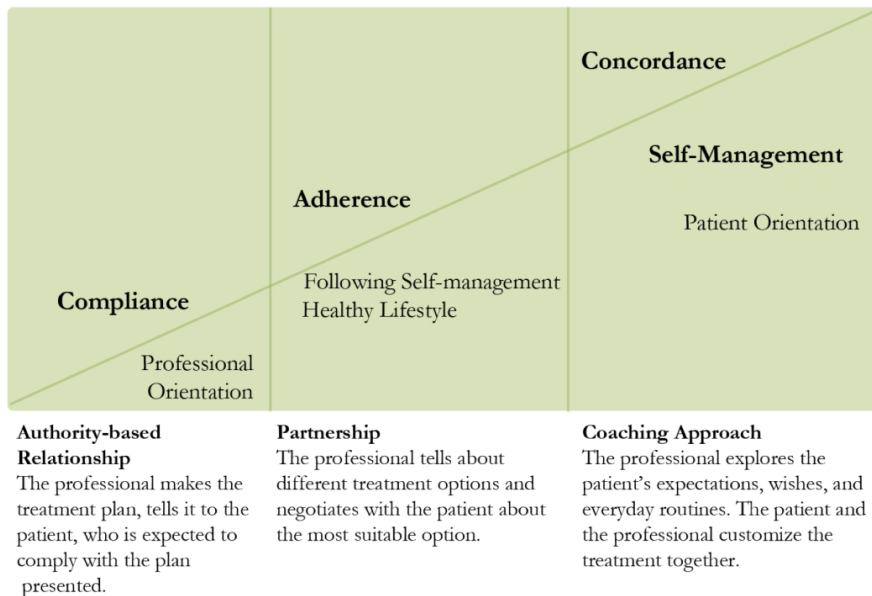
In addition to the WHO's report, some other essential documents have influenced the definition of the concept of medicine taking behaviour. Many of these widely recognized reports have been published in the UK to support the implementation of concordance and partnership thinking in the National Health Services system (NHS). The report by the National Co-ordinating Centre for NHS Service Delivery and Organisation R&D (NCCSDO) in the UK highlighted that one of the key reasons for medication non-adherence is failure to address patients' needs and preferences in healthcare (Horne et al., 2005). The medication-taking behaviour is related to other similar challenges in healthcare, e.g., smoking cessation or lifestyle changes, where there is a need to influence patients' behaviour.

Some years later in 2009, the National Institute for Health and Care Excellence (NICE) in the UK published clinical guidelines for medicines adherence (National Institute for Health and Care Excellence, 2009). The guideline underlines patients' involvement in decisions about their prescribed medicines and that the patient's decision should be an informed choice. The guidelines are intended for healthcare professionals, adult patients, and significant others. The guideline is kept updated, last checked in March 2019, with no new evidence found that affects the recommendations.

In 2013 WHO launched an European policy framework strategy Health 2020 for the 21st-century (World Health Organization, 2013). The strategy highlighted patient empowerment and patient-centred care to improve health outcomes and adherence to treatment regimens. According to the strategy, patients and their families should be part of the healthcare team when making clinical decisions, although not everyone is capable or willing to take control over treatment. Nevertheless, the strategy also considers that healthcare professionals need to be motivated and convinced to allow the patients to take a leading role in their treatment and move toward a coaching approach. The

change requires a new way of communicating with the patients about the treatment choices and considering their experiences and life situations in the planning, implementation, and monitoring of care.

Despite the existing guidelines and recommendations, medication adherence as a phenomenon has not yet been implemented so that it would have led to a breakthrough in the development of the treatment practices improving adherence higher than 50%. The figure below illustrates the required shift from compliance to concordance in health services provision as it has been presented in Finland since late 2000s (Figure 1) (Airaksinen et al., 2012; Routasalo et al., 2009).



**Figure 1** Illustration of the transition from compliance (professional orientation) towards concordance (patient orientation and coaching approach) in supporting self-management in patient care (Airaksinen et al., 2012; Routasalo et al., 2009).

## 2.2 UNDERSTANDING MEDICATION ADHERENCE: THE JOURNEY TOWARDS PATIENT-CENTEREDNESS

The journey towards patient-centered care has been long. Even though the course of action is moving towards patient-provider partnership in healthcare, we are not there yet (Kiviranta & Hämeen-Anttila, 2021; Mononen, 2020; National Institute for Care and Health Excellence NICE, 2021; National Institute for Health and Care Excellence, 2009; Royal Pharmaceutical Society & Merck Sharp and Dome Ltd, 1997). In the UK, adherence and patient centeredness have been prioritized on the long-term basis in the National Health Service (NHS) since the 1990s, emphasizing partnerships in medicine taking (Elliott et al., 2016; Elwyn et al., 2010; Horne et al., 2005; National

Institute for Health and Care Excellence, 2009; Royal Pharmaceutical Society & Merck Sharp and Dome Ltd, 1997). The UK example and its openly accessible resources have promoted adherence and patient centeredness in many other countries and encouraged to run national and local programs, e.g., in Finland (Aarnio & Martikainen, 2016; Bodenheimer et al., 2002; Finnish Medicines Agency Fimea, 2012; Kiviranta & Hämeen-Anttila, 2021; Ministry of Social Affairs and Health, 2018; Mononen, 2020; National Institute for Health and Care Excellence, 2009; Routasalo et al., 2009; World Health Organization, 2013, 2017). In Finland, these national programs include, e.g., Potku-program (the patient as a driver) based on the Chronic Care Model (Bodenheimer et al., 2002; Ministry of Social Affairs and Health, 2010), and its spill out program “Only the medicine taken will work” (Finnish Medicines Agency Fimea, 2012; Mononen et al., 2020; Routasalo et al., 2009, 2010; Routasalo & Pitkälä, 2009), as well as TIPPA-project that according to concordance-thinking, concentrated on changing the medication counselling culture in Finnish community pharmacies to become more patient-centred (Airaksinen & Peura, 2014; Airaksinen et al., 2012; Bodenheimer et al., 2002; Kansanaho, 2006; Puumalainen, 2005; Routasalo et al., 2009). National Medicines Information Strategy since 2012 and Rational Pharmacotherapy Action Plan since 2018 have been the first medicines policy documents in Finland that have explicitly put the medicine user in the centre of the policy (Finnish Medicines Agency Fimea, 2012; Kiviranta & Hämeen-Anttila, 2021; Ministry of Social Affairs and Health, 2018). This chapter focuses on discussing partnership and shared decision making and the ways to implement patient-centeredness in clinical practice to enhance medication adherence.

## **2.2.1 PARTNERSHIP AND SHARED DECISION MAKING**

Shared decision making (SDM) is a practical collaborative process in which a healthcare professional works together with a patient to decide on care (Barry & Edgman-Levitan, 2012; Elwyn et al., 2012; Légaré et al., 2018; National Institute for Care and Health Excellence NICE, 2021; National Institute for Health and Care Excellence, 2009). SDM is a helpful approach in routine clinical practice and is based on the communication and trustful relationship between the patient and the physician, or other healthcare provider. According to SDM, two equal experts are discussing together, the patient is the expert in their everyday life, and the healthcare professional is the expert in disease management. In a respectful communication, these two experts discuss together to find the best suitable treatment and medication for the patient considering the patient's hopes and preferences of the treatment outcomes (Légaré et al., 2018; National Institute for Health and Care Excellence, 2009). SDM is not just an approach to providing the patient with medicines information and leaving the patient to make the treatment decision alone. The goal is that thru trustful discussion, the patient can make the decision on their

treatment together with the healthcare professional. The decision may not be the choice healthcare professional may have suggested in the first place but the choice which matches the patient's context, preferences, and life situation (Elwyn et al., 2012; Légaré et al., 2018; National Institute for Care and Health Excellence NICE, 2021).

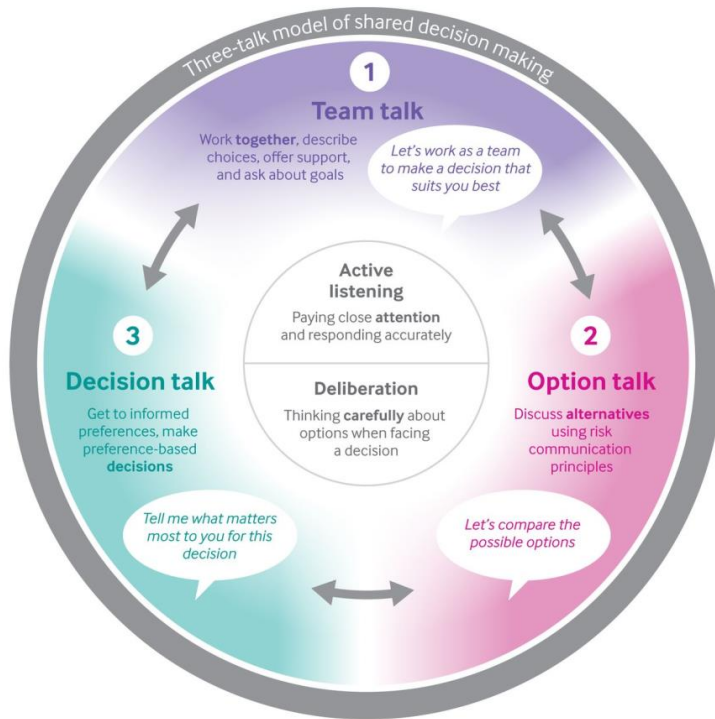
The healthcare provider works as a coach or mentor to strengthen the patient's knowledge, skills, and confidence in treatment decision-making and self-management (National Institute for Care and Health Excellence NICE, 2021; National Institute for Health and Care Excellence, 2009; Routasalo et al., 2009). The treatment outcomes that are important to the patient will influence the decision on treatment choices. The preferences vary by the patient when valuing the potential treatment benefits. The patients valued treatment benefits depend on the disease severity and the treatment toxicity, e.g., chemotherapy (Partridge, 2017; Vaz-Luis et al., 2017). Only the patient can assess whether the medicine's benefits are worth the disadvantages of the treatment. When valuing these aspects, it is important, that the patient and the healthcare provider respect the expertise of each other's (Barry & Edgman-Levitan, 2012; Elwyn et al., 2012).

There can also be limitations to using SDM, e.g., for patients with cognitive impairment, hearing loss or cultural barriers (Backman et al., 2020). Also, not all patients are willing to take responsibility for the treatment choices, but all patients must be provided with the option of being involved in the SDM. However, SDM is a practical concordance approach to support patients' self-management in everyday life to increase medication adherence. It needs to be strengthened by, e.g., training the healthcare professionals (Airaksinen et al., 2012; Diouf et al., 2016; Kansanaho, 2006; Ministry of Social Affairs and Health, 2018; World Health Organization, 2003). However, SDM also requires a change of action at the health system level so that the healthcare providers have the time required to implement SDM adequately at the clinics.

## **2.2.2 AN EXCAMPLE OF A MODEL TO ENHANCE ADAPTION OF SHARED DECISION MAKING IN CLINICAL PRACTICE**

There have been a lot of activities to increase SDM in real-life practice in healthcare, but according to Cochrane review, it has not yet been widely adapted (Légaré et al., 2018). Elwyn et al. published the three key steps, “the three-talk model”, in 2012 to provide a practical concept for healthcare providers to learn SDM (Elwyn et al., 2017; Elwyn et al., 2012). The three-talk model of shared decision making contains three steps towards the decision (Figure 2). These steps are: 1) Choice or Team Talk, where the patient and healthcare professional are starting to work as a team to make the decision, that suits the patient best. Working together means describing choices, offering support, and discussing about the goals of the treatment. 2) Options Talk for discussing alternatives using risk communication principles and 3)

Decision Talk for getting to informed preferences and making preference-based decisions. At the end of the discussion, the patient decides on the treatment together with the healthcare provider.



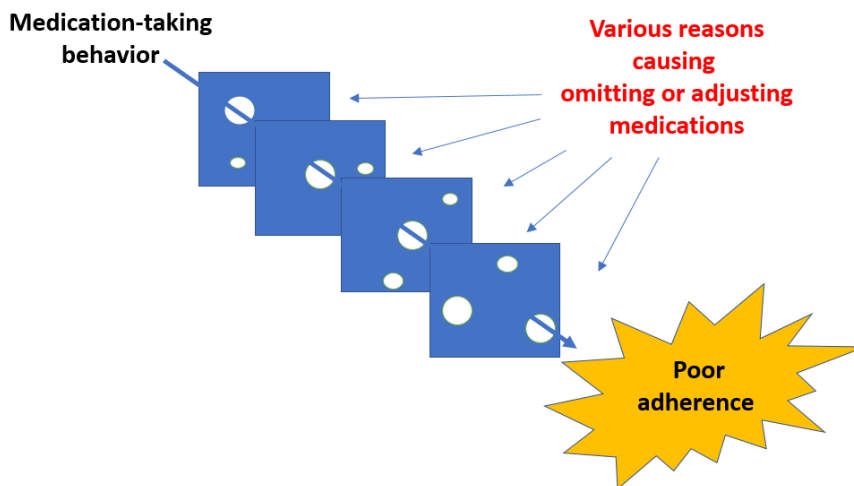
**Figure 2** Three-talk model of shared decision making (Elwyn et al., 2017)

Active listening and deliberation are in the centre of this three-steps decision-making model (Figure 2). The discussion proceeds collaboratively where the patients' priorities, concerns, personal circumstances, and environment have a significant role. What matters to the patient have a critical meaning in the decision making, and the decisions are not being made without the patients' understanding of the treatment benefits and harms (Elwyn et al., 2017).

It is important to consider, that non-adherence may result from poor decision quality and a lack of SDM (Elwyn et al., 2017; Légaré et al., 2018). The patient may be unaware of the treatment options, their benefits, and risks as well as consequences of the different treatment choices. Also, the healthcare professional may be unaware of the patients' values and preferences.

### 2.2.3 POOR ADHERENCE AS A MEDICATION SAFETY RISK

Poor adherence can be considered as a medication safety risk. Extending the risk thinking and system thinking to adherence opens a new perspective on the progressive process of what can happen if the patient is not taking the medication according to instructions and what could be the interventions promoting adherence. In systemic risk management thinking, the interventions to promote adherence can also be seen as systemic defences preventing risks related to poor adherence (Figure 3). For that purpose, risk points for poor medication adherence in the medication use process need to be identified. Risk points may be related to insufficient medication counselling or misunderstanding of instructions, or other systems-based contributing factors to poor adherence. Even though systems thinking in promoting medication safety has become common (World Health Organization, 2017), little attention has been paid to adherence and medication-taking behaviours as a factor contributing to medication safety. Therefore, it is crucial to identify the unknown reasons and contributing factors, even root causes for poor adherence that can lead to operational failures causing omitting or adjusting medications.



**Figure 3** Illustration of poor adherence as a medication safety risk using Reason's Swiss Cheese Model (Reason, 2000). Various reasons can cause a change in medication-taking behaviour leading to poor adherence and medication safety risks.

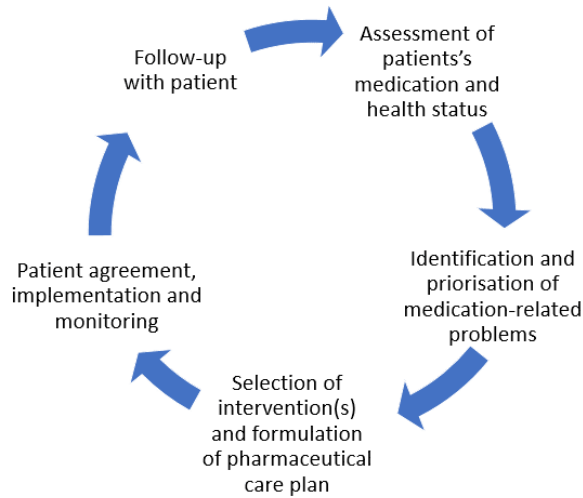
The Swiss Cheese Model by James Reason provides a practical tool to illustrate application of prospective risk management thinking to medication adherence (Figure 3) (Reason, 2000). Thus, human error thinking also applies to medication-taking behaviour. Blaming patients for not taking medication as prescribed is not a solution (World Health Organization, 2003). Instead, we need to focus on the system and identify the reasons behind the patients'

existing medicine taking behaviours. Like in the Swiss Cheese Model, there can be many holes, but only one hole in the slice is not necessarily causing nonadherent behaviour (Reason, 2000). Nevertheless, if there are many holes in several layers, they can accidentally fit together and cause behaviour leading to poor adherence and medication safety risks. By identifying reasons, contributing factors and root causes for omitting or adjusting medication it is possible to find systemic solutions to prevent potential harm. Identifying, solving, and preventing medication-taking barriers and optimizing the medication requires partnership to understand patients' reasoning for their medicine taking behaviour (Bell et al., 2007; Horne et al., 2005; National Institute for Health and Care Excellence, 2009, 2015; Routasalo et al., 2009; World Health Organization, 2003).

#### **2.2.4 IMPLEMENTING MEDICATION RISK MANAGEMENT: PHARMACEUTICAL CARE**

Pharmaceutical care is a practical patient-centred approach to increase patient involvement in their own care and to enhance rational use of medicines by prospective medication risk management (Hepler & Strand, 1990). Pharmaceutical care has been the background thinking for implementing patient-centred medication risk management interventions in healthcare, such as medicines information and medication counselling, medicine history taking and medication reconciliation, and medication reviews.

The concept of pharmaceutical care was launched in 1990 by Hepler and Strand (Hepler & Strand, 1990). They defined pharmaceutical care as “the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient’s quality of life”. (Hepler & Strand, 1990). The goal of pharmaceutical care is to improve patients’ quality of life by improving therapeutic, humanistic, and economic outcomes of the pharmacotherapy in collaboration with the patient and other healthcare professionals involved in a care team (American Society of Hospital Pharmacists, 1993; Council of Europe, 2020; Hepler & Strand, 1990). These outcomes can be achieved by identifying, resolving, and preventing medication-related problems, which can reduce medication-related harm, and optimize medication use (Council of Europe, 2020; Hepler & Strand, 1990). Actions needed in the pharmaceutical care process for medicines optimization are presented in Figure 4. The healthcare professionals are expected to actively listen to their patients, implement and monitor the patients’ therapeutic care plan and, in that way, help the patient commit to the treatment and reach therapeutic outcomes. Medication adherence can be considered an indirect clinical outcome or a behavioural outcome (Kozma et al., 1993; Légaré et al., 2018; Mononen, 2020).



**Figure 4** Pharmaceutical care process with patient-centred interventions to enhance outcomes of pharmacotherapies and patients' quality of life. Medication adherence can be considered as one of the indirect clinical outcomes (Council of Europe, 2020; Hepler & Strand, 1990).

The patient's medication therapy is intended to increase patients' quality of life (American Society of Hospital Pharmacists, 1993; Hepler & Strand, 1990). In the pharmaceutical care process (medication management process), the healthcare professionals take responsibility for optimizing the medication through suitable interventions according to each patient's preferences and daily routines (Figure 4) (Chen et al., 2014; Council of Europe, 2020; Hepler & Strand, 1990; Kobue et al., 2017). The patient's education and counselling interventions are planned to increase medicine users' understanding of the treatment. It also enhances the patients' self-management skills and prevents possible medication-related problems and risks, significantly affecting therapeutic outcomes (World Health Organization, 2003). Also, monitoring and reviewing the patients' medications during regular follow-ups are planned to help to prevent possible future medication-related harm if the patient's condition changes or some other medication-related problems affect medicine taking and self-management.

As the pharmaceutical care process is patient-centred, the patient should have the possibility to be involved in making the quality-of-life goals of the treatment together with the healthcare professionals (Council of Europe, 2020; Hepler & Strand, 1990). Interprofessional co-operation is crucial to achieve the desired treatment outcomes (Mansoor et al., 2013; Rathbone et al., 2016). The various healthcare professionals have significant roles and



responsibilities in supporting the patient's medication management through pharmaceutical care interventions (Council of Europe, 2020). The different roles of healthcare professionals need to be well-determined.

In 2020 the Council of Europe (CoE) adopted a resolution on implementing pharmaceutical care in its member countries in Europe. The content of the resolution is in line with the pharmaceutical care principles introduced by Hepler and Strand in 1990 (Figure 4) (Council of Europe, 2020; Hepler & Strand, 1990). According to the CoE resolution, the pharmaceutical care process includes assessment of patient's medication, identification of medication-related problems, selection, and formulation of the pharmaceutical care plan so that it meets the patient's needs as well as implementation, monitoring, and follow up. The interventions should be patient-centred, where the healthcare professional takes responsibility for optimizing patients' medication use and preventing medication-related problems in partnership with the patient for the patients' best interest.

## **2.2.5 TOWARDS PATIENT-CENTEREDNESS IN REAL-LIFE PRACTICE: INTERVENTIONS INCREASING PATIENT INVOLVEMENT IN THEIR MEDICATION MANAGEMENT**

There are currently widely implemented routine practices in healthcare that facilitate patient involvement in their medication therapy. These practices can be considered as systemic defences in medication risk management and they can be divided in the following three categories: 1) medicines information and medication counselling, 2) medication history taking and reconciliation, and 3) medication reviews by physicians or conducted collaboratively. These patient-centred medication management practices have evolved from the need to identify, solve, and prevent medication-related problems and risks to improve outcomes of pharmacotherapies (Bell et al., 2007; Council of Europe, 2020; Hepler & Strand, 1990; National Institute for Health and Care Excellence, 2009, 2015; National Prescribing Centre, 2014; Routasalo et al., 2009; World Health Organization, 2003, 2017). The goal is to prospectively manage medication-related problems and risks that could harm patients and cause additional preventable costs in various health care settings. These practices have evolved especially under the disciplines of clinical pharmacy and pharmaceutical care.

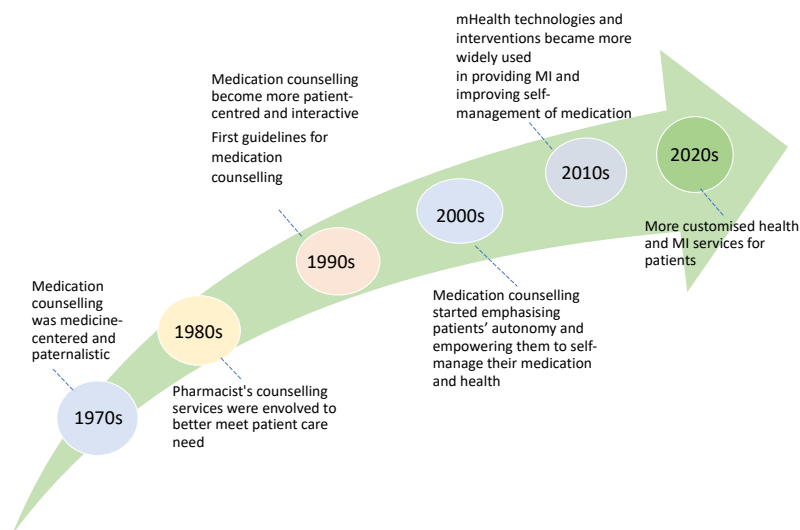
The next subchapters will introduce these practices from the patient involvement approach to describe their potential to influence adherence and self-management of pharmacotherapies.

### **2.2.5.1 Medicines information and medication counselling**

Medicines information and medication counselling are one among the interventions planned to enhance patients' understanding of the medicines

they are taking, and to support self-management of their medication (Airaksinen et al., 2012; Finnish Medicines Agency Fimea, 2012; Horne et al., 2005; Kiviranta & Hämeen-Anttila, 2021; Mononen, 2020). The goal is to affect the patient's medication-taking behaviour positively. A well-informed and trained patient can make the decision on the treatment together with the healthcare professional and self-manage the medication at home. Medication counselling should not be a one-way action, a monologue, where the healthcare provider dumps medication information, and the patient is the receiver (Airaksinen & Peura, 2014; Airaksinen et al., 2012; Horne et al., 2005; Kansanaho, 2006; Puumalainen, 2005; United States Pharmacopeia, 1997). This kind of counselling is paternalistic and authority-based, and the patient is expected to comply with the information (Airaksinen et al., 2012; Horne et al., 2005; Routasalo et al., 2009). The healthcare professionals need to empower the patients in medication self-management with interactive and collaborative discussion and active listening (Airaksinen et al., 2012; Bell et al., 2007; Kansanaho, 2006; Marinker & Royal Pharmaceutical Society of Great Britain, 1997; National Institute for Health and Care Excellence, 2009; Puumalainen, 2005; United States Pharmacopeia, 1997).

The healthcare providers' attitudes to medication counselling have varied over time from a more paternalistic manner towards cooperation with the patient (United States Pharmacopeia, 1997; World Health Organization, 2003). Not until 1980, for example, pharmacists in Finnish pharmacies were allowed to provide medicines information and counselling to the patient because it was considered a physician's duty (Airaksinen, 1996; Mononen, 2020; Vainio, 2004). Medicines information was not easily accessible to patients, and it was medicine centred (Figure 5). The patients were expected to comply with providers' orders and not question their decisions. When it became allowed to provide medicines information in community pharmacies, some physicians were particularly concerned about pharmacists' involvement in therapeutic counselling, such as telling about effects and adverse effects and indications of medications (Vainio, 2004). Also, community pharmacists saw their role more as reading the dosing instructions on the label and telling how to store the medicine at home (Airaksinen, 1996). At the same time, patients wanted to know the therapeutic effects of their medications. Since then, the situation has changed, and the medicines information to patients has become standard practice, also in Finnish pharmacies (Mononen, 2020). Furthermore, medicines information sources have diversified and become easily accessible online (Mononen, 2020).



**Figure 5** Evolution of medicines information (MI) to patients since the 1970s (adapted Mononen 2020)

Since the 1990s, medication counselling and medicines information have become more interactive and patient-tailored (Airaksinen et al., 2012; Mononen, 2020; Vainio, 2004). Particularly community pharmacists have focused on improving medication counselling services and communication on medications with their customers (Mononen, 2020). There have been systematic long-term attempts to change the counselling culture towards interactive patient-centred communication (Airaksinen, 1996; Airaksinen et al., 2012; Kansanaho, 2006; Mononen, 2020; Puumalainen et al., 2005; Vainio, 2004). This change has been supported by medication counselling guidelines and checklists, many of them being derived from clinical interviews and modified to support implementation of pharmaceutical care, such as the USP Medication Counselling Behaviour Guidelines (Airaksinen et al., 2012; Jyrkkä et al., 2017; Kansanaho, 2006; Puumalainen et al., 2005; Rollnick & Miller, 1995; United States Pharmacopeia, 1997). Also, principles of motivational interview have been applied to medication counselling practices (Jyrkkä et al., 2017; Rollnick & Miller, 1995). Common to these models is that they try to reinforce change in health care professionals' medication counselling behaviours towards partnership, concordance, and actual dialogue (Airaksinen et al., 2012; Jyrkkä et al., 2017; Kansanaho, 2006; Puumalainen et al., 2005; United States Pharmacopeia, 1997).

### **2.2.5.2 Medication history taking and reconciliation**

The keystone of the appropriate medicine use is an up-to-date medication regimen that informs the patient about what kind of medicines should be used, why and for how long, and how the medicines should be taken. Medication reconciliation is a process where the healthcare provider creates the most up-to-date list of all medicines a patient is taking and compares that list against physicians' orders (Institute for Healthcare Improvement IHI, 2011; Joint Commission on Accreditation of Healthcare Organizations, 2006; National Institute for Health and Care Excellence, 2015; National Prescribing Centre, 2014; Penm et al., 2019; World Health Organization, 2014). The concept has been further evolved to include the patient's allergies and the history of adverse effects from medications and medication aids (Penm et al., 2019).

Medication history taking and reconciliation can be seen as a systemic defence in medication risk management to prevent, identify and resolve drug-related problems (Kari et al., 2018; National Prescribing Centre, 2014). When conducting medication reconciliation, one of the sources should be patients themselves (Institute for Healthcare Improvement IHI, 2011; Kari et al., 2018; National Prescribing Centre, 2014). They know how they have used medicines at home and what problems they may have experienced (Institute for Healthcare Improvement IHI, 2011; Kari et al., 2018; National Prescribing Centre, 2014; World Health Organization, 2017). They may have stopped taking the prescribed medication or adjusted it because of DRPs. Also, they may have purchased and taken Over-The-Counter (OTC) medicines that are not documented in the patient record but may affect the prescribed medication. Through medication reconciliation, the patient may become more knowledgeable about their medicines and why they are prescribed (Kari et al., 2018).

Even though the importance of an updated medication list has been widely recognized, it is still challenging to maintain. According to the Finnish Medicines Agency's population survey in 2021, only 26% of chronically ill adult patients had an up-to-date medication list in Finland (Jyrkkä et al., 2021). Other studies show similar challenges also in other countries (Caglar et al., 2011; Mazer et al., 2011; Schepel et al., 2019). As medication reconciliation is becoming more common practice and promoted, e.g., by WHO and national patient and medication safety strategies, its potential in increasing patient-centred communication on medication use could be better exploited.

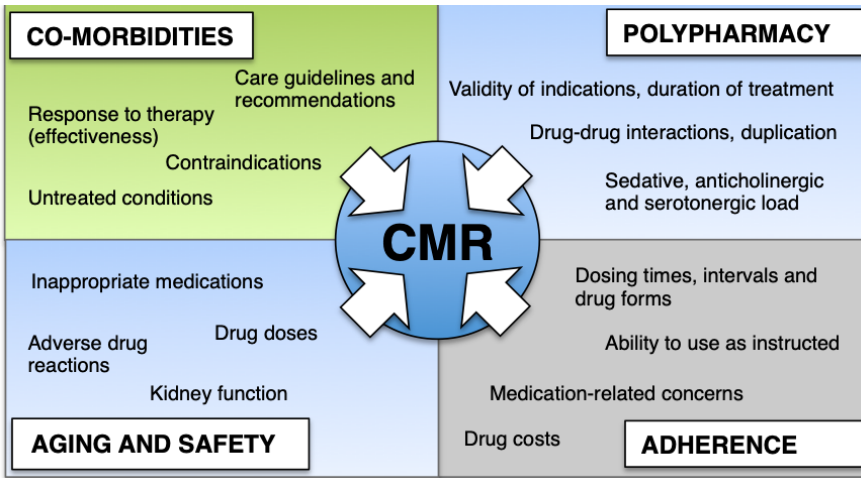
### **2.2.5.3 Collaborative medication review**

Medication reviews (CMR) is one of the practical interventions to support patient's medication taking behaviour and involve patients in their care. Part of physicians' routine practice is to review patients' medications. Medication reviews can also be conducted collaboratively involving pharmacists and other care team members (Kiiski et al., 2019; Leikola, 2012; National Institute for

Health and Care Excellence, 2015; Toivo, 2020). In Finland, collaborative medication reviews have been recommended by the Ministry of Social Affairs and Health as a means of reducing inappropriate medication in older adults since 2007 (Finnish Government, 2015; Kumpusalo-Vauhkonen et al., 2016; Ministry of Social Affairs and Health, 2007, 2011, 2018).

The Pharmaceutical Care Network Europe (PCNE) has defined medication reviews as follows: “Medication review is a structured evaluation of a patient’s medicines with the aim of optimizing medicines use and improving health outcomes” (Griese-Mammen et al., 2018). Drug-related problems (DRP) can cause medication-related harm and are defined as “An undesirable patient experience that involves drug therapy and that actually or potentially interferes with a desired patient outcome” (Strand et al., 1990). Before conducting a medication review, the patients’ medication should be reconciled.

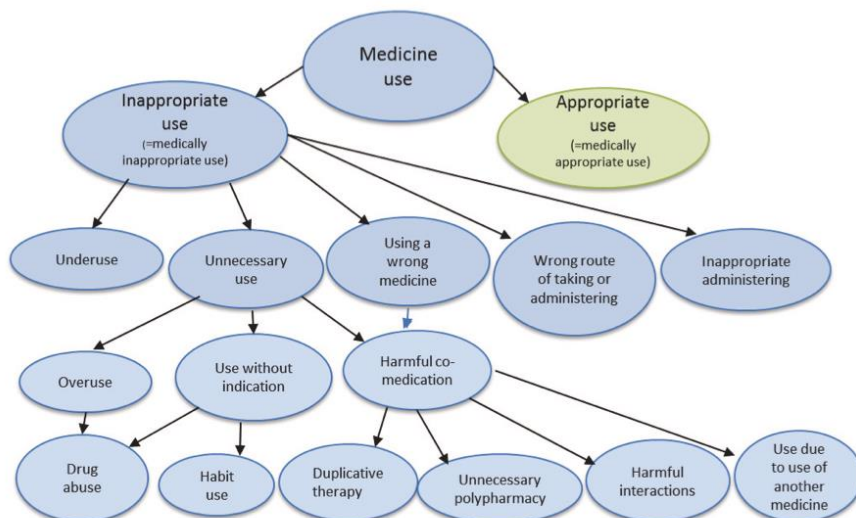
CMR is a problem-based approach where the aim is to solve identified drug-related problems, optimize medication use and increase medication adherence (AATE, 2017; Clyne et al., 2008; Kari et al., 2018; Kiiski et al., 2019; Leikola, 2012; Ministry of Social Affairs and Health, 2018; National Institute for Health and Care Excellence, 2015). A patient interview is crucial for identifying DRPs, including barriers to medication adherence and reasons for not taking medication as prescribed, deficiencies in patient knowledge about the medication or illness, as well as providing advice (AATE, 2017; Clyne et al., 2008; Dimitrow, 2016; Kari et al., 2018; Leikola, 2012). The patient's views and preferences are essential to find out because they may be different from those of healthcare professionals and impact patients' medicine use and adherence (National Institute for Health and Care Excellence, 2015). The CMR process can be divided into four main risk dimensions (Figure 6), which can have a negative impact on a patient's medication regimen, especially in older adults (Leikola, 2012). One of the four risk dimensions is medication adherence.



**Figure 6** Main dimensions of medication-related problems and risks to be covered by the collaborative medication review (CMR) procedure to ensure safe and appropriate pharmacotherapy in older patients (Leikola, 2012).

Patients have many problems in medication management, so there may be a broader need for CMR than it is used today in routine practice. Even though national and international recommendations on CMRs highlight the importance of involving the patients or their caregivers in the CMR process, evaluations of the practices indicate that this is not optimally occurring in real-life practices (Kari et al., 2018; Kiiski et al., 2019; National Institute for Health and Care Excellence, 2015). The recent population survey in Finland by the Finnish Medicines Agency illustrates the prevalence of drug-related problems from the patient perspective (Jyrkkä et al., 2021). According to the survey, 60% of patients aged 18-79 years reported that they had to accept possible adverse drug reactions related to their medication, 42% were worried about possible adverse drug reactions, and 61% had experienced at least one drug-related problem. The most commonly experienced problems were related to adverse drug reactions (47%) and medication ineffectiveness (35%). The other problems were polypharmacy (17%) and using medicines for too long time (18%).

DRP may be the reason for poor adherence or vice versa (Figure 7). Figure 7 illustrates different ways medicines can be misused (Dimitrow, 2016; Stakes & Rohto, 2006). DRPs can be caused by not taking medicines as prescribed. Polypharmacy and age-related body changes are among the factors that can increase the risk for inappropriate use of medicines and poor adherence (Dimitrow, 2016; Leikola, 2012; National Institute for Health and Care Excellence, 2015; Stakes & Rohto, 2006).



**Figure 7** Different ways medicines can be used inappropriately and this can be caused by not taking medicines as prescribed (Dimitrow, 2016; Stakes & Rohto, 2006).

CMR may be a useful intervention to solve patients' medication-related problems and improve adherence, particularly in patients with polypharmacy and multiple diseases. However, more patient involvement is needed when planning patients' medication care plans and implementing possible medication changes after CMR (Kiiski et al., 2019).

There is increasing but still contradictory evidence on outcomes of CMR. CMR may decrease medication-related harm when reducing inappropriate medicine use and prescribing, as well as the anticholinergic and sedative burden of medication (Chen et al., 2019; Kallio et al., 2018; Leikola, 2012; Thiruchelvam et al., 2017). Admission to the hospital because of ADRs may decrease (Renaudin et al., 2016; Thiruchelvam et al., 2017), although the evidence is contradictory and unclear (Chen et al., 2019; Christensen & Lundh, 2016). Also, the impact on quality of life is uncertain (Chen et al., 2019; Renaudin et al., 2016). According to one systematic review, CMR has no significant impact on mortality (Chen et al., 2019), contrary to another systematic review by Thiruchelvam et al. (Thiruchelvam et al., 2017).

A randomized clinical trial in Denmark has shown promising results that an extended pharmacist's intervention to solve DRPs contributing to poor adherence may prevent readmissions to the hospital (Ravn-Nielsen et al., 2018). Readmission within 30 and 180 days to the hospital was reduced in patients who received an extended pharmacist intervention than in those who received usual care or a basic pharmacist intervention (Ravn-Nielsen et al., 2018). The extended pharmacist intervention included medication review, three motivational interviews and follow-up with the primary care physician, nursing home and pharmacy representatives. The basic pharmacist

interventions included medication review conducted by a trained pharmacist, and the usual care did not have any particular intervention. The researchers concluded that the extended intervention intended to solve DRPs and including a non-judgmental motivational discussion with the patient might prevent readmission caused by poor adherence. As poor adherence to treatment may cause the disease to worsen, the readmission may be adherence related. More research is needed to confirm these findings and show the cost-effectiveness of these quite time-consuming interventions.

## **2.2.6 THE IMPACT OF NOCEBO ON MEDICATION ADHERENCE**

Nocebo is a common phenomenon in healthcare, although it is not widely recognized in routine clinical practice (Lansberg et al., 2018). Nocebo as a phenomenon means that a harmless substance or treatment may cause harmful side effects or worsening symptoms because the patient thinks or believes they may occur or expects them to occur (National Institutes of Health NIH, 2022). Nocebo-effect can be seen as the opposite of placebo. The effectiveness of a placebo is based on the effect of the positive illusion of the treatment intervention (Häuser et al., 2012; Lansberg et al., 2018; Planès et al., 2016). Similarly, nocebo is considered a nonspecific negative effect on the treatment or the medication (Häuser et al., 2012; Lansberg et al., 2018; Planès et al., 2016). However, both nocebo and placebo are psychobiological phenomena that can be intentionally used to achieve therapeutic goals (Häuser et al., 2012; Lansberg et al., 2018).

Nocebo is related to patients' expectations of the treatment or medication and can cause symptoms to worsen (Lansberg et al., 2018; Planès et al., 2016). The previous experiences with medicines may impact patients' experiences and expectations and cause nocebo (Häuser et al., 2012; Mohammed et al., 2016). They can induce negative learning experiences, which raise doubts about the medicine's safety or treatment safety. The symptoms may not diminish, and the patient is not receiving an explanation for the symptoms. Negative emotions may further strengthen the symptoms (Louhiala et al., 2020).

Communication between the medicine user and the healthcare provider plays an important role in nocebo as the professional's specific word choices or phrases can affect patient's medication-taking behaviour (Cox & Fritz, 2022). Patients want to discuss their concerns with the healthcare providers and get adequate medicines information (Lambert-Kerzner et al., 2015; Saleem et al., 2012). Healthcare providers should pay attention to the nocebo effect in clinical practices and pharmacies and discuss the patients' expectations, concerns, and fears about the treatment (Lansberg et al., 2018). Nocebo-effect can cause omitting the medicine taking and cause significant harm to the patient while the patient is expecting or illustrating side-effects (Dunne et al., 2014; Ju et al., 2018; Lansberg et al., 2018; Nielsen &



Nordestgaard, 2016). Adequate medicines information and patient counselling is crucial when trying to decrease nocebo-response.

While discussing with the patients about the treatment choices, healthcare professionals can also unintentionally cause nocebo-effect to the patients (Lansberg et al., 2018). Unconscious expressions or words can have a nocebo impact on the patients, and the healthcare professionals can cause non-adherence by accidentally interacting negatively with the patients (Lansberg et al., 2018). The physicians may lack time in the appointment, leading to an insufficient discussion with the patient about the treatment benefits and medication side effects and leading to misunderstandings (Lansberg et al., 2018). The same can happen in a pharmacy if many customers are in line. To avoid the possible nocebo-response, healthcare providers should pay attention to their behaviour, act, and speak with the patient. Shared decision-making and enough time while discussing with the patient their treatment choices can prevent the patient from harm (Lansberg et al., 2018).

However, nocebo-effect, as well as placebo-effect, can be used in both negative and positive ways. The placebo effect is helpful with effective treatments, but it should not be used with ineffective treatments to create a false illusion of the outcomes. The misuse of placebo effects can be, e.g., when creating excessive expectations for the patient using quackery or unnecessary medications. In contrast, to prevent overuse of antibiotics or deprescribing benzodiazepines, the nocebo effect can help highlight the potential harmfulness of continuous medication. A better understanding of the nocebo effect can impact adherence, and healthcare professionals should be better educated to be aware of its potential effects.

Medication adherence is a dynamic process and can vary from medicine to medicine. Adherence to one medicine does not mean automatically adherence to all medicines (National Institute for Health and Care Excellence, 2009; World Health Organization, 2003). Statins are an example of medicines with a common belief of serious adverse effects compared to the positive outcomes of the therapy. Consequently, nocebo-effect is common if patients expect to have adverse events when taking statins (Gupta et al., 2017; Lansberg et al., 2018; Rizos & Elisaf, 2017). It leads statin therapy to be often suboptimal. In turn, poor adherence to statin therapy may result in harmful effects by jeopardizing the prevention of cardiovascular diseases (Lansberg et al., 2018; Vonbank et al., 2017; Vonbank et al., 2013; Yan et al., 2006).

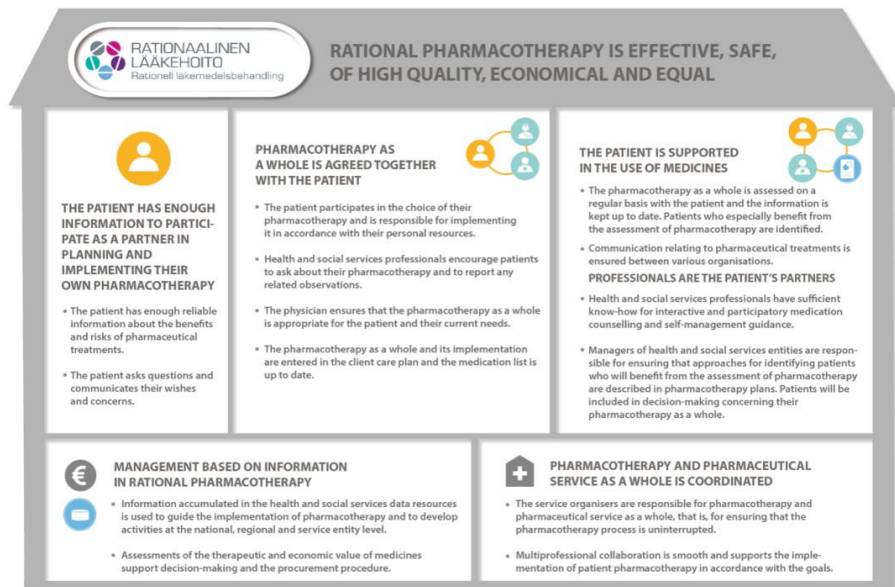
Patients' beliefs about the treatment play a significant role when they experience possible side effects (Bermingham et al., 2011; Hayden et al., 2015; Ju et al., 2018). The internet and the social media can have a negative impact on expectations or provoke fears about the medicines and, in that way, generate nocebo-effect and lead to, e.g., new symptoms, the symptoms worsening or reduced effectiveness of the treatment (Bermingham et al., 2011; Bräscher et al., 2017; Louhiala et al., 2020; McKillop & Joy, 2013a; van der Ploeg et al., 2016). Anyone with no scientific expertise can post on the internet, and these publications may spread and cast doubt on the benefits of the

medicines. Social media can increase fear and impact the discontinuation of medication (Bräscher et al., 2017; Nielsen & Nordestgaard, 2016). Statins and generic medicines are examples of the medicines exposed to this kind of negative communication in the media provoking nocebo-effect and poor adherence (Dunne et al., 2014; Lansberg et al., 2018; Nissen, 2017; Pettersen, Fridlund, Bendz, Nordrehaug, Rotevatn, Schjott, et al., 2018).

## **2.2.7 THE IMPACT OF HEALTH POLICY DECISIONS ON MEDICATION ADHERENCE**

According to WHO, policy-makers need to understand how social and economic factors influence medication adherence (World Health Organization, 2003). Those factors can be barriers or facilitators to patients' medication management (Habte et al., 2017; Rashid et al., 2014).

In Finland, the Rational Pharmacotherapy Action Plan (RPAP), based on the Government program, highlighted for the first time in 2018 the importance of a national strategy for promoting rational pharmacotherapy (Ministry of Social Affairs and Health, 2018). According to RPAP, rational pharmacotherapy is effective, safe, cost-effective, equal and of high-quality (Figure 8). For the national implementation of the Program, specified objectives were set for services organizers and providers, healthcare organizations, social welfare professionals and medicine users. RPAP emphasizes partnership, patient-centeredness, empowerment, and involvement. These principles are included in the key objectives of the Action Plan in the following way: 1) the patient has enough information to participate as a partner in planning and implementing their own pharmacotherapy, 2) pharmacotherapy regimen is agreed together with the patient, and 3) the patient is supported in the use of medicines (Figure 8). According to RPAP, implementation of these objectives is supported by evidence-informed management based on information in rational pharmacotherapy and coordinating pharmacotherapy and pharmaceutical services (Ministry of Social Affairs and Health, 2018). Implementation of these principles is still ongoing as part of Finland's social and healthcare reform (Ministry of Social Affairs and Health, 2019).



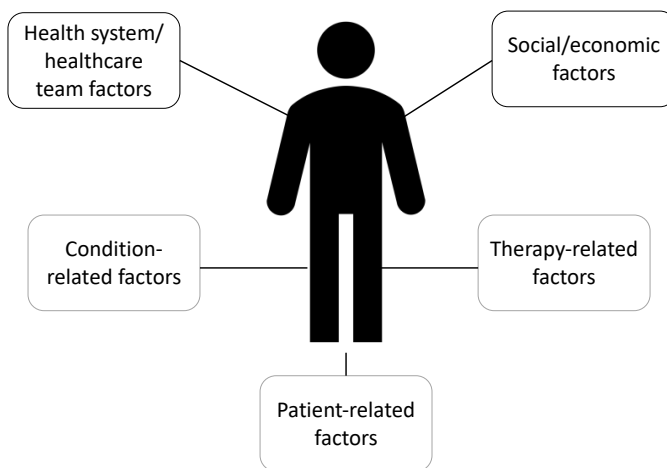
**Figure 8** Partnerships needed in ensuring rational pharmacotherapy as illustrated by the Rational Pharmacotherapy Action Plan (Ministry of Social Affairs and Health, 2018).

Another important policy-related issue influencing medicine use and adherence is medicines pricing and reimbursement policies (Chen et al., 2014; Gemmill et al., 2008; Goldsmith et al., 2017; Habte et al., 2017; Suviranta et al., 2019). Patients with multimorbidity often have multiple medications and have high medicines costs as heavy users of medicines (Saastamoinen & Verho, 2015). The high cost of medicines can impact medication management negatively, especially if the cost compensation, e.g., insurance, does not cover the medicines or covers only part of the cost (Chen et al., 2014; Gemmill et al., 2008; Goldsmith et al., 2017). Studies in Finland show that low-income patients have to compromise the medicines purchased due to a lack of money (Aaltonen, 2017; Aaltonen et al., 2013). If the prescription charges increase, it may impact the ability to buy medicines and, in such a way, affect the health (Aaltonen, 2017; Gemmill et al., 2008). The impact of these financial aspects on adherence and public health has also been highlighted by WHO (World Health Organization, 2003).

## 2.3 MEDICATION ADHERENCE AS A PHENOMENON: DIMENSIONS OF CONTRIBUTING FACTORS BY WHO

Medication adherence is a complex phenomenon and not entirely understood (Mohammed et al., 2016; World Health Organization, 2003). The WHO's report "Adherence to long-term therapies - evidence for action" in 2003 summarized existing evidence by then, identifying factors contributing to medication adherence. Furthermore, WHO highlighted the ways adherence could be improved in clinical practice.

According to WHO, healthcare professionals should be trained in adherence, and a toolkit to support adherence in clinical practice is needed. As patients should be empowered in their treatment, healthcare professionals should also be empowered in adherence management. According to WHO's definition, factors influencing medication adherence are divided into five dimensions: 1) social and economic factors, 2) health system and healthcare team factors, 3) condition-related factors, 4) therapy-related factors, and 5) patient-related factors (Figure 9) (World Health Organization, 2003).



**Figure 9** The WHO's identification of five interacting dimension of adherence to long-term therapies (World Health Organization, 2003).

According to WHO, interventions to enhance adherence should be patient-centred and individually tailored (World Health Organization, 2003). Ideally, they should positively impact all five dimensions, especially those in which the patients have obstacles. Promoting patients' responsibility for their care, medicines information and medication counselling, and the possibility to exchange experiences with others with the same disease seem to be successful interventions (World Health Organization, 2003).

### **2.3.1 SOCIAL AND ECONOMIC FACTORS**

Low socioeconomic status may impact medication adherence, although it does not appear to be an independent predictor (Goldsmith et al., 2017; World Health Organization, 2003). When the patient must consider whether to buy medicines or food, medicines are probably not a priority (Al Hamid et al., 2014; Bezabhe et al., 2014; Dehdari & Dehdari, 2019). Financial balance and insurance coverage increase medication adherence in patients with multimorbidity (Goldsmith et al., 2017; Holtzman et al., 2015). Support from the family is essential and increases adherence (Al Hamid et al., 2014; Gassmann et al., 2016; Habte et al., 2017; Hogan et al., 2014; Kelly et al., 2014; McKillop & Joy, 2013a; Ming et al., 2011; Pagès-Puigdemont et al., 2016; van Geffen et al., 2011). Despite illness, being accepted in the community and feeling supported is crucial to medication adherence (Al-Qazaz et al., 2011; Bezabhe et al., 2014; Bockwoldt et al., 2017; Dehdari & Dehdari, 2019). Also, religion and religious practices and beliefs can significantly impact adherence as well as war even after the ending (Al Hamid et al., 2014; Habte et al., 2017; World Health Organization, 2003). Race and social inequalities have also an impact on adherence (World Health Organization, 2003).

Age affects adherence, but often it depends on the condition (World Health Organization, 2003). Considering infants and toddlers, the parents have to manage their child's medication and follow the prescribers' orders. When the children grow older, they often can have more autonomy and manage more independently their medication but may still need their parents' support. Adolescents can often have difficulties in adhering to their medication and their health behaviour became more and more influenced by the social environment. Older people often have multiple diseases, and polypharmacy is more common, affecting adherence. Nevertheless, support is needed in every age group.

### **2.3.2 THERAPY-RELATED FACTORS**

According to WHO, there are plenty of therapy-related factors affecting adherence (World Health Organization, 2003). Side effects or fear of side effects impacts medication-taking practices and patients' willingness to follow the physician's orders (Habte et al., 2017; Ju et al., 2018; Rathbone et al., 2017). The patient can experience worse side effects than the symptoms of the illness, even in the case of a severe illness (Clancy et al., 2020). The patients want to discuss with the healthcare provider about the side effects and how to cope with them (Kekäle, 2016; Lambert-Kerzner et al., 2015; Saleem et al., 2012).

As mentioned before in this thesis, polypharmacy and complex medication seem to be barriers to medication adherence (Al Hamid et al., 2014; McKillop & Joy, 2013b; World Health Organization, 2003). Also, previous treatment failures, many changes in the treatment regimen and lack of support can affect negatively affect adherence. Good understanding of the illness and its

treatment to integrate medication into daily routines combined with adequate support are crucial to coping with adherence problems. The interventions to increase adherence need to be tailored according to the therapy and the patient's needs (World Health Organization, 2003).

### **2.3.3 PATIENT-RELATED FACTORS**

According to WHO, patient-related factors can be classified as the patient's resources, knowledge, attitudes, beliefs, perceptions, and expectations (World Health Organization, 2003). If the patient has inadequate knowledge about the disease and its medication, they may have difficulties understanding why good medication management is crucial (Al-Qazaz et al., 2011; Dehdari & Dehdari, 2019; Meraz, 2020). The patient may have different beliefs about the medication and previous experiences about the medicines, which can affect the perceptions and attitudes towards the medicines (Ju et al., 2018; Kelly et al., 2018; Kelly et al., 2014; Mohammed et al., 2016; Tong et al., 2011; World Health Organization, 2003).

The patient may not prioritize disease management, which may be difficult for the healthcare providers to understand (Bockwoldt et al., 2017; Hogan et al., 2014; Rowell-Cunsolo & Hu, 2020; Ågård et al., 2016). There may be other priorities that the patient value more, especially if it also requires lifestyle changes (World Health Organization, 2003; Ågård et al., 2016). There can be misunderstandings and a lack of knowledge. The patient may think adjusting the medicines and skipping some doses are not affecting the disease, and intermittent failure taking the medicines have no impact on its response (Eliasson et al., 2011). Stigma and feeling discrimination can be an obstacle and causing medication non-adherence (Ho et al., 2017; Holtzman et al., 2015; Miller et al., 2010; Schatz et al., 2019; Shalihu et al., 2014; Srimongkon et al., 2018; Tranulis et al., 2011). Stress and helplessness, negative views about medicines or thinking physicians are overprescribing medicines and worries about medicines long-time effects of medicines may be barriers to medication management (King-Shier et al., 2017; McKillop & Joy, 2013b; World Health Organization, 2003). Some diseases, such as hypertension, have no visible symptoms causing non-acceptance of the disease and harming medication adherence (King-Shier et al., 2017; World Health Organization, 2003).

Motivation, self-efficacy and behavioural skills are essential when coping adherence problems in healthcare (World Health Organization, 2003). When the patient is empowered, they know how to safely adjust the medication when the disease worsens (Habte et al., 2017; Jaffray et al., 2014). Belief in the medicine's efficacy and perceived health benefits facilitates adherence (Gassmann et al., 2016; Ho et al., 2017; World Health Organization, 2003).

### **2.3.4 CONDITION-RELATED FACTORS**

The effect of the condition-related factors affecting adherence depends on how the patient perceives the risk of their disease and how important the patient value the expected treatment outcomes (World Health Organization, 2003). If the patient value the expected outcomes high, the patient prioritizes physicians' orders and treatment follow-ups. There are some strong determinants of adherence such as symptoms severity, disease progression or availability of effective treatments. If the patient has concomitant illnesses such as depression and, e.g., diabetes or HIV, or drug or alcohol abuse, it can affect adherence negatively.

### **2.3.5 HEALTHCARE TEAM AND SYSTEM-RELATED FACTORS**

According to WHO, few studies have examined the effects of the system or healthcare team on adherence (World Health Organization, 2003). However, a good and trustful patient-provider relationship enhances medication adherence (Kelly et al., 2014; Marinker & Royal Pharmaceutical Society of Great Britain, 1997; World Health Organization, 2003). The patient needs support from healthcare professionals to manage the life with illness and enhance medication safety in everyday life (National Institute for Health and Care Excellence, 2015; World Health Organization, 2003).

There are also many factors affecting medication adherence, such as poor access to healthcare and the poor patient-provider relationship (Bezabhe et al., 2014; Garavalia et al., 2011; Ho et al., 2017; Pagès-Puigdemont et al., 2016). Long waiting times at clinics, short appointment times, and busyness are also obstacles (Miller et al., 2010; Pagès-Puigdemont et al., 2016; Schatz et al., 2019). Poor understanding of adherence and lack of interventions to enhance patients to take medication as prescribed can be barriers in healthcare and cause harm to patients.

## **2.4 BEHAVIOURAL THEORY -BASED APPROACH TO MEDICATION ADHERENCE: EVOLUTION OF THEORIES**

Health behaviour has an essential role in promoting well-being and managing long-term illnesses (World Health Organization, 2003). Behavioural theories can provide a way to understand and predict what a change in health behaviour requires from the patient when treating chronic illnesses and how the environment may affect it (National Institute of Health NIH, 2005). With the help of behavioural theory, it is possible to see a bigger picture of the factors affecting the required change in health behaviour and support the patient in achieving the desired behaviour change.

The researchers have tried to explain human behaviour with different behavioural theories over time when tackling medication non-adherence

(Michie et al., 2005). For example, WHO's adherence report introduced some behavioural theories that can help to understand patients' actions in medicine taking and why non-adherence, despite much emphasis, seems to remain unchanged for decades. However, there are numerous behavioural theories, but no clear evidence of which theories predict best health behaviour change (Michie et al., 2005).

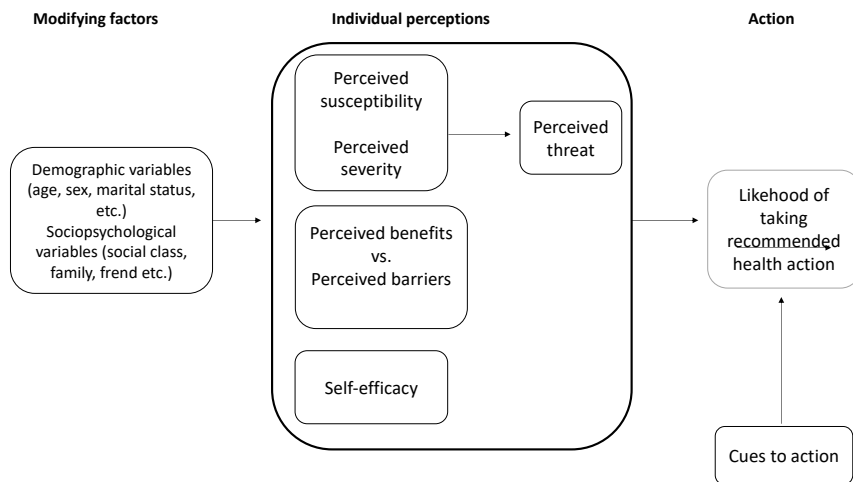
To be helpful, the chosen theory must fit the intended practice to be helpful (National Institute of Health NIH, 2005). The theories can be at the individual level, trying to explain and influence the individual's behaviour. Examples of widely used individual-level theories are the Health Belief Model, the Transtheoretical Model, or the Theory of Planned Behaviour (National Institute of Health NIH, 2005). In addition, interpersonal theories, such as Social Cognitive Theory, focus more on the person's mind or individual self, like attitude, knowledge, beliefs, and motivation. The next subchapters will introduce some behavioural theories that may influence patients' medication-taking behaviour.

#### **2.4.1 THE HEALTH BELIEF MODEL (HBM)**

The Health Belief Model (HBM) is one of the first and most widely used behavioural theories (Rosenstock, 1974). It was originally developed in the 1950s in the U.S. Public Health Service by a group of social psychologist aiming to understand why people fail when preventing the disease or adapting the screening test to spot the diseases in early states (Coleman & Pasternak, 2012; Janz & Becker, 1984; LaMorte, 2019; Morris et al., 2012; Rosenstock, 1966; Rosenstock, 1974; Shahrabani & Benzion, 2012).

According to the HBM, the person's behaviour depends on the belief of the benefits and obstacles related to the health behaviour (Janz & Becker, 1984; Rosenstock, 1966; Rosenstock, 1974). There is a possibility to predict the person's decision about the health behaviour with the factors that are affecting the incoming result (Figure 10). These factors are: 1) perceived susceptibility, i.e., how high the person thinks the risk of getting the disease is, 2) perceived severity, i.e., how severe the person assumes the disease to be, 3) perceived barriers, i.e., how major the person feels about the barriers to reach the health behaviour, 4) perceived benefits, how the person assume the possible health benefits to be when changing the health behaviour, and 5) cues to action, both internal and external factors that motivate the person to take action (Becker et al., 1974; Janz & Becker, 1984; Rosenstock, 1974). Self-efficacy, i.e., the person's capability to make the needed health behaviour changes, was not included in the original HBM. It was added to the HBM in the 1980s (Alsulaiman & Rentner, 2021; Becker et al., 1974; Janz & Becker, 1984; Morris et al., 2012).





**Figure 10** The Health Belief Model (HBM) (Becker et al., 1974; Becker et al., 1977; Champion & Skinner, 2008; Rosenstock et al., 1988)

According to the HBM, a person makes rational decisions about engaging in the desired behaviour (Becker et al., 1974; Chisolm et al., 2010; Janz & Becker, 1984; Rosenstock, 1966; Rosenstock, 1974). The person's desire to change health behaviours is based on his/her health expectations. A person may want to avoid the disease or get better if already sick if he/she believes that a specific health-related action will cure or prevent the disease. Therefore, HBM has been used to explain and predict medication compliance and adherence (National Institute of Health NIH, 2005). In the compliance study, especially the treatment of high blood pressure has been in focus because patients may not have any symptoms or feel sick, which may affect their willingness to take medicines (National Institute of Health NIH, 2005). Most lately, the HBM has been used to explain the people's intention to take the Covid-19 vaccination (Zampetakis & Melas, 2021).

However, HBM has its limitations. It does not consider the person's beliefs, attitudes, or other personal aspects linked as factors influencing person's health behaviour decisions (LaMorte, 2019; Orji et al., 2012). Social acceptance or environmental and economic factors are not considered either. HBM also presumes that every person has the same access to the information about the disease and that health efforts are everybody's priority.

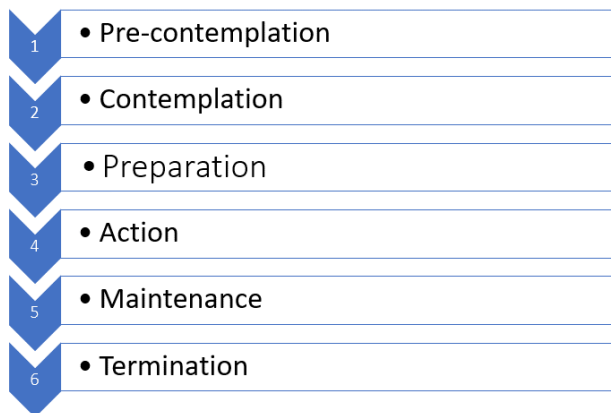
## 2.4.2 THE TRANSTHEORETICAL MODEL (TTM)

The transtheoretical model (TTM), also known as the Stages of Change model, was developed to understand the decision-making process related to people's health behaviour (Prochaska & DiClemente, 1983; Prochaska & Velicer, 1997).

The previous behaviour theory models were based on the idea that information is a dominant factor influencing health behaviours. However, the empirical studies showed that the link between knowledge and desired behaviour change was not straight. Even if people, for example, know that smoking harms their health, it was difficult for them to change their behaviour and stop smoking (Prochaska & DiClemente, 1983). TTM was developed based on observations showing that behaviour change is not a straightforward event, but rather a step-by-step process.

TTM can be used to describe how a person can overcome an addiction (LaMorte, 2019; Prochaska & DiClemente, 1983; Prochaska & Velicer, 1997). The model was initially developed in the 1980s to explain smoking cessation process and how some people could do it independently (Prochaska & DiClemente, 1983). TTM applies existing behaviour theories, intending to integrate the main features of various behavioural theories. For this reason, the theory is called TTM (National Institute of Health NIH, 2005).

The TTM model contains six different steps that lead to behaviour change: 1) pre-contemplation, in which the individual has no intention to make the change within six months, 2) contemplation, in which the individual has the intention to make the change in the next six months, 3) preparation where the individual is ready to make the change in the following months and have a plan how to do it, 4) action, where the change has recently happened, and it has been maintained for less than six months, 5) maintenance, where the change has happened for more than six months ago and is being mainly maintained to prevent relapse, and 6) termination, where the behaviour change is fully embraced and relapse no longer occur (Figure 11). The termination was not in the first version of the transtheoretical model in 1983 but was added to the end of the line in 1992 (Prochaska & DiClemente, 1983; Prochaska & Velicer, 1997).



**Figure 11** The Transtheoretical model (TTM), also known as the Stages of Change Model, adapted by Prochaska, DiClemente and Velicer (Prochaska & DiClemente, 1983; Prochaska & Velicer, 1997)

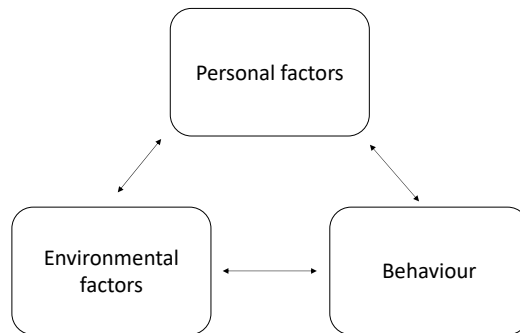
TTM has a motivational and person-centred approach in trying to understand the process of behavioural change (National Institute of Health NIH, 2005; Prochaska & DiClemente, 1983; Prochaska & Velicer, 1997). It seeks to explain changes in human behaviour that cannot be brought only by adding information TTM has been used to explain not only individual behaviour change but also organisational change (National Institute of Health NIH, 2005).

The limitation of the Transtheoretical Model is that it does not consider the individual's social context (LaMorte, 2019; UKK-Instituutti, 2020). In real-life practice, the individual does not systematically move from one stage of change to another. Nor does change necessarily require the individual to go through all the stages, nor does it require that one stage be taken in the same order. In addition, there may sometimes be times when a new habit is dumped, and the old one returns. Such flashbacks are not only a bad thing. They teach an individual to make realistic plans and prepare for the obstacles of everyday life.

### **2.4.3 THE SOCIAL COGNITIVE THEORY (SCT)**

The Social Cognitive Theory (SCT) tries to explain why individuals act as they do (Bandura, 1989). According to the SCT, the environment in which an individual grows influences behaviour and there is a constant dynamic interaction between the person, environment, and the person's behaviour (Almuqrin & Mutambik, 2021; Bandura, 1989; Bandura, 2001). The social cognitive theory is based on and evolved from the Social Learning Theory (SLT). The key part of the SLT was that a person learns when observing others, especially observing the benefits of the actions of others, not only learning from their own experiences (National Institute of Health NIH, 2005).

According to SCT people learn by observing others, and every proven behaviour can change a person's thinking (Bandura, 1989; Bandura, 2001). Hence, behaviour change occurs through personal factors and the social environment. Social norms, perceptions of the consequences of action and a sense of capability affect action. Self-efficacy affects what individuals decide to do, how motivated they are, and how they manage to maintain behaviours and avoid negative thoughts. Personal factors such as feelings and perceptions and environmental factors such as family and work influence human behaviour. The behaviour itself influences the environment and personal factors (Figure12).



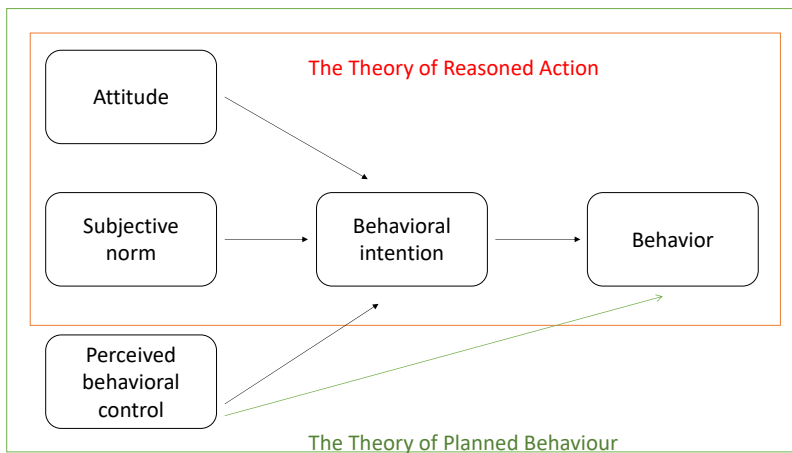
**Figure 12** The Social Cognitive theory (SCT) adapted by Bandura (Bandura, 1989)

When using the SCT to explain actions related to health, there are some limitations to consider. If the environment changes, it may not automatically change the person's behaviour (LaMorte, 2019). Also, the theory concentrates on the human capability to learn but does not consider the previous experiences, feelings or motivation that may affect the behaviour. All three factors in the SCT are considered equal, but there can be differences between the effect of the factors in real life.

#### **2.4.4 THE THEORY OF PLANNED BEHAVIOR (TPB) AND THE THEORY OF REASONED ACTION (TRA)**

The Theory of Planned Behaviour (TPB) is a widely used behavioural theory (Ajzen, 1991; Coleman & Pasternak, 2012; Morris et al., 2012). It is based on the theory of Reasoned Action (TRA) and is an improvement of the Information Integration theory trying to describe the difference between attitude and behaviour. According to TRA, the human's attitude and norm formulate an intention to behave that leads to behaviour. In the TPB, a person's perception of controlling their behaviour also influences behavioural intent and direct behaviour (Ajzen, 1991; Ajzen & Driver 1991; Bosnjak et al., 2020). According to TPB, behaviour management is an essential factor in the model besides the intent. It is related to the patient's previous experiences. These factors directly affect the patient's self-confidence, likely leading to better success if the self-confidence is high. If the patient is optimistic about the change, believes that others will approve the behaviour change and receives support, the change is more likely to happen (Figure 13). The TBP

model has been used to explain different health behaviours such as smoking cessation.



**Figure 13** The Theory of Reasoned Action (TRA) and the Theory of Planned Behaviour according (TPB) to Ajzen 1991.

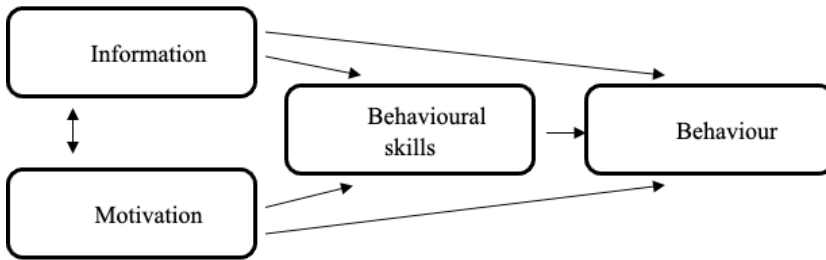
The TBP model also has limitations (Conner et al., 2013; Munro et al., 2007; Sheeran et al., 2013; Sniehotta et al., 2014). It does not consider the other things that may affect the desired behaviour and motivation to change, like fear or previous negative experiences. Despite the intent, the patient may not have the recourses to make the change.

#### 2.4.5 THE INFORMATION-MOTIVATION-BEHAVIOURAL SKILLS MODEL (IMB)

The Information-motivation-behavioural skills model (IMB) is introduced in the WHO report along with e.g. the Stages-of-Change model and Behavioural (learning) theory (World Health Organization, 2003). IMB model is a conceptualized theoretical model to explain health behaviour (Fisher & Fisher, 1992). IMB has been originally developed based on previous behaviour theories to explain the psychological factors related to HIV-risk behaviour (Bandura, 1989; Evon et al., 2015; Fisher & Fisher, 1992; World Health Organization, 2003; Yang et al., 2020).

The IMB model consist of three parts of human behaviour that influence behaviour change: health-related information, motivation, and behavioural skills (Evon et al., 2015; Fisher & Fisher, 1992; Fisher et al., 2003). According to the IMB model, information includes knowledge about the facts that affect health and automatic decisions to act after the learned information. Motivation includes both personal motivation to change the own attitude and

behaviour to reach positive outcomes, and social motivation to get support and fit into the social frame. Both information and motivation are needed to achieve the required behavioural skills (Figure 14). When a patients have enough information, are motivated to act, and have enough behavioural skills to achieve the behaviour, they will reach the wished goal with positive health outcomes. On the contrary, if the patient lacks knowledge, is not motivated, and has insufficient behavioural skills, he/she will have risk behaviour related to health and experiences unfavourable health results.



**Figure 14** The Information-Motivation-Behavioral skills model of Health Behavior (Fisher & Fisher, 1992)

According to IMB model, the information, motivation, and behavioural skills should be specific and directly related to preferred health behaviour (Fisher & Fisher, 1992; Fisher et al., 2003; World Health Organization, 2003). The model has been successfully implemented in different health behavioural interventions. Adequate information is crucial when changing behaviour, but the expected outcome will be lacking without motivation and behavioural skills. Also, a well-motivated patient may have a lack of information, or a well-informed patient may have a lack of motivation. If the patient has both motivation and knowledge, the desirable health behaviour may improve treatment adherence.

#### **2.4.6 ADHERENCE TO LONG-TERM THERAPIES, THE RECOMMENDATIONS OF WORLD HEALTH ORGANIZATION**

The WHO's recommendations of adherence provides a basic understanding of elements of the previous behavioural theories such as the Health Belief Model, Social Cognitive Theory, and the Theory of Planned Behaviour. According to WHO, it is necessary to understand the essential behavioural aspects and behavioural change models when treating patients with chronic conditions (World Health Organization, 2003). Successful treatment outcomes depend on the patient's adherence to treatment. Even the best treatment can become ineffective if the patient is not acting as assumed. Interventions based on behavioural theories seem to be effective in managing many diseases and can

change patients' behaviours and even the behaviours of healthcare professionals or how health systems work.

According to WHO, adherence is a complicated behavioural process influenced by many complementary contributing factors (World Health Organization, 2003). These include the patient's characteristics and the patient's surroundings such as social support and the health care system, as well as the illness and its treatment (World Health Organization, 2003). The medical treatments vary from disease to disease, and so does the requirement to change the behaviour. Patients may have different social, physical, and mental resources to manage the treatment or required behavioural changes, for example, modifying diet or quitting smoking. That is why adherence to treatment should be seen as a prolonged treatment journey rather than a one-time experience trying to face the behavioural changes required by the disease (Kekäle, 2016). It is also essential to specify what can be seen as a sufficient adherence rate to each treatment and how intensive the behavioural change should be (World Health Organization, 2003).

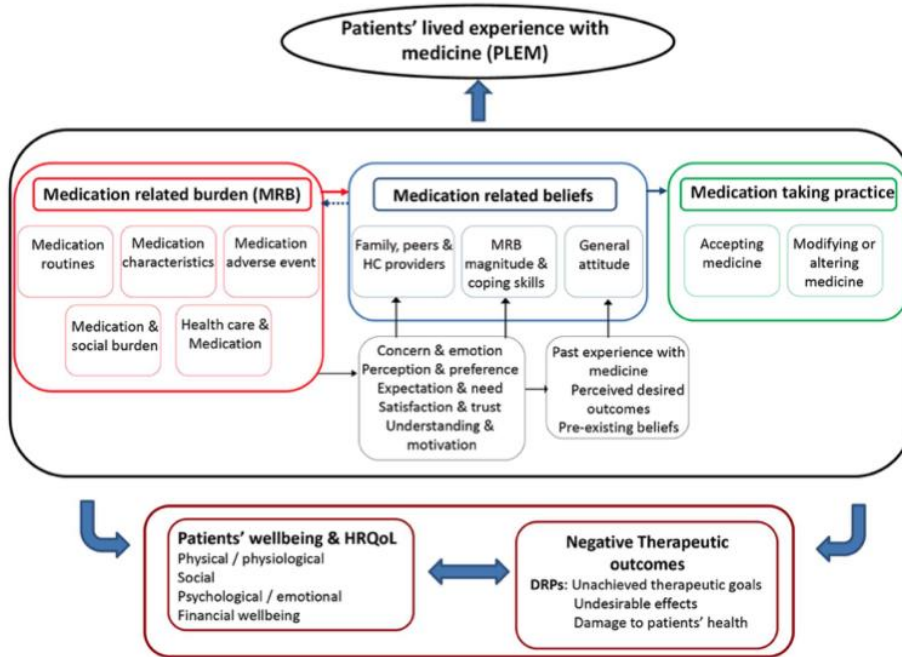
WHO highlight the provider's behaviour, health system factors and patient attributes as critical behavioural determinants of adherence (World Health Organization, 2003). The most important determinants of adherence are patient-provider communication. However, today patients receive information, and disinformation, increasingly from the internet, outside of the patient-provider relationship, which challenges healthcare. More research is needed to find out how the internet and digital technology may have impacted medication adherence.

According to WHO, there is no specific patient attributes or behavioural pattern that can predict non-adherence or adherence to treatment (World Health Organization, 2003). Almost all the patients have difficulties adhering to treatment, especially if there are some self-management requirements. A patient's beliefs and expectations of the treatment affect success. The factors contributing to adherence seems to be the susceptibility to the illness, disease severity, self-efficacy, and ability to control health behaviour. If the symptoms decrease rapidly due to treatment, it may increase the adherence to treatment or do quite the opposite. It seems that only increasing knowledge over illness is not sufficient to increase adherence, although it seems to increase it in acute illnesses.

#### **2.4.7 MEDICATION-RELATED BURDEN (MRB) AND PATIENTS' LIVED EXPERIENCE WITH MEDICINE (PLEM) INFLUENCING ADHERENCE**

A new viewpoint related to influencing factors affecting the use of medicines came into the discussion when Australian researchers published a meta-synthesis on the medication-related burden (MRB) and patients' lived experience with medicine (PLEM) based on qualitative studies in 2016 (Mohammed et al., 2016). According to the new conceptual model, the

patient's lived experiences with medicines may influence medication-taking practices and treatment outcomes by causing medication-related burden (Mohammed et al., 2016). MRB can be related to 1) the burden of medication routines, e.g., how to manage the medication in daily life, 2) the burden of medication characteristics, e.g., pill size or shape, number of medicines, or exchange of medication brands, 3) the burden of adverse events, e.g., its impact on everyday life, 4) medication-associated social burden, e.g., how the medicines use impacts social life, such as holidays or visiting friends, or social stigma, and 5) healthcare-associated medication burden, e.g., complex healthcare system or financial aspects (Figure 15). According to the conceptual model, the medication-related burden affects the patient's health and well-being, beliefs, and behaviour towards medicines. They, in turn, may result in non-adherence and unreachable therapeutic outcomes.



Abbreviations: DRPs= Drug Related Problems, HC = Health care, HRQoL= Health related quality of life

**Figure 15** Conceptual model of Patients' Lived Experience with medicines PLEM (Mohammed et al., 2016)

The conceptual model of Patients' Lived Experience (PLEM) provides a new systemic perspective on poor medication engagement and its contributing factors (Mohammed et al., 2016). In Finland, PLEM has been operationalised and validated to form a set of 10 statements (Mikkola, 2021) that was included



in the biannual population survey called Medicines Barometer by the Finnish Medicines Agency in 2021 (Jyrkkä et al., 2021).

### **3 AIMS OF THE STUDY**

This study aimed to enhance understanding of the complexity of medication adherence by studying why patients do not take their medication as prescribed. The goal was to systematically collect research evidence on the factors influencing medication adherence by using studies that applied qualitative methods (Study I) and by exploring primary care physicians' and patients' insights in medicine taking and adherence (Studies II and III).

The specific objectives of the study were (the number of the original publication is provided in brackets):

- To systematically gather research evidence on the factors contributing to medication adherence in patients with a chronic condition (I)
- To investigate general practitioners' insights into barriers and facilitators to medication adherence in primary care (II)
- To identify reasons for non-adherence in patients with multimorbidity in primary care and to start building up a conceptual framework for factors contributing to non-adherence (III)

## 4 MATERIALS AND METHODS

In this study, both qualitative and quantitative research methods were applied although the emphasis is on qualitative research (Table 1). Study I was a scoping review of qualitative studies, Study II applied a focus group discussion method for primary care physicians and Study III is a study protocol for quantitative study based on pharmacist-patient interaction during medication reconciliation in primary care clinics. Study I collected the existing research evidence on barriers and facilitators related to medication adherence using the qualitative research method. Study II explored potential challenges and solutions related to medication adherence identified by primary care physicians in real-life clinical practice. Study III is a research protocol for building up a conceptualised framework identifying contributing factors to medication adherence.

**Table 1** Outline of the study (I-III).

STUDY	STUDY AIMS	METHODS	DATA SOURCE	ANALYSIS
I	To understand the barriers and facilitators to medication adherence from patient's perspective	Scoping review based on systematic literature search following the PRISMA-ScR guideline	Original peer-reviewed qualitative studies (n=89) from selected databases MEDLINE (Ovid), Scopus, and the Cochrane Library from January 2009 to June 2021	Qualitative content analysis
II	To examine GPs' insights into non-adherence and ways of overcoming it	Focus group discussion	General practitioners (n=16) in primary care interviewed in 4 focus groups	Qualitative content analysis
III	To identify reasons for non-adherence for building up a conceptual framework of these reasons in primary care (a study protocol)	Patient interview during medication reconciliation	Patients (approx. n=250) in primary care	Quantitative analysis, descriptive statistical analysis

## **4.1 FACTORS CONTRIBUTING TO MEDICATION ADHERENCE IN PATIENTS WITH A CHRONIC CONDITION: A SCOPING REVIEW OF QUALITATIVE RESEARCH (STUDY I)**

### **4.1.1 SEARCH STRATEGY**

The literature search for eligible qualitative studies was conducted on September 23, 2019, using MEDLINE (Ovid), Scopus, and the Cochrane Library, with the assistance of an information specialist at the Helsinki University Library. The search was updated on June 9, 2021. Articles published from January 2009 to June 2021 were included in the study to focus on the most recent publications. We limited the article search to English language studies and articles published in peer-reviewed journals. A wide range of search terms related to medication, drug, medicine, adherence, non-adherence, compliance, non-compliance, patient, experience, fear, beliefs, knowledge, attitudes, behaviour, communication, reason, and cause was used (Study I, Figure I). Relating to the study design and methodology, the search terms were qualitative, interview, focus group, questionnaire, observation, study, and research.

### **4.1.2 INCLUSION AND EXCLUSION CRITERIA**

The qualitative studies with the primary focus on understanding the complexity of medication adherence as described by patients who were being treated for chronic conditions were included (Table 2). The original qualitative studies and systematic reviews were also included if the study population consisted of people  $\geq 18$  years and had at least one chronic condition. As the primary focus was on patients' experiences and attitudes towards medication adherence, control groups were not required. The use of qualitative methods both for data collection and data analysis was mandatory. The focus of the study was to understand the phenomena in general, so we excluded studies in which a primary study population consisted of children or adolescents under 18 years, or patients with an acute illness who were pregnant or who were drug or alcohol users. Also, conference papers, studies applying quantitative methods or mixed methods, as well as studies that collected data using qualitative methods, but in which data was analysed using quantitative methods, were excluded. Articles written only in English were included.

**Table 2** The inclusion and exclusion criteria of the study articles (Study I)

	<b>Inclusion criteria</b>	<b>Exclusion criteria</b>
<b>Population (P)</b>	<ul style="list-style-type: none"> <li>• 18 years or older patients with at least one chronic condition</li> </ul>	<ul style="list-style-type: none"> <li>• &lt;18 years old patients, patients with an acute illness who were pregnant or drug or alcohol users</li> </ul>
<b>Control</b>	<ul style="list-style-type: none"> <li>• Not required</li> </ul>	
<b>Time</b>	<ul style="list-style-type: none"> <li>• Published from January 2009 to June 2021</li> </ul>	<ul style="list-style-type: none"> <li>• Published before 2009</li> </ul>
<b>Concept (C)</b>	<ul style="list-style-type: none"> <li>• The patients' experiences, attitudes, and opinions towards medication adherence</li> <li>• Different settings and methods were accepted</li> <li>• The use of qualitative methods both for data collection and data analysis</li> </ul>	<ul style="list-style-type: none"> <li>• The study does not include patients' experiences, attitudes, or opinions towards medication adherence</li> <li>• Conference papers, quantitative methods, mixed methods studies, studies that collected data using qualitative methods, but in which data was analysed using quantitative methods</li> </ul>
<b>Context (C)</b>	<ul style="list-style-type: none"> <li>• Outpatient or community settings, outpatient clinics</li> </ul>	<ul style="list-style-type: none"> <li>• Patients' medicines taking in hospital setting</li> </ul>
<b>Other</b>	<ul style="list-style-type: none"> <li>• Published in English</li> <li>• Full text available at the University of Helsinki Library</li> </ul>	<ul style="list-style-type: none"> <li>• The publication is not available</li> </ul>

#### 4.1.3 STUDY SELECTION

The systematic searches for eligible articles retrieved 4,404 studies (Figure 16). After duplicates were removed, three researchers independently screened the titles and abstracts for eligibility using the online software, Covidence. If one or two reviewers identified the article as relevant, a full-text review was carried out. All disagreements were solved via discussions and reaching a consensus. After the title and abstract screening, two reviewers independently screened the full text of selected articles. Disagreements were resolved through discussions with the third reviewer for final inclusion. The articles were selected in several parts, which allowed the reviewers to have a regular discussion of the eligibility criteria, ensuring the same understanding of the criteria, and the criteria remaining the same throughout the article selection phase. As in many scoping reviews, the goal was to describe the phenomena surrounding patients and medication adherence; the risk of bias of included studies was not assessed.

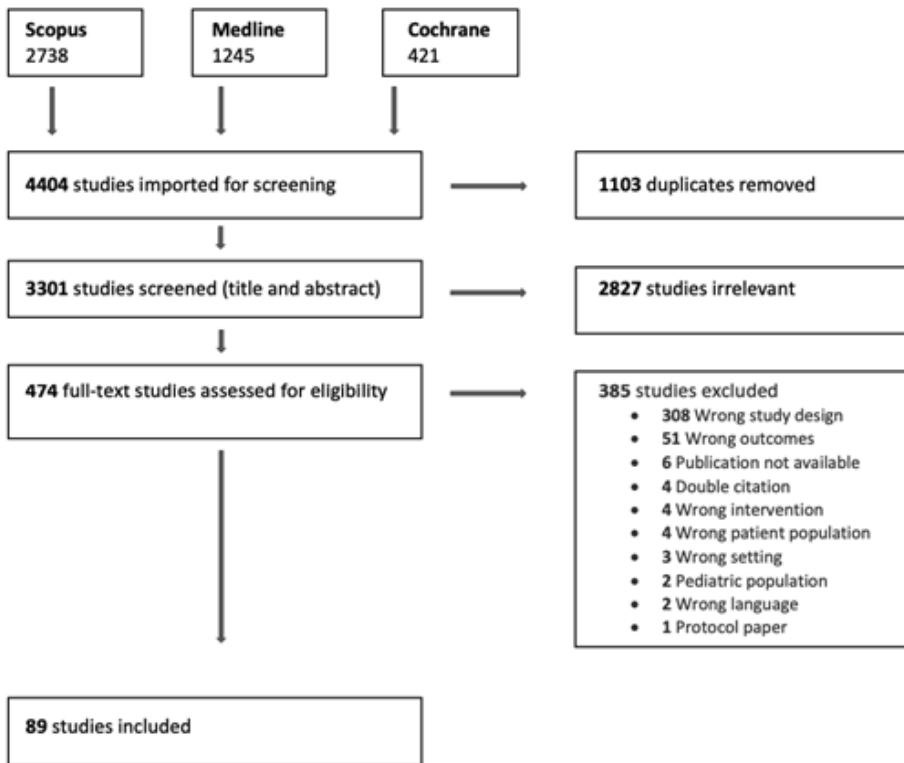


Figure 16 PRISMA flow diagram of the article selection process (Study I)

#### 4.1.4 DATA EXTRACTION

The data extraction template was constructed using the Covidence online platform. Two reviewers independently extracted the data, and the results were reviewed and verified by both reviewers for quality and clarity. The discrepancies were resolved by discussions and reaching consensus. The data extraction template first focused on the study design, illness, context, and concept of the studies, as well as barriers and facilitators to medication adherence.

After extracting a third of the studies, a more specific classification for barriers and facilitators to medication adherence was constructed, and the material was re-extracted from the beginning with the wider list of items. This classification was further elaborated during the analysis of the results. In the extraction process, patients' knowledge of their illness and its treatment were noted. Motivation and behaviour skills seemed to be essential and correlated to good medication self-management during the analysis. Therefore, the IMB model was applied as part of the classification of facilitators to medication adherence (Fisher & Fisher, 1992; Fisher et al., 2003).

## 4.2 BARRIERS AND FACILITATORS TO MEDICATION ADHERENCE: A QUALITATIVE STUDY WITH GENERAL PRACTITIONERS (STUDY II)

### 4.2.1 STUDY SETTING, PARTICIPANTS AND STUDY DESIGN

The study was conducted in the Kirkkonummi Health Centre, a municipal public health service for the 36,000 inhabitants of Kirkkonummi, Southern Finland. Kirkkonummi Health Centre is a single centre administratively but operates in three venues: the main health centre in Kirkkonummi centre and two smaller regional health centres in the Kirkkonummi area (in Masala and Veikkola). GPs working in the health centre were invited to participate in focus group discussions, that were held in all the three regional service areas between October 2010 and May 2011. The qualitative design was chosen to understand GPs' perceptions of medication adherence and the problems GPs thought patients might have experienced in following instructions for their medication treatment.

### 4.2.2 INTERVIEW GUIDE, DATA COLLECTION, AND ANALYSIS

In this study, a topic guide of semi-structured questions was used to allow the GPs to come to the topic from a personal point of view (Table 3). Two convenors ran the focus groups: a moderator (pharmacist) and a facilitator (either MD or another local GP). The interviewees knew the backgrounds of the researchers.

**Table 3** Topic guide for the focus group discussion (Study II).

All questions were open-ended and aimed at encouraging discussions
1. In your opinion, how active are your patients in managing their chronic conditions? How do they succeed with their self-management?
2. How do you coach their self-management?
3. If it were possible to refer some patients to a pharmacist for a consultation, what type of patients would you refer?
4. Which are those groups of patients that have the largest problems with self-management? Do they have something in common?
5. How do you help patients to commit to their treatments? What are the challenges?

6. How do you find the inter-professional collaboration in the coordination of care?

In this study, purposive sampling was used. The interviews were audiotaped and transcribed verbatim. The GPs were recruited in the focus groups by email invitation, and the recruitment process was continued until the data was saturated. Age, gender, experience, and workplace were considered in the recruitment process. Because of workload or absence from work, all the invited doctors could not participate in the study.

The data were analysed by conventional inductive content analysis (Silverman, 2013). The meaningful units of the transcripts were first manually coded. The following categories were derived from these units and finally condensed during the analysis. The results and the conclusions were confirmed by discussion and consultation.

### **4.3 WHY MEDICINES ARE USED DIFFERENTLY THAN PRESCRIBED: A PROTOCOL FOR A PROSPECTIVE PATIENT-ORIENTED OBSERVATIONAL CASE STUDY TO INVESTIGATE REASONS FOR NON-ADHERENCE IN PRIMARY CARE (STUDY III)**

#### **4.3.1 STUDY DESIGN AND SETTING OF THE STUDY**

The study is a prospective observational case study that will be carried out in the public primary care clinics in the city of Vantaa, located in the capital region of Finland. The research method will contain the pharmacist-conducted medication reconciliation, including a patient interview in a 30-minute appointment. The pharmacist-conducted medication reconciliation practice was implemented in 2019 in Vantaa and is in routine use. The data will be collected through patient interviews during pharmacist-led medication reconciliation. The conclusions will be confirmed by discussion between all authors. The data will be analysed and reported in a peer-reviewed scientific journal.

#### **4.3.2 STUDY CONTEXT, POPULATION AND REQRUITMENT PROCEDURES**

The data will be collected in four public outpatient clinics in Vantaa during medication reconciliation conducted by pharmacists. Physicians, nurses, and pharmacists will identify patients who are eligible for this study (Table 4). Patients 55 years of age or older will be included, as they most commonly have multiple medications and illnesses. The patient will be provided with both oral and written information about the study. If the patient is willing to participate



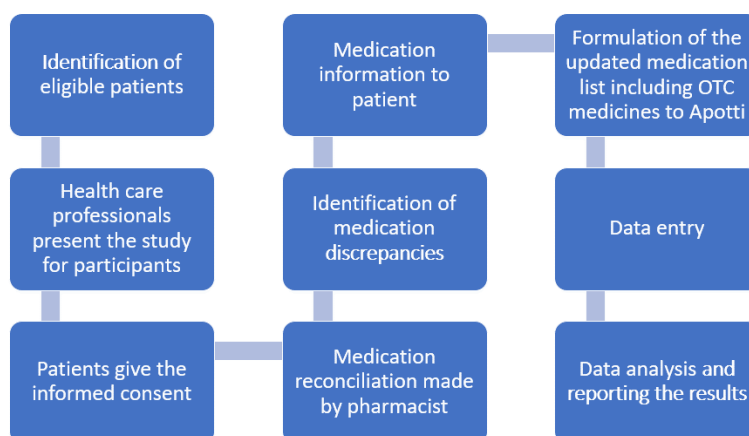
and sign the informed consent, they will be included in the study. The study will include 250 patients who attend the public outpatient clinics in Vantaa, Southern Finland. Since this is an observational cross-sectional study, we will not perform sample size calculations but estimate that 250 patients will allow enough observations for adequate and sound conclusions.

**Table 4** Inclusion and exclusion criteria for the study participants in Study III.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> <li>• Males and females (Finnish speaking)</li> <li>• Age ≥ 55 years</li> <li>• Patients with multimorbidity (more than one chronic disease)</li> <li>• Living at home and managing daily life independently</li> <li>• Willing to take part and sign the informed consent</li> </ul>	<ul style="list-style-type: none"> <li>• The patient does not understand Finnish</li> <li>• Under 55 years old</li> <li>• Diagnosed Alzheimer or another cognitive disorder</li> <li>• Needs help to manage daily life</li> <li>• End of life care</li> </ul>

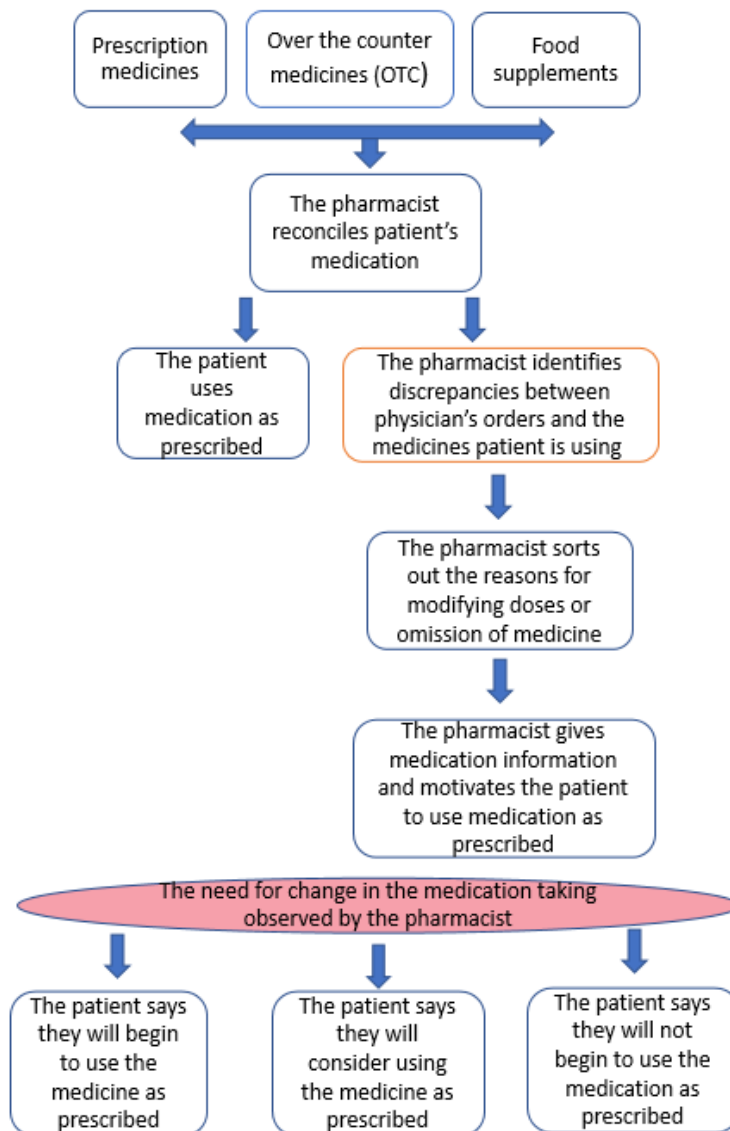
#### 4.3.3 MEDICATION RECONCILIATION INTERVENTION AND DATA COLLECTION

Healthcare professionals (physicians, nurses, and pharmacists) present the study to patients (oral and written information) who meet the inclusion criteria and give written informed consent. The patients will have time to consider their participation (Figure 17).



**Figure 17** The study process. It starts with identifying eligible patients willing to participate and ends with the analysis of the collected data and reporting the results.

The data will be collected during the pharmacist-led medication reconciliation and entered in the pseudonymized form to the secured HUSeCRF database (Figure 18, HUS electronic case report form presented in Table 5). All the pharmacists will use the same interview and documentation technique (Figure 18, Table 5). Medication reconciliation will take place upon admission to the public outpatient clinic, usually before an appointment with a physician. The pharmacist will, with the patient, go through all medicines prescribed to him/her according to the Apotti database (Oy Apotti Ab), and also consider non-prescription medicines, and food supplements to assess the actual medicines used by the patient (Figure 18). If the pharmacist identifies medication discrepancies between the physicians' prescriptions and the patient's self-reported use of the medicines, the pharmacist will ask the patient about the reasons for adjusting the medication. Based on this process, the pharmacist will formulate the updated medication list, also including clinically appropriate non-prescription medicines in the patient record system, Apotti, where the physician will verify it.



**Figure 18** Flow chart of the pharmacist-conducted medication reconciliation process at the public outpatient clinic in the city of Vantaa and which will be used as a data collection point for this study (III).

**Table 5** Variables that will be documented to the data collection template.

<b>Characteristics of the patients and outpatient clinic</b>	<b>The data related to patients' diseases and medications</b>	<b>Medication discrepancies</b>
Subject ID	Diagnoses	Medication specific discrepancies (yes/no)
Age	The number and type of prescription medicines	The generic name and dosage form of the medicine the patient is using otherwise than prescribed
Sex	The number and type of non-prescription medicines	The reasons for discrepancies reported by the patient
The outpatient clinic	Total number of all medicines	Has the patient used medications as prescribed? (more/less than prescribed)
Date of appointment	The year when the medication list has last been reconciled	Will the patient consider taking the medication as prescribed after the discussion with the pharmacist? (yes/no)

If the pharmacist identifies any medicine-taking problems or barriers, the pharmacist will clarify the possible misunderstandings or concerns influencing medication use by discussing with and explaining to the patient how to self-manage their medication appropriately and safely. The barrier can be, for example, unintentional non-adherence such as forgetting to take the medicine or poor medication administration techniques. The pharmacist will find the best solution from the patients' perspective together with the patient. The solution may be, for example, to go through with the patient the correct medication taking technique or find out the appropriate memory aid. If a barrier is difficult for the patient to overcome, the pharmacist will report it to the physician. If the pharmacist identifies urgent drug-related problems (DRPs), the pharmacist will inform the clinicians about them immediately. The urgent DRPs can include for example inappropriate prescribing, drug interactions, severe adverse effects or medication that is potentially inappropriate for the patient.

#### **4.3.4 ANALYSIS**

The data will be documented in a structured format in the HUSeCRF database (Table 5) and analysed by descriptive statistical analysis. The quantitative analysis will focus on the following variables and measures: 1) the number of medication discrepancies between physicians' prescription orders and patients' self-reported medication use, 2) type of discrepancies, 3) the list of medicines most commonly reported to have been taken differently than prescribed (identification of high-risk medicines for non-adherence), and 4) reasons for taking medicines differently than prescribed. The qualitative part of the analysis will focus on 5) forming a preliminary conceptual model for patient-reported reasons for non-adherence.

##### **4.3.4.1 Quantitative analysis**

We will calculate the prevalence of discrepancies from the data and how many discrepancies we will find altogether (frequency, %). We will categorize the types of discrepancies, e.g., omissions, duplications, contraindications, unclear information, changes (n, %). The occurrence of discrepancies (n, %) according to the therapeutic group and active ingredient will be analysed using Anatomical Therapeutic Chemical (ATC) Categorization (World Health Organization Collaborating Centre for Drug Statistics Methodology (WHOCC), *Last updated: 2018-02-15*). The most common (top 10) drug substances and ATC-groups of reported discrepancies will be analysed to identify the medicines at high risk of non-adherence. The quantitative data will be analysed using IBM SPSS Statistics 26 software.

##### **4.3.4.2 Qualitative analysis: constructing the preliminary conceptual model of reasons for non-adherence, the iceberg model**

We will analyse the small amount of qualitative data, which the pharmacist has written from the patient's reasoning uncoded. We will further synthesise our qualitative findings with our quantitative findings into meta-synthesis, where the results of this study and two previous qualitative studies (Study I and II) are combined to construct a preliminary conceptual model of reasons for non-adherence.

Our aim is to develop an iceberg model in which the medication discrepancies are the tip of the iceberg, a visible part, and the underlining reasons for the discrepancies are hidden below the surface. According to this model, the more product-specific and in-depth reasons for non-adherence can be identified during the medication reconciliation process with the patient. This is important because these underlying reasons for adjusting or stopping taking medicine may not be discussed with the patient during a routine doctor's appointment but are crucial for medication-taking behaviours. Understanding the underlining reasons for non-adherence from the patient's

perspective provides the possibility to support the patient most effectively and build systemic defences in the medication use processes in a way that will facilitate appropriate medication taking.

#### **4.4 RESEARCH ETHICS**

All the studies I-III were conducted in accordance with good scientific practice guidelines and the Declaration of Helsinki (Finnish National Board on Research Integrity TENK, 2019).

Study I was based on published research articles, to which we had access either as open-access publications or through the Helsinki University Library.

For Study II the Board of the Kirkkonummi Health Centre granted the study permission. Based on the Finnish research ethics regulation, pre-evaluation by the ethics committee was not required as the study was health services research not involving patients (Finnish National Board on Research Integrity TENK, 2019). All participants were healthcare professionals and gave their written informed consent for voluntary participation.

Study III has been approved by the Ethics Committee of Helsinki University Hospital (protocol code HUS/1037/2020) and the Institutional Review Board of Vantaa (protocol code VD/4977/13.00.00/2020). Informed consent will be obtained from all patients involved in the study. Current data protection guidelines are also followed.

## **5 RESULTS**

### **5.1 CHARACTERISTICS OF INCLUDED STUDIES (STUDY I: SCOPING REVIEW)**

Eighty-nine (89) peer-reviewed articles were included in the scoping review (Study I, Figure 16). The study design in all the articles was qualitative and carried out in community or outpatient settings. The context of most of the studies was an outpatient setting, either in primary or secondary care. The studies' concept varied from the rationale of taking medication to understanding patients' beliefs, practices, and reasons for non-adherence. The studies were conducted in 36 different countries: the United States (n=19), the United Kingdom (n=10), South Africa (n=4), Australia (n=3), Canada (n=3), Malaysia (n=3), the Netherlands (n=2), Sweden (n=2), Indonesia (n=2), Iran (n=2) and one study from each of the following countries: Belgium, Norway, Portugal, Spain, Switzerland, Germany, Ireland, France, Italy, Singapore, New Zealand, Taiwan, Jordan, Pakistan, Kuwait, Saudi-Arabia, Vietnam, Uganda, Tanzania, Kenya, Eswatini, Ethiopia, Namibia and Lesotho. There was one study in which both Nepal and Australia were involved and one study in which Italy, Portugal, and Poland were involved.

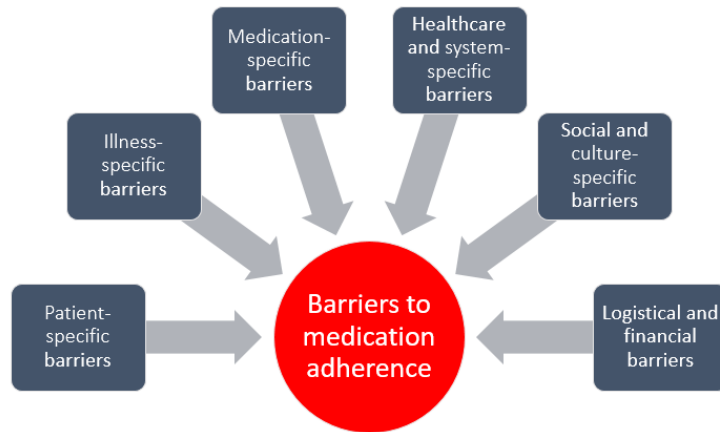
The scoping review covered 13 systematic reviews on medication adherence (Article I: Table A3). Seven of them focused on patients with cardiovascular disease or type two diabetes, one on patients with rheumatoid arthritis, one on patients with breast cancer, two on patients with chronic kidney disease or kidney transplants and two with no specific illness.

There were 17 studies that had a behaviour theory-based approach to medication adherence (Article I: Table 1). The theories that appeared were Andersen's Behavioural Model, Roy Adaptation Model, Common-Sense Model of Self-Regulation, Social-Ecological Model, Therapeutic Alliance, Dowell's Therapeutic Alliance Model and Leventhal's Common-Sense Model, Health Literacy Pathway Model, ABC Taxonomy and Three-Factor Model, Health Belief Model, Naturalistic Decision Model and Stages of Change Model. One of the studies did not have a theory-based approach in the beginning, but many of the findings fitted together with the Information–Motivation–Behaviour Model.

### **5.2 BARRIERS TO MEDICATION ADHERENCE (STUDY I)**

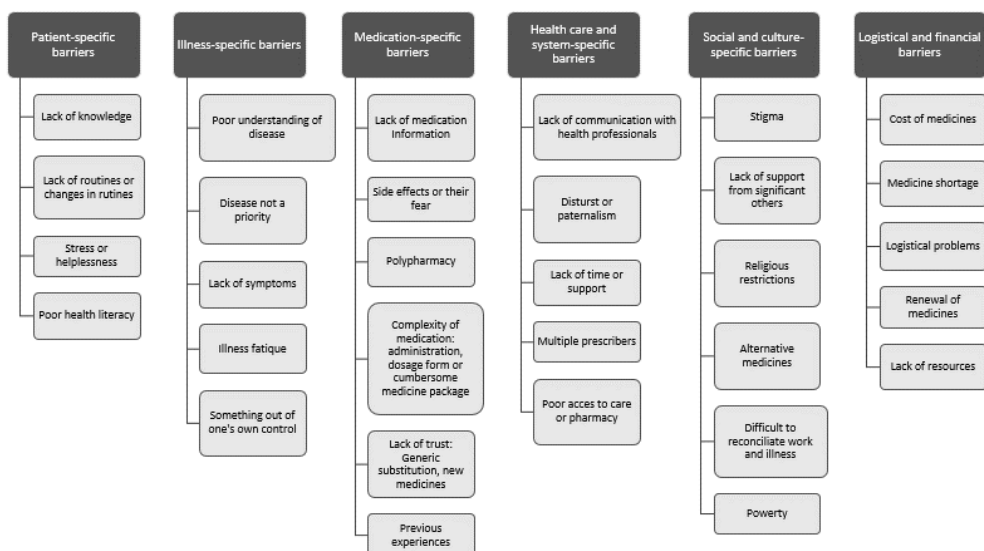
The studies included in the scoping review (n=89) reported more barriers than facilitators to medication adherence (Study I). Six subject areas with subcategories were inductively identified related to barriers to medication adherence (Figure 19). The classification was data-driven and compiled after

extracting evidence from a third of the studies. After that the data were re-extracted from the beginning with the improved categorization (Figure 19 and Figure 20).



**Figure 19** The identified key barriers to medication adherence based on the included qualitative studies (n=89).





**Figure 20** Subcategorization of barriers to medication adherence arising from the include qualitative studies (n=89).

## 5.2.1 PATIENT-SPECIFIC BARRIERS

Patients may lack information or knowledge to understand their medication regimen properly. At the beginning of their disease, the patient may have received medication information and adherence counselling but then no follow-up, leading to patients being forgetful (Axelsson et al., 2015). If the patient is extremely ill at the time of counselling, it may be challenging to adapt the information provided, and misunderstandings can occur.

Patients can have poor awareness about the need to take medication as prescribed, and they tend to adjust their doses according to their understanding (Al-Qazaz et al., 2011b; Meraz, 2020). They may have incorrect or erroneous beliefs about medication (Tranulis et al., 2011). They can lack motivation and think the disease is something they cannot control (Ågård et al., 2016). A lack of routines, being busy, or changes in practices for special occasions are risk points for medication adherence and can easily lead to missing doses or sleeping through dosing times (Evon et al., 2015).

Stress and helplessness can affect medication adherence (Shaw et al., 2018). Different administration routes can be a barrier and changing oral tablet form to injectable dosage form can increase non-adherence (Bockwoldt et al., 2017). Injectable drugs may feel unpleasant, and a patient may think injecting will destroy the body (Ågård et al., 2016). Patients' physical disabilities can also be a barrier when administering the medicine, which may require good eyesight or a steady hand (Stryker et al., 2010). Poor health literacy increases the adherence problem, and there can also be difficulties in understanding written language, especially if it is not written in a patient's mother tongue (Huang et al., 2020; Schatz et al., 2019). Comorbidity may increase the probability of non-adherence (Ho et al., 2017).

### **5.2.2 ILLNESS-SPECIFIC BARRIERS**

Contrary to healthcare professionals' expectations, the disease is not always the priority for the patient (Bockwoldt et al., 2017; Rowell-Cunsolo & Hu, 2020; Ågård et al., 2016). It can be an unwanted episode, but not as important as other matters in life. A patient may have an adverse emotional reaction to the illness and judge life before the illness as more valuable. The required life changes may not be a priority. Patients may also rationalise that the disease is not so severe that they need to take their medication precisely as prescribed. Choosing to take or not to take medicines may depend on how serious the patient assesses their situation to be (Koh et al., 2018).

Sometimes the challenge is that the patient has not accepted the illness or thinks it is someone else's fault. The negative beliefs about illness or multiple diseases can increase barriers to medication adherence though it can differ from condition to condition (Jarab et al., 2018). Cancer can be understood as more life-threatening than diabetes, although diabetes can have grave consequences when not treated as required. The disease itself can cause fatigue and overwhelming tiredness, which negatively impact adherence (Gassmann et al., 2016).

### **5.2.3 MEDICATION-SPECIFIC BARRIERS**

At the time of the onset of the illness, patients may lack information of their condition or of the medication they need (Habte et al., 2017; Harrold et al., 2010). They can feel confused about the illness duration and prognosis (Garavalia et al., 2009; Garavalia et al., 2011). Treatment can often seem time-consuming and complex to them (Hogan et al., 2014; Jarab et al., 2018). Taking medication can be associated in patients' minds with being sick, which can negatively influence adherence (Bockwoldt et al., 2017). Difficulties in integrating medication into daily life can prevent patients from taking medication as prescribed. Working life may require shift work, and night shifts may make it difficult to have regular routines (Vaanholt et al., 2018). Besides, the illness may not have visible symptoms, and patients may not feel unwell

(King-Shier et al., 2017). Patients also fear that once they start a medication, this means they must continue taking it throughout their life (Van Loggerenberg et al., 2015).

If the medication information for a patient is inadequate and does not meet the patient's needs, they may use alternative information sources such as the internet (Hayden et al., 2015). A patient information leaflet in a medicine package may be difficult to understand. Warnings of side effects in the package sometimes make a patient decide not to take the medicine. Generic substitution may cause suspicions about the effect of a generic drug compared with the original product, thereby negatively affecting adherence (Pettersen, Fridlund, Bendz, Nordrehaug, Rotevatn, Schjøtt, et al., 2018). Media can also influence opinions of the quality of drugs (McKillop & Joy, 2013a). The desire of patients to self-regulate their lives may sometimes lead them to use non-prescription drugs instead of prescribed medicines (Kobue et al., 2017).

Struggling with side effects seems to be a common barrier to medication adherence. Fear and the thought of not being safe with their medication may keep patients from taking it (Habte et al., 2017). There are also physical barriers surrounding medication-taking: the size of the tablet can make it difficult to swallow, there can be unpleasant metallic after-taste or throat pain (Gassmann et al., 2016). Needle phobia can prevent injecting insulin. A change from oral tablets to injectable drugs can be a drawback for patients (Bockwoldt et al., 2017).

#### **5.2.4 HEALTHCARE AND SYSTEM-SPECIFIC BARRIERS**

Poor access to healthcare and long waiting times causes poor medication adherence (Ho et al., 2017). Fragmentation of treatment between multiple prescribers, a lack of communication between a general practitioner and a community pharmacist and poor coordination between primary, secondary and tertiary care can lead to treatment problems. These, in turn, can lead to the discontinuation of care (Ho et al., 2017; Jeragh-Alhaddad et al., 2015; Souter et al., 2014).

A lack of support and empathy from healthcare providers and a paternalistic manner can negatively impact adherence (Bezabhe et al., 2014; Garavalia et al., 2011; Ho et al., 2017; Pagès-Puigdemont et al., 2016). Poor patient-provider relationships lead to insufficient patient counselling and leave the patient struggling alone with medication problems (Garavalia et al., 2011). Without trust-based patient-provider communication, patients cannot freely discuss side effects and other concerns related to their medication (Lambert-Kerzner et al., 2015; Saleem et al., 2012). The inability of healthcare professionals to discuss adherence problems with patients and take their concerns and experiences seriously can impact the self-efficacy of patients (Rifkin et al., 2010; van Geffen et al., 2011). A lack of trust in doctors and questioning of their expertise may increase the burden of the illness and have an essential influence on a patient's adherence behaviour (Habte et al., 2017).

### **5.2.5 SOCIAL AND CULTURE-SPECIFIC BARRIERS**

A stigma is a common reason for non-adherence, especially with HIV/AIDS and with non-communicable diseases (Bezabhe et al., 2014). Patients may not want anybody to know about their illness. The fear of being stigmatized can be so intense that the patient prefers not to take their medication if there is a possibility that someone might be watching. It can be difficult to reconcile work and illness (van Geffen et al., 2011). A lack of support from significant others can have a substantial impact on adherence and control of the illness (Alhomoud et al., 2015; Dehdari & Dehdari, 2019).

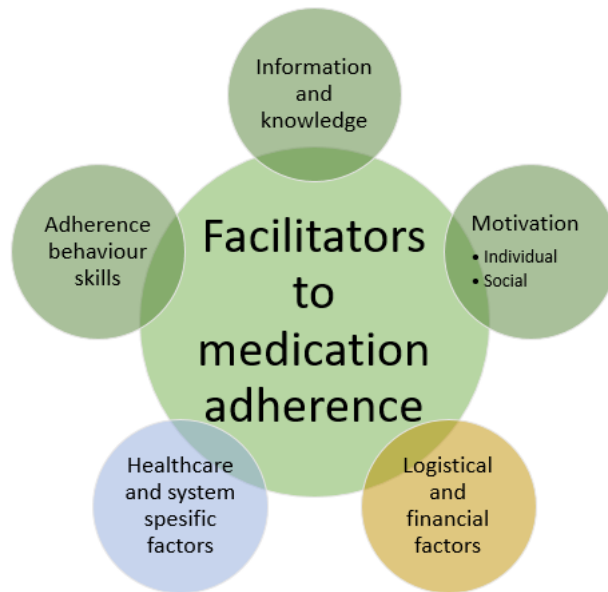
Patients can prefer traditional alternatives or homeopathic remedies or methods instead of conventional medicine because these are more “natural” (Alodhaib et al., 2021; Rahmawati & Bajorek, 2018; Saleem et al., 2012). Patients can have a strong religious faith and prioritize religious rituals instead of taking medicines. Fasting during Ramadan and holy water can have a significant impact on medication management and may be the leading reason to adjust the medication to fit better with religious situations and routines (Bezabhe et al., 2014). Patients may stop the medication if they believe that praying can cure them (Lyimo et al., 2012).

### **5.2.6 LOGISTICAL AND FINANCIAL BARRIERS**

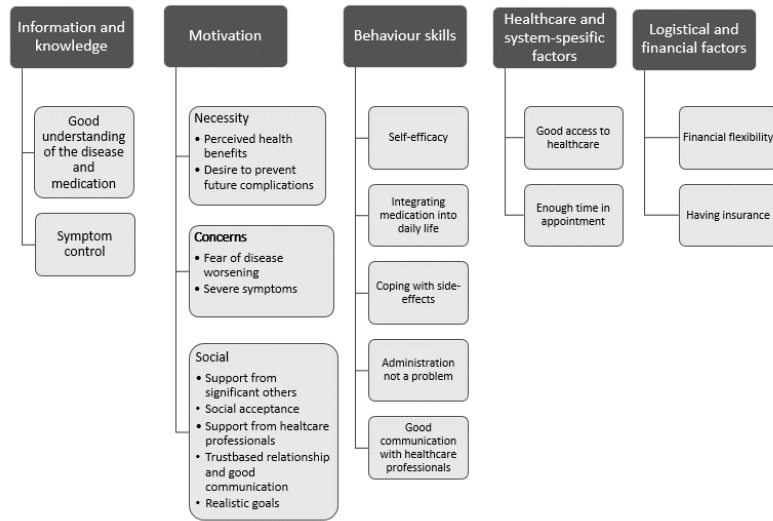
Financial burdens and costs of medicines are significant barriers to medication adherence (Chen et al., 2014). Unemployment and economic difficulties can affect the ability to buy medicines. If a patient does not have enough money to buy necessities such as food and clothing, medicines are unlikely to be a priority (Goldsmith et al., 2017). Difficulties travelling to the clinic, especially in developing countries, can hinder good medication self-management (Garavalia et al., 2009). If insurance coverage is not comprehensive enough or there is no insurance, the cost of medicine can be unbearable (Goldsmith et al., 2017). A medicine shortage and the availability of medicines at the clinic or pharmacy, especially in developing countries, can become a significant problem for the continuity of care (Habte et al., 2017).

## **5.3 FACILITATORS TO MEDICATION ADHERENCE (STUDY I)**

Five subject areas related to facilitators of medication adherence were identified (Study I). Because medication taking is related to individual behaviour, the Information–Motivation–Behavioural Skills Model (IMB) was used as a starting point for the analysis (Fisher & Fisher, 1992; Fisher et al., 2003). As medication adherence is a complex entity in addition to reflecting human behaviour, healthcare and system-specific factors and logistical and financial factors were also observed (Figure 21 and Figure 22).



**Figure 21** The identified key facilitators to medication adherence based on the included qualitative studies (n=89).



**Figure 22** Categories and subcategories of facilitators to medication adherence arising from the included qualitative studies (n=89, Study I). The Information–Motivation–Behavior Skills (IMB) model was used as part of the classification.

### 5.3.1 INFORMATIONAL, MOTIVATIONAL AND BEHAVIOURAL FACTORS

A good understanding of the illness and its treatment and how medicines promote the quality of life is essential for adherence (Kobue et al., 2017). The ability to integrate medications into daily life improves adherence in self-managing chronic conditions (Chen et al., 2014). Low toxicity, mild adverse effects, and an oral route of administration seem to promote medication adherence (Chen et al., 2014; Hayden et al., 2015). There are different tools to assist with medicine taking, such as pillboxes, clocks, or mobile alarms, or taking medications during regular TV and radio programmes (Axelsson et al., 2015; Ho et al., 2017).

The patient's motivation is an essential facilitator. Motivation improves if the patient understands the necessity of the medication, and it contributes to positive health benefits (Goldsmith et al., 2017). Significant life events can have a positive effect on medication adherence. If a serious complication occurs, the importance of preventing complications and maintaining health is highlighted and may lead to a re-evaluation of the patient's priorities (Bockwoldt et al., 2017; King-Shier et al., 2017; Ming et al., 2011). The desire to return to normal life is a powerful facilitator for medication adherence (Shaw et al., 2018).

The concerns related to illness may improve adherence and motivation to take medication as prescribed (Chen et al., 2014; Peláez et al., 2016). If

patients have lived through the experience of their disease and its further negative impact on functional abilities, medication adherence may increase (Peláez et al., 2016). Knowing that interrupting or changing medications would result in the disease worsening can increase the desire to self-manage medication better (Chen et al., 2014). The treatment goals must be realistic and achievable for the patient (Ågård et al., 2016).

Support from family and friends and colleagues at work support adherence. It may require the disclosure of the illness, which can be scary for the patient (Bezabhe et al., 2014; Habte et al., 2017). Social acceptance helps the patient to cope with the illness. Self-efficacy is an essential skill when coping with practical problems in daily life. If the patient takes ownership of self-managing the medication and knows how to adjust medicines if the disease worsens, the chances for better adherence are higher (Habte et al., 2017; Jaffray et al., 2014). Feeling responsible and having a strong belief in the efficacy of medication promote self-empowerment and create a positive attitude towards the medication (Gassmann et al., 2016).

### **5.3.2 HEALTHCARE AND SYSTEM-SPECIFIC FACILITATORS**

A trust-based, collaborative, and respectful patient-provider relationship is crucial for medication adherence (Ho et al., 2017). Good access to healthcare and enough time for discussions are necessary for patients (Koh et al., 2018).

Sometimes a desire to please healthcare providers or fearing them may also facilitate adherence (Ho et al., 2017). Patients wish for confidential communication and an ongoing dialogue with health care professionals (Richardson et al., 2016). Support from healthcare providers and freely accessible care appear to increase adherence (Van Loggerenberg et al., 2015).

### **5.3.3 LOGISTICAL AND FINANCIAL FACTORS**

Financial flexibility is necessary for medication adherence. The balance between revenue and expenditure of the household makes it possible to buy essential commodities such as food, clothes, and medicines without prioritizing (Goldsmith et al., 2017). Additionally, having good insurance coverage guarantees secure finances in contrast to having no insurance at all.

## **5.4 CHARACTERISTICS OF PARTICIPANTS (STUDY II: FOCUS GROUP DISCUSSION WITH GPS)**

Four focus group discussions, with a total of 16 general practitioners (n=16) were convened. The interviews lasted from 60 to 90 minutes. Two of the focus groups took place in the main health centre of Kirkkonummi, one was conducted in Veikkola and another in Masala, the two regional health centres

of the municipality. Both young and more experienced GPs were represented in the interviews (Table 6).

**Table 6** Characteristics of the GPs (n=16) interviewed in the focus group discussions (n=4).

<i>Variable</i>	<i>(n)</i>	
<i>Gender</i>	Female	12
	Male	4
<i>Age</i>	25-30	4
	31-40	4
	41-54	6
	55≥	2
<i>Education</i>	Licensed medical doctor	5
	Medical doctor in the specialist training of general practice	4
	Specialist in general practice	7

## 5.5 POOR ADHERENCE IN MEDICATION MANAGEMENT (STUDY II)

The first main theme that was identified during the coding process was poor medication adherence. According to the GPs, the main barriers to good adherence were related to patient-specific factors, the role of the doctor and the health system (Study II). Table 7 presents a detailed list of the extracted themes of the perceived barriers.



**Table 7** Barriers to good medication adherence according to the GPs (n=16)

<b>Patients</b>
<ul style="list-style-type: none"> <li>• Poor knowledge of the illness and medication</li> <li>• Administering and dosage of the medication</li> <li>• Independent pausing, stopping, or controlling of the medication</li> <li>• Lack of competence in self-management</li> <li>• Hiding the drug information (e.g., drugs prescribed by private doctors)</li> <li>• Fear of drugs</li> <li>• Media and neighbours as a source of medication information</li> <li>• Diseases where poor control does not yet present symptoms</li> <li>• Challenges with lifestyle changes</li> <li>• Replacing prescription drugs with self-administered drugs</li> </ul>
<b>GP</b>
<ul style="list-style-type: none"> <li>• Reviewing the full medication information is challenging and time-consuming</li> <li>• Accurate knowledge of the actual home medication is difficult to attain</li> <li>• Sometimes an overly authoritative role for doctors</li> <li>• Unsatisfactory skills in coaching self-management</li> </ul>
<b>Drug therapies</b>
<ul style="list-style-type: none"> <li>• Complex medications</li> <li>• Polypharmacy</li> <li>• The duration of the medication (temporary, permanent) and withdrawing the medication</li> <li>• Adverse effects</li> </ul>
<b>Health care system</b>
<ul style="list-style-type: none"> <li>• Shortage of GP appointments</li> <li>• Poor access to care</li> <li>• Problems with keeping the medication lists up to date</li> <li>• IT systems and poor communication within health care systems</li> </ul>

### 5.5.1 PATIENT-RELATED FACTORS OF SELF-MANAGEMENT

According to the GPs, the patients were quite burdened with medication non-adherence. The patients managed their chronic disease incorrectly, and the GPs agreed that probably at least half of their patients' experienced difficulties with their medication adherence. The GPs also noticed that problems accumulated in specific patient groups.

The GPs thought, there was a massive variation in self-management in general and medication management in particular among different patient groups. A few treated their disease exactly as ordered using their own Excel tables to document the care outcome. Others did not attend GP's appointments or manage their disease as agreed. The GPs thought these

patients were confused with their medication and often did not know how to take the medicines. The GPs said that the patients did not always understand why the GP had prescribed the medicines for them. Patients might assume the GPs were interfering when they asked about medication even though the GPs intent was to clarify the issues and find the best alternative to treat their disease. The GPs knew the patients made independent decisions on their treatment, and they hoped those decisions would not be harmful.

The GPs wanted to discuss their especially problematic patients, who had many diseases and multiple medications in all four focus group discussions (Table 8). Medication adherence was considered even more challenging related to the home care clients and their caregivers, mostly because of lack of time.

**Table 8** Examples of especially challenging patient groups in regard to medication adherence according to the GPs (n=16).

Challenging patient groups	Citations
Hypercholesterolemia patients	I cannot see why there is not more discussion of simvastatin. I'm in a true simvastatin rumba with my patients...[refers to media attention]
Asthma patients	Many patients with asthma take their medication in a totally irrational manner. For example, if they have symptoms and they have to walk the dog, they may take first the treatment drug and then the opening drug. They so easily stop taking the drug if they are in good balance.
Diabetes patients	Diabetes and hypertension are the difficult ones as they do not give symptoms.
Patients with hypertension	I have had those hypertension patients who only take the drugs when they feel a little dizzy.
Patients with a serious cardiovascular disease	The patients with cardiovascular disease, after they have been treated and are symptom free, may stop wanting to take their medications... they may not understand the drugs in fact may cure. First you are all well, then in secondary care you are prescribed a magnitude of drugs, it's often difficult to understand.
Patients who are discharged from hospital	They are so busy there [in secondary care] and need to get these patients out quickly, so they don't have time to motivate them to take the medications correctly.

Caregivers	I've met caregivers who do not have information of the appropriate care. If they are not present when the medication is prescribed, they may not understand it and be able to assist in the medication management.
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### 5.5.2 THE ROLE OF THE DOCTOR

The GPs (n=16) thought the doctor's authoritative role might demotivate patients from taking responsibility for their medication management. The doctors knew that patients did not always tell them the truth about their medicines. The GPs' opinion was that they sometimes lacked the skills to support patients regarding guidance on day-to-day issues and counselling at home.

### 5.5.3 THE HEALTH SYSTEM

According to the GPs, the short length of appointments and the GPs' expected workload often did not match. The GPs regarded supporting self-management as challenging because they did not have adequate time to complete all the crucial facts.

The various IT systems made it challenging to keep the patient's medication lists up-to-date. The GPs see only the medication lists of the health records in the public health system. When a private doctor or a specialist make changes in the medication list, the changes are not easily obtainable. However, the GPs considered the patients are not always aware of this and do not understand that they should tell them of all medications they were taking and how they were administering them at home.

## 5.6 BETTER MEDICINES INFORMATION FOR THE PATIENT (STUDY II)

The second major theme in focus group discussions was the increased need for medicines information. The GPs highlighted the need for medicines information to increase medication adherence (Study II). According to the GPs (n=16), the risk groups mainly needed more medicines information. The GPs proposed possible solutions for medication non-adherence (Table 9). Many of them were related to better inter-professional cooperation.

**Table 9** Facilitators to better medication adherence according to the GPs (n=16) (Study II).

<b>Patient</b>
<ul style="list-style-type: none"> <li>• Focus on health outcomes of self-management of drug therapies</li> <li>• Support for patients to better understand their disease and its management</li> <li>• Pharmacists as coaches for drug therapies</li> <li>• Medication counselling for caregivers</li> <li>• Peer groups for chronic conditions and training in peer groups</li> </ul>
<b>Doctor</b>
<ul style="list-style-type: none"> <li>• Inter-professional practices for reconciling the medication lists before annual check-ups</li> <li>• Continuity of care and permanent doctor-patient relationships</li> <li>• Equal relationships with patients, with a coaching attitude</li> <li>• Setting achievable goals</li> </ul>
<b>Drug therapies</b>
<ul style="list-style-type: none"> <li>• Inter-professional interventions: medication reconciliation (nurse or pharmacist), medicines optimization (pharmacist) and medication review (pharmacist)</li> <li>• Combination products to minimize the number of medicines</li> <li>• Checking and teaching the right use of medical devices</li> </ul>
<b>Health care system</b>
<ul style="list-style-type: none"> <li>• Inter-professional practices</li> <li>• Inter-professional interventions: medication reconciliation, medicines optimization and medication review</li> <li>• Health care wide shared patient information and better IT systems</li> </ul>

### 5.6.1 MORE PATIENT EMPOWERMENT

The GPs wished the patients would take more responsibility for their care, although the GPs generally agreed about taking charge of medications. According to the focus group discussions (n=16), the GPs (n=16) did not resist changing their role from authoritative to more like a coach.

The GPs acknowledged that they needed better communication strategies. It takes time to create trustworthy relationships with patients. The GPs stated that a stable GP-patient relationship is a strengthening factor for medication adherence. The GPs thought that if they, together with the patient, set achievable goals and followed how the patients achieved them, the patient would probably be committed to them and motivated to achieve them. According to the GPs, the instructions should be repeated because patients easily forget the information they received.

The GPs thought peer support was a strengthening factor for patients' medication adherence. However, the doctors highlighted that there should be a healthcare professional to moderate the group discussion.

### **5.6.2 MORE INTERPROFESSIONAL PRACTICES**

One way to tackle the non-adherence, according to the GPs (n=16), would be with more inter-professional support for the patient. It would allow for more support and depth for medication management. The GPs' appreciated help from other healthcare professionals, especially with patients with multimorbidity and multiple medications. There was a need for more interprofessional cooperation between GPs and other healthcare professionals to tackle the problems of polypharmacy. Interactions and adverse effects weaken medication adherence and self-management and hinder achieving the desired outcome. The doctors would appreciate nurses' help with annual appointments for chronic diseases. If the nurse interviewed the patient before the appointment with the GP, and the medication list was updated before the patient saw the GP, the GP would have all the necessary information to make decisions.

Better interprofessional processes would help the doctors collaborate with other healthcare professionals on the healthcare level. According to the GPs, it would benefit all health care because "no one person would need to do everything". Sometimes the lack of indication for medication was not questioned at GP appointments because it was prescribed in secondary care. Medications prescribed initially for acute reasons may have become regular medications. Especially those patients with severe cardiovascular events were often confused about the situation. The patients seem to be discharged from the hospital quickly without a proper understanding of the disease. According to the GPs, the patient's admission from secondary care would need more medication counselling and guidance with the self-management of their medication.

### **5.6.3 THE ROLE OF THE PHARMACIST**

Medication reconciliation and rational use of medicines were among the tasks for which doctors would like pharmacists' help. If a pharmacist figured out the actual use of medicines the patient is using at home and the medication list was updated before the appointment with the GP, this would be welcomed by GPs.

The GPs agreed that the medication reviews made by the pharmacist for patients with multiple medications or new symptoms would support them in decision-making and help patients cope with the medication. Sometimes the GPs experienced challenges when considering if the symptom was an adverse effect, interaction, or a new illness. In those cases, the pharmacist's medication review might help them in decision-making. It might also be a solution in cases where the patient's status has worsened due to an unclear reason. The GPs welcomed the pharmacist to the inter-professional care team. They thought it would offer better possibilities for the rational use of medicines and support patients' medication adherence.

## 5.7 SUMMARY OF FINDINGS (STUDY I-II)

In Study I, an extensive range of barriers and facilitators to medication adherence was identified, and the studies were more often concerned with barriers than facilitators. The barriers were classified as patient-specific, illness-specific, medication-related, healthcare and system-related, sociocultural, and logistical and financial factors. The facilitators were classified as information and knowledge of the disease and medication, individual and social motivation, adherence behaviour skills, healthcare and system-specific factors and logistical and financial factors. Some of these factors can act as barriers and facilitators, such as healthcare and system-related factors and logistical and financial factors.

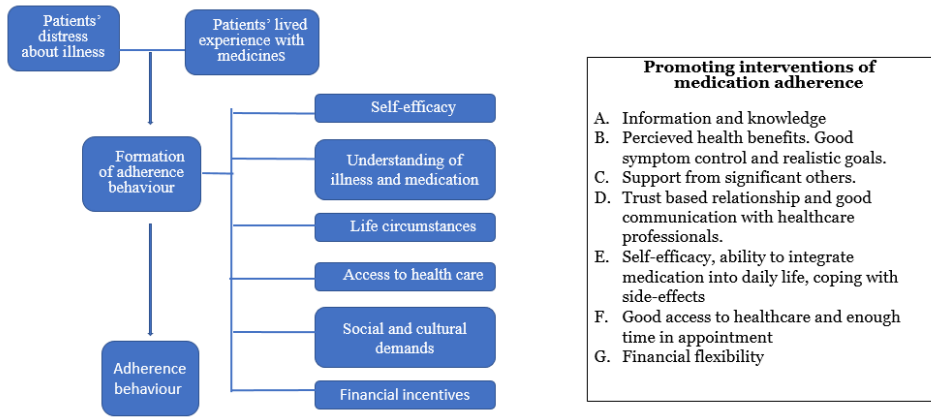
Our scoping review covered 13 systematic reviews ((n=13, Article I: Table A2) and 76 single studies (n=76, Article I: Table A1). The findings of the systematic reviews were in line with the single qualitative studies.

Some of the included studies had a theory-based approach to medication adherence (n = 17) (Study I: Table 1). Using different theories helped to understand and explain patients' actions related to taking their medication (Study I: Table 1).

In Study II, the GPs (n=16) were concerned with poor medication adherence, which they considered the central problem in guiding the self-management of people with chronic disease. They suggested better inter-professional cooperation and more open communication with patients to overcome the problems. They wished to work closely with nurses and pharmacists to help people with chronic diseases. The GPs also highlighted the need for better IT systems to keep patients' medication information up-to-date and that more priority should be given to counselling patients about medicines.

When planning interventions to promote adherence, we need to consider the different dimensions affecting adherence (Study I-II). Based on the study results, the preliminary concept of possible behaviour affecting medication adherence may be formulated (Figure 23). According to the study results, the patients' distress about illness and lived experiences with medicines may form the patients' adherence behaviour. The patient's ability to change her behaviour as the disease requires depends on complex internal and external factors. The patient needs to have various skills, adequate knowledge, and a safe living environment to promote adherence behaviour. By understanding the adherence behaviour and identifying the reasons behind the patient's medication-taking behaviour, the healthcare professionals can in routine clinical practice, support the patient to achieve the treatment goals and increase the quality of life. To promote formation of adherence behaviour, the patient needs to have self-efficacy to manage the illness and its medication, good understanding about illness and medication, optimal life circumstances (e.g., support from significant others), good access to healthcare as well as

trustful relationships with healthcare professionals, social and cultural support, and financial incentives.



**Figure 23** The concept of medication adherence behaviour based on the results (Study I and II).

## **6 DISCUSSION**

### **6.1 MAIN FINDINGS (STUDIES I-III)**

Every encounter with the patient is an opportunity to support the patient in the rational use of medicines. Our research provides evidence for developing more patient-centred interventions to enhance medication adherence in patients' daily life. This doctoral dissertation adds to the knowledge of medication-taking behaviours from a patient approach, particularly deepening the understanding of the factors contributing to medication adherence. The two studies, one of which extensively reviewed qualitative research (Study I) and the other of which gathered evidence from GPs (Study II), are in line with each other. The results of the local small-scale study (Study II) validate the analysis made from the more comprehensive data (Study I).

Findings of this thesis confirm that medication adherence is a complex phenomenon that can be analysed from different perspectives. The adherence situation has not essentially changed in two decades (World Health Organization, 2003). A wide range of factors seems to impact medication adherence positively or negatively or both ways. These findings seem to be similar regardless of the research concept. Based on our research, it can be observed which issues would be highlighted in future practices to promote medication adherence. However, there were more studies on barriers to medication adherence than facilitators (Study I), indicating that barriers may be more accessible to identify than facilitators. According to our findings, it would be essential to focus on finding facilitators so that, with their help, it would be possible to build up effective new practices to improve medication adherence. To our knowledge, Study I is the first scoping review on patient-related factors of medication adherence based on qualitative research.

According to the scoping review (Study I), information and knowledge of diseases and their treatment, communication, trust in patient-provider relationships, support, and adequate resources appeared to be the essential facilitators in medication adherence from the patient perspective. Patients are willing to discuss their concerns about medications. They have many worries about their illnesses, and it seems that they do not always have adequate information to make decisions to self-manage their care. Better communication and better information about medicines appear to be the critical factors for patients.

In Study II, GPs reported that poor medication adherence is one of the most significant challenges in primary care. The GPs had to tackle complex medication management issues, especially with an ageing population. According to GPs, there was an increased need for medicines information. They also reflected significant individual differences in patients' needs and skills, which further complicated the guiding of patients' self-management.



The GPs thought that better interprofessional cooperation would facilitate medication management as they have often a lack of time in a short appointment.

Our study protocol presented in Study III wants to bring new patient-oriented insights into medication-taking behaviours, particularly why patients take their medicines differently than prescribed and the high-risk medicines in this respect. We need more detailed information to identify better drug-specific adherence problems and how to affect them most effectively. Medication discrepancies can indicate non-adherence, and healthcare professionals can make the most of this information when determining the underlying reasons behind patients' behaviour (Study III). Patients may use the prescribed medicines differently than how the prescriber has planned. There can be intentional or non-intentional poor adherence, and the patient may have a rational reason to modify doses. The GPs in Study II were concerned about the patient's un-updated medication lists. They wished for better IT systems to keep the medication list updated. The national medication information database Kanta, where all healthcare providers have access to the patient's prescription data, will give one solution to this concern (Finnish Institute for Health and Welfare THL, 6/2020; Kanta Services). However, the patients can use the medicines differently as prescribed and recorded in the Kanta list. Medication reconciliation is still necessary to ensure how the patient has used the medication at home. In our study protocol (Study III), medication reconciliation will be used to monitor medication adherence and identify patients' medicines use against the physician's instructions in routine clinical practice. It provides a new perspective on finding non-adherence in healthcare.

Based on the findings of this doctoral thesis, there is a need to continue developing a theoretical model related to adherence. The model could consider previous theories related to medication adherence, patient perspective and the research evidence constructed by qualitative methods.

### **6.1.1 PATIENTS VALUES AND PRIORITIES REFLECTING MEDICATION-TAKING BEHAVIOURS**

Our scoping review (Study I) pointed out that patients' values may differ from the healthcare professionals' expectations. According to the scoping review, the disease and its management are not always the priority for the patient, which the healthcare professionals may not consider. It may be influenced by the fact, that healthcare professionals have learned to think disease-specific, and for them, good disease management is the priority, making it difficult to consider other priorities. The patients may judge the life before the illness was diagnosed as more valuable and the possible life changes required by the illness as a burden. Similar findings are presented in the previous systematic review and meta-analysis concentrated on the medication-related burden (Mohammed et al., 2016). The patients may experience the complex

medication or the injectable medicines as obstacles as well as taking the medication on time. Strategies to improve adherence, such as reminders may be useful when the patient is motivated (McSharry et al., 2016), but forgetting can also indicate lack of motivation to take the medicines or lack of belief in medications (Al-Qazaz et al., 2011).

According to our scoping review (Study I) the patients may feel ashamed and stigmatized, and the negative thoughts of illness and the limitations on life it may impose, may cause poor adherence. Patients have an effort to avoid the factors that cause burden (Mohammed et al., 2016). The situation can be worse if there is no support from significant others. Support from healthcare providers as well as significant others seem to be essential to medication adherence. What matters to the patient has a critical meaning in patients' decision making, affecting self-management and medication adherence.

More attention should be paid to the patients' fears of side effects (Study I and II). According to our findings, it seems to be a common obstacle and causes poor adherence. It may cause skipping doses, omitting, or adjusting medicines. The patients want to discuss their concerns about side effects with the healthcare professionals. They may be afraid to tell the healthcare providers about their negative experiences when thinking that the medicine that, however, helps may be taken away from them. According to some systematic reviews related to cardiovascular diseases and diabetes, drug-related problems are a significant threat in healthcare (Al Hamid et al., 2014; Ju et al., 2018; Marshall et al., 2012; McSharry et al., 2016; Rathbone et al., 2017). Our findings indicate that DRPs are essential threats also in other diseases affecting patients' daily life negatively and causing unwanted medication-taking behaviour. The situation seems not to have essentially changed from the WHO's report in 2003 (World Health Organization, 2003).

The reasons for not taking medication as prescribed can be various, and it can differ from disease to disease, which requires the actions to support the patient to be more patient specific (Study I-III). Patients may not have enough medicines information to make rational decisions about medication regimens. There can be a lack of routines or changes in routines, negatively affecting medication self-management. Motivation for self-management and to be empowered can be lacking, and there can be much stress related to medication and illness. A good relationship with the healthcare provider improves adherence, mainly if the patient receives assistance adapting the medication into daily routines.

### **6.1.2 FACTORS RELATED TO HEALTHCARE AND PATIENT-CENTEREDNESS**

Both Studies I and II highlighted the importance of a trustful patient-provider relationship for medication adherence. The patients should have faith that the healthcare providers are on their side. The GPs in Study II considered that changing their role from an authoritative person to more like the patients'

coach was a positive development. According to them, the change has happened relatively quickly in one career's lifetime.

The healthcare professionals need to understand patients' priorities and preferences because these affect medication self-management and treatment outcomes. The complexity of the topic may explain why many interventions to improve medication adherence have not been successful (Nieuwlaat et al., 2014). There is much research about interventions to increase adherence, but the interventions are either complicated and challenging to put into practice or focus only on some part of the patients surrounding (Amankwaa et al., 2018; Haynes et al., 2008; Mohammed et al., 2016; Nieuwlaat et al., 2014; World Health Organization, 2003).

Patient-centred care may be standard in theory but putting it into practice may be challenging. The actions towards enhancing medication adherence through concordance should be put more effort into. According to our studies, the healthcare provider's authoritative role may hinder patients from talking about their problems. The patients may try to please the healthcare providers and not tell if they have used medicines against the prescriber's order. The GPs tried to determine patients' adherence by observing the frequency of prescription renewals (Study II). However, they thought it was not a very reliable method. On the other hand, the healthcare professional's ability to interact with the patient may also vary and needs to be strengthened. According to the GPs', they sometimes lack the skills to support patients regarding guidance on day-to-day issues and appreciate the help of nurses.

According to NICE guidelines, patients' involvement in care allows patients and providers to share their thoughts about the treatment options, benefits, and risks in a confidential relationship (National Institute for Care and Health Excellence NICE, 2021; National Institute for Health and Care Excellence, 2009). It also allows discussion of the other essential issues, such as the duration of the treatment or monitoring requirements and the likelihood of experiencing adverse effects. Also, in Finland, the Ministry of Social and Health has taken a stand to promote the patients' involvement in their care (Ministry of Social Affairs and Health, 2018). Even though the awareness of taking the patients into the centrum of their treatment decisions seems to be strengthening, our study findings indicated we are not there yet. According to our studies, there is still a considerable need to improve the patient-provider relationship and move patients from passive recipients to active participants. The new method to investigate medication non-adherence in routine clinical practice may give more information about interventions that may be put into consideration in the future (Study III).

According to our studies (Study I-II), long queues for treatment in healthcare can affect medication adherence negatively. The GPs believed that a long-term patient-provider relationship increases adherence. This finding supports the WHO, highlighting that the patients seem to be more adherent when receiving care from the same provider (World Health Organization, 2003). In Finland, the model of family doctors in health centres has risen in

public debate as it is suggested to increase the mutual trust as well as continuity of care (Pennanen, 2022).

The GPs thought there was a need to improve the healthcare system. The patient's clinical pathway from, e.g., secondary, or tertiary care to primary care needs to be more seamless (Study II). The GPs wished for shared IT systems to help transfer medication information to everyone involved in the patient's care. Developing the national Kanta medication list in Finland, where all healthcare providers have access to the patient's prescription data, is a step towards this. Kanta medication list is meant to be launched in outpatient care at the end of 2024 (Finnish Institute for Health and Welfare THL, 6/2020). (Finnish Institute for Health and Welfare THL, 6/2020). It has been prioritized in the national actions to implement rational pharmacotherapy as part of ongoing social and health services reform (Ministry of Social Affairs and Health, 2022).

There is a need for interprofessional cooperation. The GPs in Study II pointed out that if the appointment time for a patient with multimorbidity is short, there cannot be many problems to be addressed. Lack of time in health care appointments often makes it challenging to discuss the patients' problems and priorities without a hurry.

However, a shift toward patient-centred healthcare requires also political will. If there is a huge workload (Study II), the goal of shared decision-making, medication counselling, and finding out patients' priorities cannot be reached. There should be enough resources to implement concordance-thinking in practice.

According to the findings of this doctoral thesis, there is a growing need to consider poor adherence as a significant patient safety risk. Low medication adherence keeps patients from reaching treatment outcomes. Medication adherence could also be promoted better in national legislation, guidelines, and organizational instructions.

Overall, better inter-professional cooperation is needed. Every healthcare professional has a role in enhancing medication adherence (Rathbone et al., 2016). The pharmacist's involvement in patient care strengthens the inter-professional care team and may improve treatment safety (Cheema et al., 2018; McNab et al., 2018; Mekonnen et al., 2016). There is a need to reorganize the system and medication management process and to make it more interprofessional, involving more, e.g., community pharmacists in patient care (Kallio, 2021; Tahvanainen et al., 2021; Toivo, 2020). According to the GPs (Study II), the pharmacist can be a valuable support to physicians when figuring out patients' actual use of medicines and reasons for using medications against physicians' orders at home and solving problems in polypharmacy with the care team.

### **6.1.3 FINANCIAL FACTORS TO BE CONSIDERED**

According to the scoping review (Study I), financial problems can affect medication adherence. If the patient has lack of money, medicines are hardly the priority. Our results show that medicines costs, especially in low-income patients, may affect patient medication adherence negatively.

It may be that changes in legislation affecting drug pricing may also affect the patient's ability to buy medicines. In 2017, the reimbursement rate for antidiabetic medicines, except for insulin, was lowered in Finland to achieve expected savings in government-funded medicines cost (Suviranta et al., 2019; Valtioneuvoston kanslia, 2015). It caused the patient's antidiabetic medicines to become more expensive and seems to have negatively impacted medication adherence (Suviranta et al., 2019).

Poor adherence causes a cost to society and the patient as well when the treatment outcomes are not achieved. If the patient must choose whether to buy medicines or necessities such as food, the patient may not prioritize medicines. Therefore, new legislation affecting patients' ability to buy medicines should be made with a sufficiently broad knowledge base, considering factors affecting patients' capability to buy medicines. It may also be considered if there should be more financial support for developing adherence-enhancing interventions applying e.g., technologies.

### **6.1.4 THE BEHAVIOURAL THEORY APPROACH**

Behavioural theories can explain why patients do not take their medication as prescribed. Usually, they explain only partly behaviours influencing medicine taking. A theory-based approach clarifies the patient's actions and behaviours related to medication-taking practices. In the scoping review (Study I), 17 studies applied a theory-based approach to medication adherence.

The Health Belief Model was the most used theoretical model found in our scoping review on medication adherence (Study I) (Garavalia et al., 2009; Garavalia et al., 2011; Oshotse et al., 2018; Rahmawati & Bajorek, 2018). According to this behavioural model, health-related decisions are rational and based on patient-perceived threats, barriers, and benefits. These factors may explain a lot of medication adherence but not all. The Social Cognitive Theory considers the environment better. In the scoping review (Study I), many factors outside patients' behaviour, such as social context, resources, family, and culture, have a role in medication adherence. More behaviour-based theories may be needed to explain adherence behaviour fully. The conceptual model of Patients' Lived Experience with medicines PLEM is one example of a new conceptual approach to the factors related to the use of medicines from the patient's perspective (Mohammed et al., 2016).

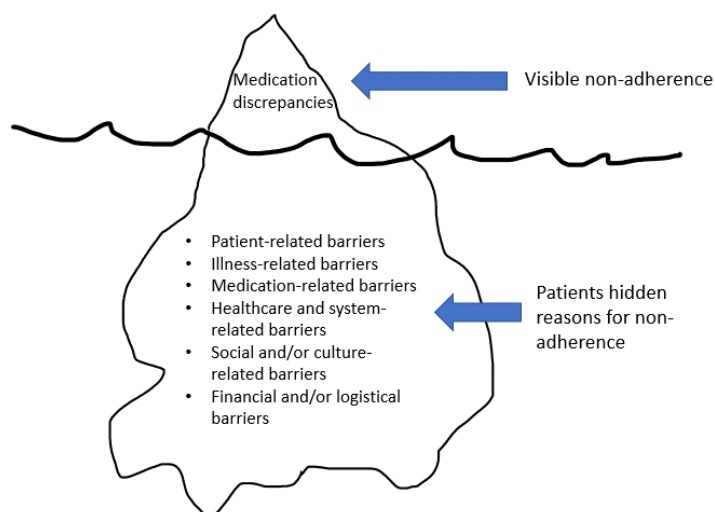
Nevertheless, the decisions related to medicines are not always based on rational thinking. Theories by Argyris and Schön, which did not appear in our study, emphasize more unconscious matters behind decisions (Argyris & Schön, 1982). These researchers call the rationally based actions espoused

theories, while theory-in-use describes the more complicated theory that explains how we behave.

As a result, there is a need to further develop the theory-based approaches to medication adherence since the existing behavioural theories are not wholly explaining the complicated phenomenon of adherence. A better understanding of human behaviour and what is needed to make a behaviour change seems to be essential and should be considered.

#### **6.1.5 THE CONCEPTUAL MODEL OF NON-ADHERENCE, THE ICEBERG MODEL**

Medicines discrepancies may indicate medication non-adherence and according to the study findings can be illustrated as an iceberg in the ocean (Study III, Figure 24). The ocean illustrates the current life situation the patient is living in, and the iceberg patients lived experiences with the illness or medicine. The iceberg's peak is a visible part of issues leading to non-adherence. The visible part of non-adherence can appear as adjusting or modelling the doses or omission of medicine. The non-adherence is hidden underneath and can vary from patient to patient (Mohammed et al., 2016). If the reasons are not adequately getting to the bottom of the problem, the outcomes of the patient's prescribed medication regimen will be highly likely lacking. This iceberg model based on our studies is intended to explain the complexity of medication adherence by illustrating a coherent whole from many studies (Study I, Study II, Study III). The iceberg model provides an essential viewpoint on how patients' abnormal use of medicines can supply further knowledge on matters that may be obstacles to the patients and lead to adjusting medicines. It also provides practical implications for examining a patient's non-adherence in the typical clinical pattern and helps to use medication reconciliation in observing medication adherence. It also helps determine, solve, and prevent challenges related to non-adherence.



**Figure 24** The conceptual iceberg model of medication non-adherence.

In certain circumstances, medication reconciliation can be used to identify non-adherence. The reasons for discrepancies can be solved in a confidential atmosphere without blaming the patient's decision, also according to WHO (World Health Organization, 2003). Even though medication reconciliation allows finding out underlying non-adherence, discussing and identifying problems in medication self-management should be part of every healthcare visit. The GPs wished for better IT systems to which everyone involved in care has access (Study II). The development of the national Kanta medication list will be launched in outpatient care at the end of 2024 (Finnish Institute for Health and Welfare THL, 6/2020). Despite the Kanta medication list, medication non-adherence may remain hidden. The patient is the only reliable data source related to the actual medication management at home (Institute for Healthcare Improvement IHI, 2011; Joint Commission on Accreditation of Healthcare Organizations, 2006; Kari et al., 2018; National Institute for Health and Care Excellence, 2009, 2015; World Health Organization, 2014).

Interviewing the patient about why they are not taking medication as prescribed, and discussing this with them, are essential elements of good professional practice. The new conceptual model of adherence, the iceberg model, may help healthcare professionals identify non-adherence in routine clinical practice or pharmacy.

## 6.2 RELIABILITY AND VALIDITY OF THE RESEARCH METHODS (I-III)

### **Study I: Scoping review**

To ensure the quality of Study I, the PRISMA-ScR checklist was used (Tricco et al., 2018). The strengths of the study include an extensive literature search and review, followed by a thorough categorization of the barriers and facilitators according to medication adherence. The literature searches were done with the help of the professional librarian. There is good coverage of qualitative studies in which the primary focus is patients' experiences and attitudes towards medication adherence. In the selection process, three researchers were involved to avoid the selection bias. The data was thoroughly extracted and analysed to define the overarching categories.

A limitation is that since we focused on the qualitative factors, we cannot conclude the magnitude of the effect of several aspects influencing adherence. We also limited our search to studies in English, and it may be a source of bias. The studies reported more barriers than facilitators, which may be another limitation. On the other hand, this suggests, that barriers have been better identified than facilitators.

### **Study II: Focus group discussion with GPs**

We used the COREQ-checklist to ensure the quality of the Study II (Tong et al., 2007). The strength of the study was a broad sampling of the GPs of all the three healthcare centres in Kirkkonummi municipality. The physicians interviewed included both the experienced and the novices. The interviews were carefully analysed to find the overarching themes and the subthemes. We continued the recruitment until any new information was received and the data was saturated.

The limitation of the study was that the GPs were recruited from only one medium-large municipality health centre. Participating physicians may have been more interested in inter-professional collaboration and medication adherence than those who did not participate; there were 16 GPs out of 25 who participated in the focus groups. Because of the small sample size, the results cannot necessarily be generalized to other healthcare centres, but the findings may contribute to a wider understanding of medication adherence. This qualitative study in primary care aimed to understand the GPs' everyday challenges with self-management. As the study was conducted ten years ago, it might not reflect current practices, and the GPs' views might have changed.

### **Study III: Using Medication reconciliation to identify non-adherence**

The strength of this study protocol is that it provides a new perspective on finding non-adherence in routine clinical practice. The study is planned to test a new way to find out the reasons for non-adherence and provides possibilities to plan tailored interventions to promote the rational use of medicines. Medication discrepancies can indicate non-adherence or problems in the use



of medicines. This conceptual model can be standardized and put into operation at other healthcare sites. Medication reconciliation is a standardized process, and pharmacists participating in this study are experienced. The study process and questions are standardized and available in writing, and the pharmacists are trained in the process.

One limitation of this study protocol is that it will be conducted at four primary care outpatient clinics in one city in Finland, and the results cannot necessarily be generalized to other healthcare sites. Another limitation is the process of patient recruitment as, during Covid-19, outpatient clinics and hospitals have started using digital or remote appointments, in which case the patient consent may be difficult to obtain. A patient-specific limitation is the possibility that the patients will not tell the pharmacist the actual use of medicines. However, this study may help those who plan further interventions to find out reasons for non-adherence and develop tailored interventions to support adherence in primary care.

## **6.3 PRACTICAL IMPLICATIONS**

### **Study I: Scoping review**

This study clarifies the contributing factors of non-adherence and why the outcomes of interventions to improve adherence have not been very successful. The study emphasizes the need to understand the medication adherence complexity. There is a gap between the patient and the healthcare provider in medication adherence thinking that should be rectified. This study broadens the understanding of patients' reality. It may also be used as a teaching material when educating healthcare professionals in medication adherence and partnership thinking, e.g., in HUS Pharmacy. The outcomes presented in this study are helpful when planning more effective interventions, comparing existing adherence scales, and building up more comprehensive theoretical models of medication adherence to increase medication adherence. This study highlights the potential of behavioural theories to understand the factors affecting medication-taking behaviour and provides a good basis for building up more comprehensive theoretical models of medication adherence.

### **Study II: Focus group discussion with GPs**

The GPs welcomed pharmacists to participate in the care team to solve in collaboration with other healthcare professionals' medication-related problems. They recognized medication reconciliation as challenging and welcomed pharmacists and nurses to optimize medication use in interprofessional collaboration. The pharmacist has become more and more part of the interprofessional care team, and pharmacist-led medication reconciliation and CMR have started to expand in primary, secondary and tertiary care as well as in social care, e.g., in HUS (Kallio et al., 2018; Kiiski et

al., 2019; McNab et al., 2018; Mekonnen et al., 2016; Ravn-Nielsen et al., 2018; Schepel et al., 2019; Toivo, 2020). Study III is implementing this approach into practice.

The GPs hoped for shared IT solutions to which everyone involved in care has access to more reliable patients' medication information. The GPs had difficulty keeping the medication lists updated. There is a wealth of various IT systems in health care. The GPs wished for shared IT systems to which everyone involved in care has access and where the most current information is available. The development of the Kanta medication list in Finland is a step in this direction, and it will be launched at the end of 2024 (Finnish Institute for Health and Welfare THL, 6/2020).

### **Study III: Using Medication reconciliation to identify non-adherence**

This study protocol will provide practical implications for investigating the patient's non-adherence in routine clinical practice. Our study may help to utilize medication reconciliation in monitoring medication adherence. It may also help to identify, solve, and prevent the challenges related to non-adherence in routine clinical practice. The iceberg model may provide a new perspective on how patients' deviant use of medicines can provide further information about concerns that may be a barrier to the patient and lead to adjusting of medicines. When a healthcare professional notices medication discrepancies related to a physician's orders, it may lead to a more detailed discussion with the patient and to interventions for increase medication adherence. Creating a high-alert list of non-adherence medications can make it possible to increase medication adherence proactively with medicines that patients typically have difficulties with. To improve the level of trust in patient-provider interaction, it is essential to identify patients at risk of using medications against physicians' orders. The pharmacist can be a useful support to physicians when figuring out patients' actual use of medicines and reasons for using medications against physicians' orders at home.

## **6.4 TOPICS FOR FUTURE RESEARCH**

There is a need for better recognition of facilitators for medication adherence. More research should be focused on the factors that have been able to help patients to commit to their treatment and medication self-management, as well as to elaborate on new theoretical models. There is also a need to develop better data systems to support medication management both for patients and healthcare professionals. Better self-management apps for the patients and comprehensive pharmacotherapy management systems for healthcare professionals are needed. Our research makes it possible to develop more patient-centred interventions and approaches to increase medication adherence, compare existing adherence scales, and build more comprehensive theoretical models of medication adherence. Medication reconciliation may be

a suitable method to study further patients reported variant use of medicines and possible non-adherence by recording the interviews between the pharmacist and the patients. This way, it could be possible to obtain more profound information about the patients' and healthcare providers interactions. This information could be used to educate the healthcare professionals to better interact with the patient. It also gives broader information to create a conceptual model of the patients' reasons for not taking medicines as prescribed when at home.

## **7 CONCLUSIONS**

There is a wide range of possible barriers and facilitators to medication adherence. The barriers seem to be better known than the facilitators. There is a need for better recognition of facilitators.

Qualitative research of medication adherence can help better understand the patients' lived experiences that direct their medicine-taking behaviour. This information is needed to find new interventions and approaches to increase medication adherence, compare existing adherence scales, and build up more comprehensive theoretical models on medication adherence.

Better communication and information on medicines appear to be among the most crucial factors for patients. Patients wish to discuss their worries and concerns about medications. Highlighting these factors may help clinicians who communicate with patients having issues with adherence.

Factors contributing to medication adherence presented in this doctoral thesis may help those who plan further interventions to build up a more comprehensive approach to improve medication adherence.

The GPs were concerned about poor medication adherence, which they considered the major problem in guiding the self-management of patients with chronic disease. They suggested better interprofessional cooperation and more open communication with patients to overcome the problems. They wished to work closely with nurses and pharmacists to help people with chronic diseases.

The GPs highlighted the need for better IT systems to keep medication information updated. They also thought that more focus should be given to advising patients on medicines.

There is a need to further develop the theory-based approaches to medication adherence since the existing behavioural theories are not wholly explaining the complicated phenomenon of adherence. A better understanding of human behaviour and what is needed to make a behaviour change seems to be essential and should be considered.

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