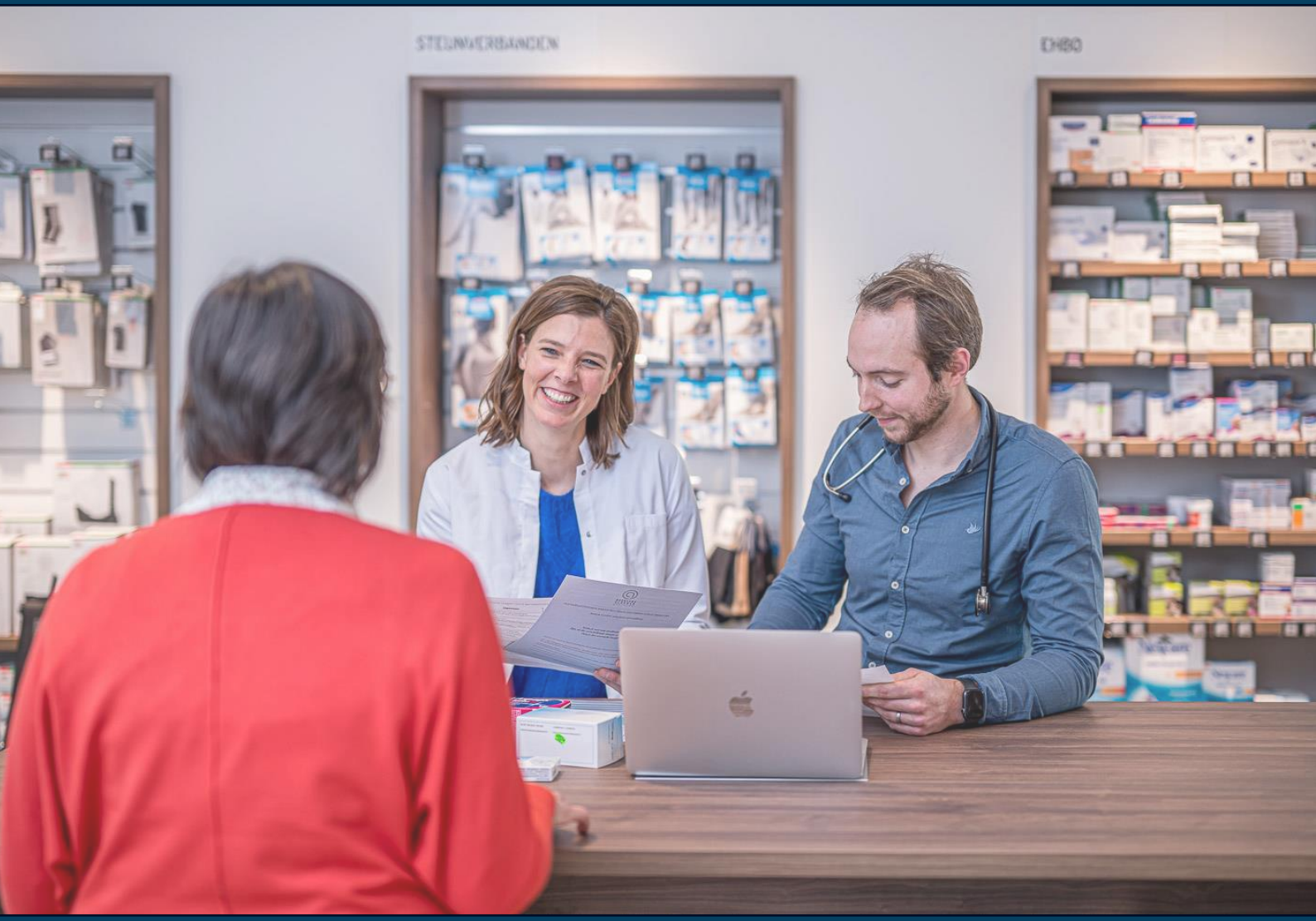
Implementation of type 3 medication review in Flanders: obstacles and opportunities

Implementatie van type 3 medication review in Vlaanderen: obstakels en opportuniteiten



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Proefschrift voorgelegd tot het behalen van de graad van doctor in de farmaceutische wetenschappen aan de Universiteit Antwerpen en Vrije Universiteit Brussel te verdedigen door Anneleen Robberechts

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List of abbreviations

APA	Belgian pharmacy Academics and Pharmacists active in professional Associations
AphA	American Pharmacists Association
AUR	Antibiotic utilization review
BRANT-MERQS	Brussels Antwerp Medication Review Quality Score
CMM	Comprehensive Medication Management
CMR	Comprehensive Medication Review Collaborative Medication Review
CMS	Chronic Medication Service
CMTM	Comprehensive Medication Therapy Management
COREQ	COnsolidated criteria for REporting Qualitative research
DMMR	Domiciliary Medication Management Review
DRP	Drug-Related Problem
DRR	Drug Regime Review
DRUM	Dispensing Review of Use of Medicines
DUE	Drug Usage Evaluation Drug Use Evaluation
DUR	Drug Utilization Reviews Drug Use Review
EU	European Union
FIP	International Pharmaceutical Federation
GDPR	General Data Protection Regulation
GheOP³S	Ghent Older People's Prescriptions community Pharmacy Screening
GP	General Practitioner
GUM	Good Use of Medicines
HCP	Healthcare Provider
HMR	Home Medicines Review
IPSA	Instituut voor Permanente Studie voor Apothekers (or Continuing Education Institute for Pharmacists)
ISF	Interactive Systems Framework
JCAHO	Joint Commission on Accreditation of Hospitals
KAVA	Koninklijke Apothekersvereniging Van Antwerpen (or Royal Pharmacists Association of Antwerp)

KNMP	Koninklijke Nederlandse Maatschappij ter bevordering Pharmacie (or Royal Dutch Society for the Advancement of Pharmacy)
LE	Life Expectancy
LSS	Lean Six Sigma
MAI	Medication Appropriateness Index
MAP	Medication-related action plan
MCDA	Multicriteria Decision Analysis
MR	Medication Review
MR1	Type 1 Medication Review Medication Review Type 1
MR2	Type 2 Medication Review Medication Review Type 2a
MR2a	Type 2a Medication Review Medication Review Type 2a
MR2b	Type 2b Medication Review Medication Review Type 2b
MR3	Type 3 Medication Review Medication Review Type 3
MRF	Medication Review with Follow-up
MTA	Medicines Therapy Assessment
MTM(S)	Medication Therapy Management (Services)
MTR	Medication Therapy Review Medicine Therapy Review
MUE	Medicine Use Evaluation
MUM	Medication Use Management
MUR	Medicine Use Review Medication Use Review
NCD	Non-Communicable Disease
NICE	National Institute for Health and Care Excellence
NIHDI	National Institute for Health and Disability Insurance
NMS	New Medicine Service
OECD	Economic Co-operation and Development
ORT	Opioid Risk Tool
OTC	Over-The-Counter

PIAF	Periodic Individual Pharmacotherapy Analysis
PCNE	Pharmaceutical Care Network Europe
PMR	Personal Medication Record
PREMs	Patient-Reported Experience Measures
PRISMA	Praktijk Research In Samenwerking Met Apothekers (or Practice Research in Collaboration with Pharmacists)
PROMs	Patient-Reported Outcome Measures
QUM	Quality Use of Medicines program
RA	Rheumatoid Arthritis
RCT	Randomized controlled trial
RMMR	Residential Medication Management Review
SDOH	Social Determinants of Heath
SES	Socio-Economic Status
SMR	Structured Medicine Review
START	Screening Tool to Alert doctors to Right Treatment
STOPP	Screening Tool of Older Person's Prescriptions
STRIP	Systematic Tool to Reduce Inappropriate Assistant
T2DM	Type 2 Diabetes Mellitus
TMR	Targeted Medication Review
WHO	World Health Organization

Chapter 1: General introduction

Part I: Medication review: what's in a name and what's it about?

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Part II: Introduction of Belgium's Health situation in connection to pharmaceutical care

Anneleen Robberechts, Stephane Steurbaut, Guido De Meyer, Hans De Loof

Chapter 1

Part I: Medication review: what's in a name and what is it about?

1.1 Abstract

Background: Medication review is a multifaceted service aimed at optimizing the use of medicines and enhancing the health outcomes of patients. Due to its complexity, it is crucial to clearly describe the service, its variants, and components to avoid confusion and ensure a better understanding of medication review among healthcare providers.

Objective: This study aims to bring clarity to the origins, definitions, abbreviations, and types of medication reviews together with the primary criteria that delineate key features of this service.

Method: A narrative review approach was employed to clarify the diverse terminology associated with "medication review" services. Relevant references were initially identified through searches on PubMed and Google Scholar, complementing the existing literature known to the authors.

Results: The study uncovers a complicated, and sometimes convoluted history of "medication review" in different regions around the world. The initial optimization of medicine use had an economic purpose before evolving subsequently into a more patient-oriented approach. A selection of abbreviations, definitions and types were outlined to enhance the understanding of the service.

Conclusion: The study underscores the urgent need for comprehensive information and standardisation regarding the content and quality of the services collectively referred to as "medication review".

Keywords: medication review; medicines use review; medication therapy management; drug utilization review; community pharmacy services; pharmaceutical services, narrative review.

1.2 Introduction

Looking back in history, the pharmacy profession has experienced significant growth, change, and development and has expanded its scope of practice. Pharmacy was seen as a bridge between the health and chemical sciences. Historically, pharmacists crafted drug products *secundum artem* (according to the art), mostly for medicinal purposes (1). By the 1950s, the pharmaceutical industry's mass production and the enforcement of prescription-only legal status for many therapeutic agents had reoriented pharmacists' roles, focusing on medicine dispensing. In 1960, the concept of "clinical pharmacy" was mentioned for the first time (2). Interventions aiming at optimizing "medication use" were initiated but this endeavour was often a largely economic systemwide activity invisible to the individual patient (3). In 1990, in their pivotal and highly cited paper (4), Hepler and Strand, alarmed by the high prevalence of drug-induced hospital admissions, expressed the need for further professional reorientation to ensure safe and effective drug therapy through pharmaceutical care as a new philosophy of patient-centred practice (4). Pharmacy services became gradually more patient-centred but pinpointing the exact origin and first mention of "medication review" in the literature is rather challenging. To address this challenge, it is necessary to clarify some confusion about word usage and definitions.

Searching "medication review" by country, using the search options in Google, produces a wide array of results that can easily lead to confusion among people unfamiliar with the topic. However, one of the searches yielded a valuable definition sourced from the guidelines of the National Institute for Health and Care Excellence (NICE).: "Medication review is a structured, critical examination of a person's medicines

with the objective of reaching an agreement with the person about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste" (5).

The complex nature of "medication review" is evident in its comprehensive scope, encompassing the identification of medication-related issues, exploring a patient's pharmaceutical history, ensuring continuous data exchange among healthcare providers, incorporating the Social Determinants of Health (SDOH) and facilitating consultations between these providers and the patient (6-8). All these efforts aim to optimize the patient's use of medications in the face of the ever-expanding complexity of the pharmacotherapeutic landscape. It is, however, crucial to define the content, common language, and definitions of "medication review" before making comparisons, especially when prioritizing quality and examining stringent endpoints (9-11).

1.3 Materials and methods

For this investigation, a narrative review approach was adopted to clarify the diverse terminology associated with "medication review" services and to offer a historical context for this pharmaceutical service within primary care. Initially, pertinent references were identified by searching PubMed and Google Scholar, supplementing the literature already known to the authors. The keywords used included "medication review", "medicines use review", "medication therapy management", and "drug utilization review". Subsequently, the search was broadened through citation tracking (12). Finally, the grey literature was explored, mainly using Google Scholar and citation tracking, for various definitions and guidelines related to medication review and other pharmacy services, including drug utilization review.

Considering the substantial heterogeneity in terminology, procedures, contexts, and outcomes associated with the research question, the application of a traditional systematic meta-analysis was deemed unsuitable.

1.4 Results

1.4.1 History of medication review

By the mid-1960s, pharmacists transitioned towards a more patient-centred approach, introducing the concept of clinical pharmacy (1, 2, 4), the beginning of an evolution detailed further in Figure 1.1. Pharmacists actively participated in optimizing patient medication therapies within hospital settings (13). While pharmacists have been examining medicine charts and offering recommendations to prescribers since the 1980s, this practice was not yet widely adopted in primary care settings during that period (4, 14).

Nevertheless, there were early efforts in the 1960s in the United States to implement "drug utilization reviews" (DURs), laying the groundwork for the current concept of medication reviews (MRs) (14, 15). In 1969, the US governmental commission named the Task Force on Prescription Drug published a document titled "Approaches to Drug Insurance Design: Background Papers" marking an early significant milestone in the realm of DUR or MR (16). To reduce confusion over terms and abbreviations Table 1.1 presents an overview of many of these related services linked somehow to "medication review".

DUR is an authorized, structured, ongoing review of prescribing, dispensing and medicines use (17). DUR and related procedures were concerned with monitoring and assessing population-level medication utilization (15) to ensure its quality and cost-effectiveness (3, 14).

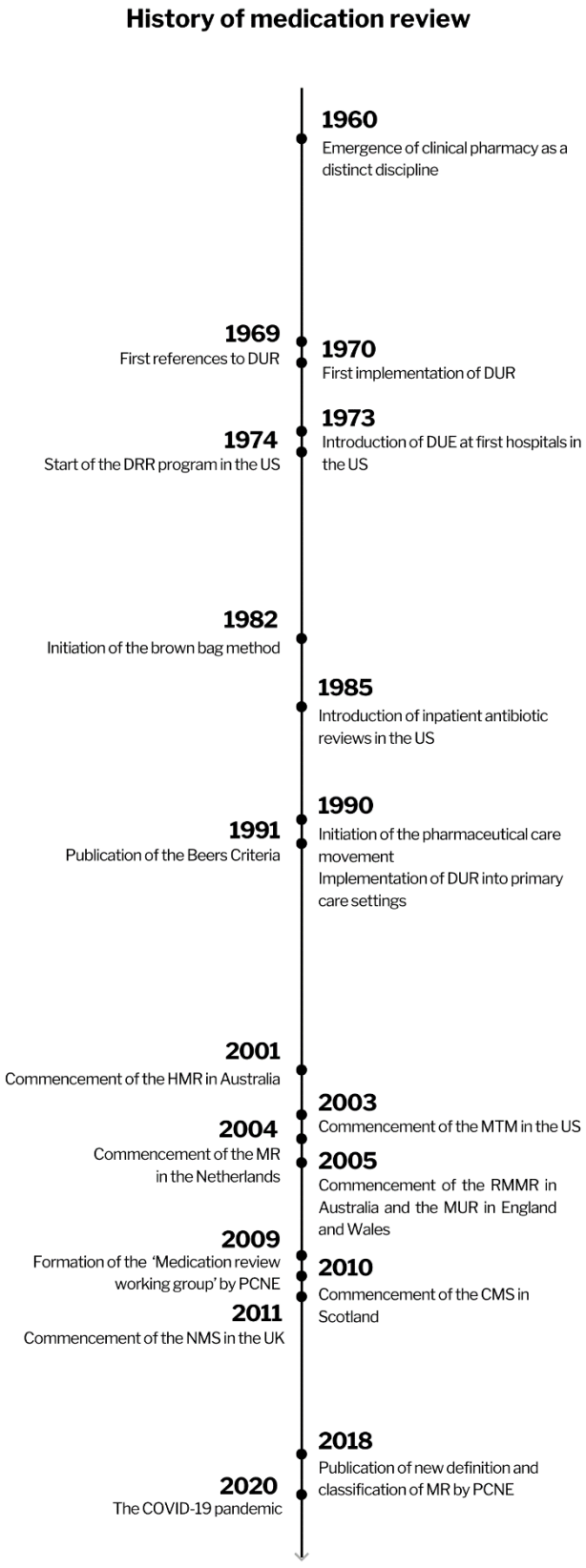

Figure 1.1: The history of medication review.

In 1970, the first DUR program was conducted by a private pharmaceutical company in the United States (14). Three years later, in 1973, the US-based organization, the Joint Commission (formerly known as JCAHO – the Joint Commission on Accreditation of Hospitals), introduced Drug Usage Evaluation (DUE), which was a more advanced analysis of medications, their uses and their contributions to various patients'

outcomes. DUE represented an interdisciplinary and systematic approach to evaluating and improving medication use, particularly at the patient level, unlike DUR. Another term, Drug Regimen Review (DRR), one of the earliest examples of DUR, was introduced in 1974 as part of a quality assurance program for the care of Medicaid recipients in the United States. During the program, pharmacists were required to conduct monthly drug reviews among nursing home residents. They would assess patients' prescribed medications to identify any potential drug-related problems, and then provide recommendations to the healthcare team for adjustments to the drug regimen (15).

Table 1.1: List of used abbreviations and their respective services related to medication review.

Abbreviation	Service	Description
AUR	Antibiotic Utilization Review	DUR performed among hospitalized patients treated with antibiotics (18).
CMM **CMTM**	Comprehensive Medication Management Comprehensive Medication Therapy Management	An individualized care plan to achieve the intended goals of therapy with appropriate follow-up to determine actual patients' outcomes, involving their active participation (19). A CMM program includes several similar elements to a CMR, yet it extends its scope to address additional facets of the patient's overall care (20). CMM not only incorporates the patient's history into recommendations, similar to CMR, but it also aims to influence elements of that history through measurable clinical outcomes (20).
CMR	Collaborative Medication Review	An internationally accepted term for medication review practices involving pharmacists collaborating closely with other healthcare professionals to review patients' medicines. Their shared goal is to optimize the use of medications and prevent inappropriate medication use (21).
CMR	Comprehensive Medication Review	A comprehensive, annual, systematic review of all available patient-specific information and medication assessments to identify and resolve potential medication-related problems. CMR involves collaboration between the patient, pharmacist, and prescriber to determine appropriate options for resolving identified problems (22, 23).
CMS	Chronic Medication Service	A service established at pharmacies in Scotland dedicated to helping patients with long-term conditions to help them manage their medicines (24).
DRUM	Dispensing Review of Use of Medicines	A review of the use of medicines with the purpose of helping patients understand their medicines and to identify medicines-related problems (6).
DUE	Drug Use Evaluation Drug Usage Evaluation	A group of structured reviews of prescribing, dispensing, and use of medication to ensure their appropriate and safe use while also optimizing the economic aspect of drug utilization (15, 18).
DRR	Drug Regimen Review	
DUR	Drug Utilization Review Drug Use Review	
MUE	Medication Use Evaluation	
MUM	Medication Use Management	
DMMR **HMR**	Domiciliary Medication Management Review Home Medicines Review	An Australian MR program involving pharmacists conducting a domiciliary visit to review patient's medications (25, 26).
MAP	Medication-related Action Plan	One of the core elements of an MTM service; it is a patient-centred document equipped with a list of action steps for the patient to use in

		tracking progress for self-management of medication-related problems (23).
MR	Medication Review	A structured evaluation of a patient's medicines with the aim of optimizing medicine use and improving health outcomes (27).
MR1	Medication Review type 1	
MR2	Medication Review type 2 *Intermediate medication review*	
MR3	Medication Review type 3 *Clinical medication review* *Advanced medication review*	
MRF	Medication Review with Follow-up	An ongoing and structured assessment of the patient's pharmacotherapy performed in Spain that comprises of detection of drug-related problems and negative outcomes related to medicines (NOMs), development of a care plan and monthly follow-up to provide continuing care (28).
MTA	Medicines Therapy Assessment	A clinical MR program conducted in New Zealand by pharmacists in collaboration with prescribers to review the use and understanding of prescribed therapy, identify medication-related problems and work with the patient and wider healthcare team to resolve these issues and optimize medication use (29).
MTM **MTMS**	Medication Therapy Management Medication Therapy Management Services	A distinct service or group of services to optimize therapeutic outcomes for individual patients (30). The MTM service model can be divided into the five core elements: Medication Therapy Review (MTR), intervention and referral, Personal Medication Record (PMR), Medication-related Action Plan (MAP), and documentation and follow-up (23).
MTR	Medication Therapy Review Medicine Therapy Review	One of the core elements of an MTM service; a systematic process that involves collecting patient-specific information, evaluating medication therapies to identify medication-related problems, creating a prioritized list of these problems, and devising a resolution plan. MTR can be comprehensive (CMR) or targeted (TMR) (23).
MUR	Medicines Use Review	A subtype of MR where pharmacists partner with patients to improve their medicines use and adherence (31). Referring to the Pharmaceutical Care Network Europe (PCNE) definition type MR2a includes MUR (32).
NMS	New Medicine Service	A service providing help and advice about medicines to patients who are prescribed a medicine to treat a long-term condition for the first time (33).
PMR	Personal Medication Record	One of the core elements of an MTM service; it contains an up-to-date list of medications helping patients manage their pharmacotherapy (20).
QUM	Quality Use of Medicines	A package of services performed by Australian pharmacists to support the quality use of medicines, including HMR and RMMR (26).
RMMR	Residential Medication Management Review	An Australian program involving pharmacists conducting MRs of patients residing in aged care facilities (26, 34).
SMR	Structured Medicine Review	A review of a patient's medication, taking into consideration all aspect of the patient's health in the form of shared decision-making conversations between a clinician and a patient (35).
TMR	Targeted Medication Review	Ongoing medication monitoring to assess medication use and identify and address specific actual or potential medication-related problems (20). TMR involves follow-up with a healthcare professional or a patient to resolve identified medication-related problems. TMR must be performed quarterly, which enables identifying issues on a more regular basis than through yearly CMR (20).

In the 1980s, the Joint Commission made the implementation of Drug Use Evaluation (DUE) into hospital procedures one of the items to be audited. Initially, the program would only focus on the use of antibiotics for hospitalized patients. Over time, this evaluation process expanded to all medications (15, 18). Another concept that contributed to the development of MR was a "brown bag review". The method was developed in 1982 under the name of the "Brown Bag Prescription Evaluation Program" in the United States (36). Its name originates from the brown supermarket bags in which patients would bring all their medications and supplements that they had at home (including those prescribed by physicians, over-the-counter medications, supplements or complementary medicines), to a healthcare appointment (37). A healthcare professional, usually a pharmacist or a physician, would review all patient's medications comprehensively, address and resolve any medication-related problems and ultimately, educate the patient about the proper use of medications (36, 37). The "brown bag review" presented a new, patient-centred approach and closely mirrored some of the objectives of today's MR.

Due to the Omnibus Budget Reconciliation Act of 1990 (OBRA '90), pharmacists in the United States were mandated to incorporate DUR outside hospitals as part of their healthcare for Medicaid beneficiaries (18, 38). All the DUR-related programs served similar functions. Nevertheless, the concepts of DRR and DUE relied on reviewing the appropriateness of an individual patient's therapy, whereas DUR constituted an analysis of a larger number of prescription profiles (15). The term "drug utilization review" can easily be confused with "drug utilization research" or "drug utilization studies", concepts embraced within the pharmacoepidemiology discipline that are time-limited investigations focused on measuring drug usage, without necessarily evaluating individual appropriateness or attempting to bring about changes in a particular patient's therapy (14).

The transition to the 2000s represented a notable period of progress for MR programs (7), illustrative of the momentum of the pharmaceutical care movement that started a decade earlier (4). Projects were initiated in Australia, the United Kingdom, Switzerland, New Zealand, the United States, Canada, the Netherlands, Germany, Sweden, and Denmark (7). Moreover, the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, published in 1991 by Mark H. Beers, an American geriatrician, and updated by the American Geriatrics Society (AGS) in the following years, provided a standardized tool for identifying potentially inappropriate medications and improving medication management (39). Since that time, numerous other tools have been developed to enhance the medication management of the elderly. A study conducted in 2019 identified a total of 76 such tools (40). Among these additional tools, START/STOPP stands out as one of the most widely acknowledged, having been established in 2008. Since its inception, it has undergone two subsequent versions, and its implementation is often customized to align with the specific contexts of different countries (41). In addition to these explicit tools, an implicit method is also used, which involves the Medication Appropriateness Index (MAI) to identify potential inappropriate prescriptions. Although this implicit method may be more time-intensive and challenging to implement, it has the potential to be more comprehensive (42, 43).

In the early 1990s, national health departments and related entities as well as various international organizations, such as the World Health Organization (WHO) and the International Pharmaceutical Federation (FIP), developed the first guidelines and frameworks to implement medication reviews in primary care (44). All these initiatives throughout the years reinforced the role and responsibility of pharmacists in patient care and drug therapy management service delivery.

The first countries to formally integrate medication review into primary care were Australia (2001), the United States (2003), and the United Kingdom (2005) (26, 45). The Australian Home Medicines Review (HMR), also known as the Domiciliary Medication Management Review (DMMR), was launched in 2001 and it was perceived as a forerunner to many of the subsequent medication reviews (6, 26). The Australian pharmacists provided home visits to evaluate the patient's current medication regimen and then consult with a clinician about any potential drug-related problems (46). The Residential Medication Management

Review (RMMR) was launched in Australia in 2005 providing medication reviews for occupants of these care facilities. The HMR and RMMR support the Quality Use of Medicines (QUM) initiative in Australia (26).

In 2003, the American Pharmacists Association (APhA) introduced the concept of Medication Therapy Management (MTM) in the United States (47) as a group of services to optimize therapeutic outcomes for individual patients (47). Comprehensive medication review constitutes one of the pharmaceutical services within the MTM (48). Other examples of MTM are intervention and referral, a personal medication record, a medication-related action plan, documentation and follow-up (20). In the UK, government policy documents, including the National Service Framework for Older People, have integrated medication reviews into primary care (49), with Medicines Use Reviews (MURs) introduced in England and Wales in 2005, and the Chronic Medication Service in Scotland in 2010 (6). Another evaluation – the New Medicine Service (NMS) – was launched in 2011 to improve the adherence and outcomes of patients starting new medications (33). Two years later, the National Health Service (NHS) published its overall “Medicines Optimisation Agenda” to improve patient outcomes through better use of medicines with reviews of patients’ medication regimens as one way to reach that goal (50). Nevertheless, despite the presence of shared features and objectives, these reviews exhibited notable variations in the terminology employed. In 2009, the Pharmaceutical Care Network Europe (PCNE) established a "Medication review working group" to standardize the terminology and practice of this service performed by pharmacists (27). Subsequently a global spread of medication review projects can be recorded (51-53). Starting in 2016, pharmacists have been able to retrieve a Summary Care Record (SCR) containing crucial clinical details, such as medication history, allergies, and adverse reactions, sourced from the patient's GP record (54). In April 2021, the Medicines Use Review (MUR) program was discontinued in the UK and replaced by Structured Medication Reviews (SMR) (55).

Considering more recent events, the COVID-19 pandemic has highlighted the community pharmacists' proficiency in identifying and effectively addressing medication-related problems (56) and ensuring the safe and effective use of long-term medications (56, 57). Together with the pandemic's demand for testing and vaccinations, this has further underscored the indispensable non-dispensing-related roles of community pharmacists.

1.4.2 Definitions and various types of medication review

As the implementation of medication review continues to grow, it is essential to clearly define what this pharmaceutical care service entails. The most important definitions are shown in Table 1.2. Zermansky et al. (58) in 2002 formulated one of the first definitions: “the process where a health professional reviews the patient, the illness, and the drug treatment during a consultation. It involves evaluating the therapeutic efficacy of each drug and the progress of the conditions being treated. Other issues, such as compliance, actual and potential adverse effects, interactions, and the patient’s understanding of the condition and its treatment, are considered when appropriate. The outcome of the review will be a decision about the continuation (or otherwise) of the treatment”.

The authors of the "Oxford Handbook of Clinical Pharmacy" of 2007 also presented a concise and useful definition: “a structured critical examination of a patient’s medicines by a healthcare professional reaching an agreement with the patient about treatment, optimizing use of medicines, minimizing the number of drug-related problems, and avoiding wastage” (59).

Nowadays, an often-used definition is the one developed by PCNE in 2018 that characterizes medication review as a structured evaluation of a patient’s medicines with the aim of optimizing medicine use and improving health outcomes. This definition entails detecting drug-related problems and recommending interventions (27).

Table 1.2: The most important definitions of medication review, sorted by publication date.

Definition	Source	Year
A structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimizing the impact of medicines, minimizing the number of medication-related problems and reducing waste (60).	Medicines Partnership	2002
A structured, critical examination of a patient's medicines by a healthcare professional: reaching an agreement with the patient about treatment, optimizing the use of medicines, minimizing the number of medication-related problems, avoiding wastage. Regular medication review maximizes the therapeutic benefit and minimizes the potential harm of drugs. It ensures the safe and effective use of medicines by patients. A medication review provides an opportunity for patients to discuss their medicines with a healthcare professional. Medication review is the cornerstone of medicines management (59).	Oxford Handbook of Clinical Pharmacy, 1nd edition	2007
A structured, critical examination of a person's medicines with the objective of reaching an agreement with the person about treatment, optimizing the impact of medicines, minimizing the number of medication-related problems and reducing waste (31).	National Prescribing Centre (NPC)	2008
A structured evaluation of a patient's medicines with the aim of optimizing medicine use and improving health outcomes. This entails detecting drug-related problems and recommending interventions (27).	Pharmaceutical Care Network Europe (PCNE)	2018

The initial classification of various levels of medication review that received significant recognition was introduced in 2002 in "Room for Review" published by the National Prescribing Centre (NPC), an NHS organization supported by the British Department of Health (31, 60):

- Level 0 – Ad hoc – unstructured, opportunistic review.
- Level 1 – Prescription review – a technical review of the list of a patient's medicine;
- Level 2 – Treatment review – a review of medicines with the patient's full notes;
- Level 3 – Clinical medication review – a face-to-face review of medicines and conditions.

Subsequently, the classification that has gained widespread acceptance was published in 2008 within the NPC's updated document "A Guide to Medication Review". In accordance with this classification, the following types of MR were delineated (31):

- Type I – Prescription review – addresses technical issues relating to the prescription; the patient is usually not involved; it is a review of medicines.
- Type II – Compliance and concordance review – addresses issues relating to the patient's medicine-taking behaviours; the patient is usually involved; it focuses on medicine use. This type includes MURs.
- Type III – Clinical medication review – addresses issues relating to the patient's use of medicines in the context of their clinical conditions; the patient is always involved and there is also always access to patient information (e.g. clinical conditions and laboratory test results). It reviews medicines and conditions.

In some countries, the extension of Type III - Clinical review with prescribing, also known as Type IV – exists as well and includes prescribing authority (53).

Currently, the classification published by PCNE in 2018, which divided medication review into three types, is in widespread use (32):

- Type 1 – Simple MR (MR1) – is based solely on the patient's medication history available in the pharmacy; it enables the detection of drug interactions, some side effects, unusual dosages, and some adherence issues. This type of MR is part of routine dispensing.
- Type 2 – Intermediate MR – classified into two subtypes:
  - Type 2A (MR2A) – based on the medication history and patient information, thus it is useful when the patient can be interviewed; detects drug interactions, drug-food interactions, side effects, unusual dosages, effectiveness, and adherence issues, but also issues with OTC medications.
  - Type 2B (MR2B) – based on the medication history and clinical information obtained from the general practitioner (GP) or physician; detects drug-interactions, drug-food interactions, side-effects, unusual dosages, adherence issues, effectiveness issues, indication without a drug and drugs without indication.
- Type 3 – Advanced or Clinical MR (MR3) – based on a complete medication history, an extensive patient interview and clinical data obtained from the GP or the physician; detects drug-drug interactions, drug-food interactions, issues with OTC drugs, side effects, unusual dosages, adherence issues, effectiveness issues, indication without a drug and drugs without indication.

Nevertheless, the definition, comprehensiveness, levels of interprofessional collaboration and remuneration of MR still vary among different countries, mainly due to their specific processes, guidelines, and terminology (10).

Table 1.3 presents an overview of several key guidance documents about MR. MR may also be associated with other pharmaceutical or medication management services, such as medical reconciliation, deprescribing interventions or the previously mentioned drug utilization reviews.

Table 1.3: List of various guidance documents concerning medication review.

Organisation and country	Guideline	MR type by PCNE	Year
American Pharmacists Association; National Association of Chain Drug Stores Foundation, USA	Medication therapy management in pharmacy practice: core elements of an MTM service model (version 2.0) (23)	3	2008
Patient-Centred Primary Care Collaborative, USA	The Patient-Centred Medical Home: Integrating Comprehensive Medication Management to Optimize Patient Outcomes Resource Guide (19)	3	2012
Saskatchewan Ministry of Health, Canada	Saskatchewan Medication Assessment Program (SMAP). Procedures and guidelines for Saskatchewan pharmacists (61)	3	2013
Royal Pharmaceutical Society, UK	Medicines Optimisation: Helping patients to make the most of medicines (50)	2a	2013
National Institute for Health and Care Excellence (NICE), UK	Medicines Optimisation: The Safe and Effective Use of Medicines to Enable the Best Possible Outcomes (5)	2a	2015
Ontario Ministry of Health and Long-Term Care, Canada	Professional Pharmacy Services Guidebook 3.0. MedsCheck, Pharmaceutical Opinion and Pharmacy Smoking Cessation Program (62)	2a	2016
Comprehensive Medication Management in Primary Care Research Team, USA	The Patient Care Process for Delivering Comprehensive Medication Management (CMM): Optimizing Medication Use in Patient-Centred, Team-Based Care Settings (63)	3	2018

Pharmaceutical Society of Ireland (PSI), Ireland	Guidelines on the Counselling and Medicine Therapy Review in the Supply of Prescribed Medicinal Products from a Retail Pharmacy Business (64)	2a	2019
Pharmaceutical Society of Australia (PSA), Australia	Guidelines for pharmacists providing Residential Medication Management Review (RMMR) and Quality Use of Medicines (QUM) services (65)	3	2019
Pharmaceutical Society of Australia (PSA), Australia	Guidelines for Quality Use of Medicines (QUM) services (66)	3	2020
Pharmaceutical Society of Australia (PSA), Australia	Guidelines for comprehensive medication management review (67)	3	2020
The Royal Dutch Pharmacists Association (KNMP), The Netherlands	Guideline for conducting clinical medication review in community pharmacy (68)	3	2020
National Health Service (NHS), UK	Structured medication reviews and medicines optimisation: guidance (69)	3	2020
Department of Health and Aged Care, Australia	Guiding Principles for Medication Management in the Community (70)	3	2022
General Pharmaceutical Council of Spain, Spain	Practical guide to Clinical Professional Pharmacy Services (CPPS) in Community Pharmacy (71)	3	2022

1.4.3 The principal criteria delineating key features of medication review

1.4.3.1 Participating healthcare providers

A MR should be carried out by a skilled healthcare professional. Current literature and practice suggest that pharmacists, GPs, or nurses are typically the ones conducting MRs, listed in descending order of prevalence (72).

Interprofessional collaboration is a fundamental component of the MR process and enhances its quality by providing a more comprehensive understanding of patients and their medications (6, 73, 74). Healthcare providers must trust the reviewing practitioner and engage in open discussions about potential recommendations to prescribers during patient regimen evaluation. Relying solely on written recommendations from pharmacists to GPs is less effective, highlighting the importance of a strong collaboration between GPs and community pharmacists for effective MRs (6, 75).

Another significant factor pertains to the patients' accessibility to community pharmacists (76, 77). Diversity in healthcare structures among various countries may contribute to variations in how MRs are carried out (51). For instance, in some countries, patients can closely cooperate with community pharmacists, who monitor their pharmacotherapy and guide them in medication use (20, 26, 75).

1.4.3.2 Target group of patients

Currently, there are no globally recognized standards yet that conclusively identify the patients who are to be prioritized for MRs. Eligibility can differ based on the country and healthcare system, and it usually depends on a combination of factors that have been correlated with drug-related problems such as multimorbidity, the complexity of the medication schedule (including polypharmacy), the patients' age and frailty, and the presence of high-risk medicines (78, 79). Effectiveness research should ultimately determine who benefits most. Furthermore, it is essential to recognize that compensation should be proportionate to the complexities of the case, incorporating the Social Determinants of Health. There is a rising recognition that healthcare should consider individuals' physical, mental, and socioeconomic well-being, taking into account subjective experiences and recognizing the SDOH to effectively address drug-related problems (80). The integration of this additional dimension substantially increases the complexity of MR.

Medicines are for real people who grapple with real-world problems, leading to less-than-ideal adherence and an array of preventable drug-related problems. Failing to incorporate this into a patient-centred pharmaceutical care philosophy will result in an inadequately powered MR and a significant number of patients being denied the full benefit of pharmacotherapy.

1.4.3.3 The most crucial outcome studies

The process of MR offers a diverse range of potential advantages, including clinical, economic, humanistic, and other related outcomes. Although the purported effects of MRs appear realistic and achievable, irrefutable proof from RCTs substantiating their positive outcomes remains scarce and, in some cases, inconclusive. Among the positive effects of MRs, the most consistent and substantial are the reduction of inappropriate prescriptions, the reduction of drug-related problems, and increased adherence (81-83).

The effects on mortality and morbidity related to MR have been studied, but there is a lack of unequivocal findings (83). In the case of hospitalizations, the outcomes are inconsistent (81, 83). Nevertheless, Mizokami et al. (84) reported that MR interventions might be effective in inpatient settings but found no such results in outpatient settings (84). Moreover, the same authors suggested that a reduction in hospital admissions was more likely for MR3 as compared to MR1 and MR2 (84). There are a small number of studies presenting a positive impact on the level of laboratory values such as low-density lipoproteins, cholesterol, and HbA1c as well as blood pressure (52, 53, 85). Moreover, MR contributed to the decrease in the number of falls among patients (82). However, studies on patient with frailty have not provided clear conclusions yet (86) but as there is no universally accepted definition or assessment of frailty this is not very surprising (87).

In terms of the patients quality of life, most studies showed no significant impact on this aspect, apart from one systematic review that reported the benefit of MTM services on patient's physical outcomes, while minimal effect was observed in mental outcomes (81-83).

Regarding the impact of MR on cost-effectiveness, the evidence is also limited and mixed. A small number of studies have demonstrated substantial cost savings due to reduced healthcare utilization and medication expenditures (52, 81, 83).

1.5 Discussion

The history of MR reflects a distinct and extensive journey to reach its current state. In its early stages, approaches to drug optimization, such as DURs, were largely driven by economic considerations. In contrast, MRs are now primarily focused on improving and ensuring the optimization of patient treatment, complemented by patient education initiatives (3).

MR extends beyond a mere definition. Although the content of MRs can vary widely, different types often converge on similar principles, as shown in previous studies (10, 11). For example, Medication Therapy Management (MTM) comprises various components, with MR being one of them (20). Upon closer examination, many of the other components are frequently integral to MR. Conversely, the MR process in Spain, referred to as medication review with follow-up (MRF), involves not only a structured assessment of the patient's pharmacotherapy but also ongoing monthly follow-ups (28). The complex nature of MRs renders the assessment and comparison of tangible outcomes challenging, particularly in the absence of a standardized methodology and given the variations in processes and healthcare systems across projects and countries.

The lack of definitive evidence regarding the positive outcomes of medication reviews from randomized controlled trials has raised questions about its validity and necessity. First, it is worth noting that assessing the effectiveness of MRs is complex and poses challenges in study design and implementation. The process

or feasibility of performing such studies is not immediately clear or simple. However, while randomized controlled trials (RCTs) are considered the gold standard for evaluating the effectiveness of a single well defined and easily replicable intervention, today these characteristics do not align with MRs. The complex and multifaceted nature of MR makes it challenging to measure or assess using RCTs. There remain however, enough arguments from clinical expertise, guidelines, qualitative studies, observational studies, and simple logic to support and further invest the effectiveness of MRs (88, 89).

Other complex interventions, like deprescribing, also encounter challenges in evaluating their effectiveness (90, 91). What MR and deprescribing mutually share is also the goal of combating inappropriate prescribing, which is the primary contributor to multimorbidity. It is not yet possible to compare or compile the results of trials assessing the effect of these services in a convincing meta-analysis. Many studies, for instance, limited the scope to specific outcome measures, selected different group of patients, included various times of follow-up. Furthermore, there is a vast discrepancy in MR terminology, not only when it comes to defining the process itself, but also regarding terms used to describe and define activities undertaken for this purpose. A standardization of the terms related to MR would enable researchers to compare data from similar interventions and studies (10).

Additionally, it is also crucial to ensure a comprehensive quality assessment of MRs (9) before launching into a large-scale reliable and repeatable evaluation of their outcomes. As demonstrated in this review paper, certain countries have a longer history of conducting various forms of medication reviews, while others are just embarking on this journey (7, 51). Standardization holds the potential to improve the reliable implementation of this practice in more countries, similar to the benefits observed in adherence research through the definition of adherence terms (92).

1.6 Conclusion

This review paper described the origins, variety, types, and historical background of “medication review”. Additionally, it aimed to enhance its comprehension by collecting definitions and compiling a list of guidelines about the MR process. Although Blenkinsopp et al. (6) reported a decade ago on the state of the art of MR in the UK, this review paper explored MRs from an international perspective while pointing towards the progress made in recent times.

Regardless, there remains a pressing need for internationally supported standardization and a more comprehensive description of the service’s content and quality to enable comparisons between studies and facilitate a broader implementation. This should also allow more reliable assessments of MRs’ outcomes and strengthen the uptake of this service, all with the final goal of improving pharmaceutical care for patients with complex medication needs.

Author Contributions

Conceptualization, A.R. and H.D.L.; methodology, M.B, A.R. and H.D.L.; validation, all authors.; data curation, M.B, A.R. and H.D.L.; writing—original draft preparation, M.B. and A.R..; writing—review and editing, M.B, A.R, H.D.L, G.R.Y.D.M., S.S; visualization, M.B..; supervision, A.R. and H.D.L.; All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

Part II: Introduction of Belgium's Health situation in connection to Pharmaceutical Care

1.7 Population of Belgium

Before the COVID-19 pandemic, the life expectancy (LE) had steadily increased over decades, reaching 82.1 years in 2019, a gain of 4 years since the turn of the century (93, 94). Women have a 4.5 year advantage over men (78.6 years for men and 83.1 years for women) (94). The LE is highest in Flanders, followed by Brussels and Wallonia. LE in Belgium is slightly lower than the European Union (EU)-15 average (95). LE decreased by one year in 2020, falling to 80.9 years, due to the high mortality in the first year of the COVID-19 pandemic (93, 94).

Nearly 30% of Belgians aged 15 years and older live with at least one chronic disease, a percentage that increases to 44% among individuals aged 75 years and older (93, 94). Since 1997, there has been a notable rise in the occurrence of multimorbidity, which is characterized by the presence of at least two major non-communicable diseases (NCDs) such as chronic lung disease, heart disease, hypertension, diabetes, cancer, and arthropathy. This upward trend in multimorbidity continues even after accounting for age, suggesting that factors other than aging such as obesity, poverty, and a lack of social infrastructure are contributing to this increase (96, 97). Given that most non-communicable diseases are chronic, the terms are often used interchangeably, despite their differences (93). Individuals with a higher socio-economic status (SES) tend to live longer. In 2020, the gap in life expectancy at birth between the highest and lowest SES groups, defined as the last and first quartile of a multidimensional SES score, was 9.3 years for men and 6.3 years for women (93). Belgium invests a smaller share of its healthcare budget on public health and disease prevention compared to the EU average, allocating only 1.6% compared to the 2.9% average across the EU (94).

Multimorbidity is linked to the utilization of multiple medications, commonly referred to as polypharmacy (98). In the context of polypharmacy, inappropriate prescribing is associated with higher chances of drug-drug interactions (99-102), adverse drug reactions (100-104), drug-related hospitalizations (99, 100, 102, 104), falls (99, 104), mortality (99, 104), and reduced quality of life (104). Various risk factors associated with hospital admissions or readmissions related to medication have been recognized, including the use of high-risk medications, polypharmacy, therapy nonadherence, advanced age, renal disease, congestive heart failure, cognitive impairment, comorbidities and the duration of hospital stays (105). Established interventions that might contribute to a reduction in hospital readmissions related to medication include the engagement of a pharmacist, educational programs, and transition-care interventions (105). Admission rates for asthma and COPD remained well above the EU average in 2019, which suggests room for improvement in primary care to better manage these conditions. New care pathways for people with diabetes have been developed in recent years, with multidisciplinary teams involving GPs, specialists and other healthcare providers (94).

1.8 Accessibility of community pharmacies in Belgium

In Belgium, medicines are readily accessible through a widespread network of community pharmacies, with a ratio of one pharmacy for every 2,253 individuals in 2019 (106). There is a requirement for pharmacies to participate in out-of-hours services (106). Pharmacies in Belgium are staffed by at least one pharmacist who oversees and performs pharmaceutical acts, such as offering guidance on proper medication usage, providing essential information related to health promotion and disease prevention, and making referrals to other healthcare providers (107). Pharmacists forge a robust bond of trust with many of their patients

through their close and personal interactions (74, 108). Community pharmacists are frequently acknowledged as the most accessible component of the health system and the initial point of contact for the public (109).

The Netherlands encountered a surge in GP workload in 2006 (110), and Belgium's 2021 Organisation for Economic Co-operation and Development (OECD) report highlighted a looming shortage of primary care physicians, with an alarming 44% of them are nearing of exceeding the age of 55 (94, 111). Research worldwide supports the integration of pharmacists into primary care settings to streamline patient care and medication management, leading to a more efficient and robust healthcare system (112).

1.9 Reimbursement of pharmaceutical services in Belgian community pharmacies

The funding structure for public pharmacies in Belgium consists of three main components: (i) economic margin: a percentage of the sales price of all medications, covering the costs of dispensing, (ii) reimbursement fee: a per-package fee for dispensed medications, compensating for intellectual services and (iii) pharmaceutical care fee: a specific fee for advanced services, such as inhalation corticosteroid guidance for asthma patients (106, 113). Even though the third component is still under development, substantial data backs the investment in broadening pharmacist services (114). This is especially true for services centred on long-term chronic conditions, such as medication reviews (MRs) (114). Amid rising global drug costs and escalating pharmaceutical expenditures (115), evidence supports investing in initiatives that promote the appropriate use of medication. Tackling the issue of medication non-adherence is a vital strategy to alleviate the strain on healthcare systems (116). It is one of the numerous methods through which pharmacists can help cut costs, particularly in the management of chronic diseases (117).

One of the reasons for pursuing this PhD was to contribute scientific support and to aid in the development of medication review type 3 (MR3) in Belgium. Compensation for such advanced pharmaceutical care is a strategic investment in preventive measures, an area where Belgium has been lagging behind its European counterparts (94).

1.10 Implementation of type 3 medication review in Belgium

The Royal Pharmacists Association of Antwerp (KAVA) is a professional association of pharmacists dedicated to enhancing the value and interests of individual pharmacists in healthcare for the betterment of patients and society. KAVA sets itself apart through a proactive and customer-oriented approach (118). The focus is on innovation, which is why I received approval from the KAVA board to attend the Periodic Individual Pharmacotherapy Analysis (PIAF) MR training course in the Netherlands in 2016 (Figure 1.2). This course was the extended version of all MR courses designed for Dutch pharmacists, integrating MR3 into their professional practice.

Subsequently, we tailored the content and structure of this program to suit the Belgian context. Since 2017, KAVA has been organizing numerous training sessions for pharmacists to facilitate the integration of MR3 into their professional routines. Pharmacists underwent training on conducting structured MR3s, accurately interpreting lab values, handling diverse information sources, and understanding guidelines. Additionally, before the COVID pandemic, communication training was also incorporated into lessons. Finally, practical application occurred through hands-on practice with real-life cases. Pharmacists were encouraged to adopt these practices effectively and received the necessary support. To provide the project with a robust scientific foundation, we collaborated with the University of Antwerp and the Vrije Universiteit Brussel on a PhD program launched in 2018. Furthermore, a collaborative initiative with Domus

Medica, an association for general practitioners in Flanders, for medico-pharmaceutical consultations on MR3 has been officially authorized by the National Institute for Health and Disability Insurance (NIHDI) since 2021 (119). This allows the organization of local meetings between community pharmacists and GPs, facilitating the deployment of this service. Despite its complexity and future-oriented approach, it's worth highlighting that in 2023 this MR3 program was ranked as the fifth most requested in Belgium among all medico-pharmaceutical consultations programs (120). Programs addressing the phasing out of benzodiazepines, polymedication in the elderly, and collaborative efforts between general practitioners and community pharmacists achieved slightly higher popularity (120).

During the Covid pandemic, the training course was temporarily shifted to an online format. From 2022 onward, we optimized this training in collaboration with the Continuing Education Institute for Pharmacists (IPSA), which covers all of Flanders (121). Since then, there has also been a joint effort to organize training courses across Flanders.

In conducting our study, we diligently collected and thoroughly analysed outcomes from the in-depth training sessions and projects we organized in collaboration with KAVA and later IPSA. This approach was designed to ensure that the study's results and conclusions actively contributed to the improvement of the training sessions. Consequently, this established a robust foundation for continuous exploration and advancement of MR3 in future studies, all aimed at effectively implementing MR3 and enhancing patient care.

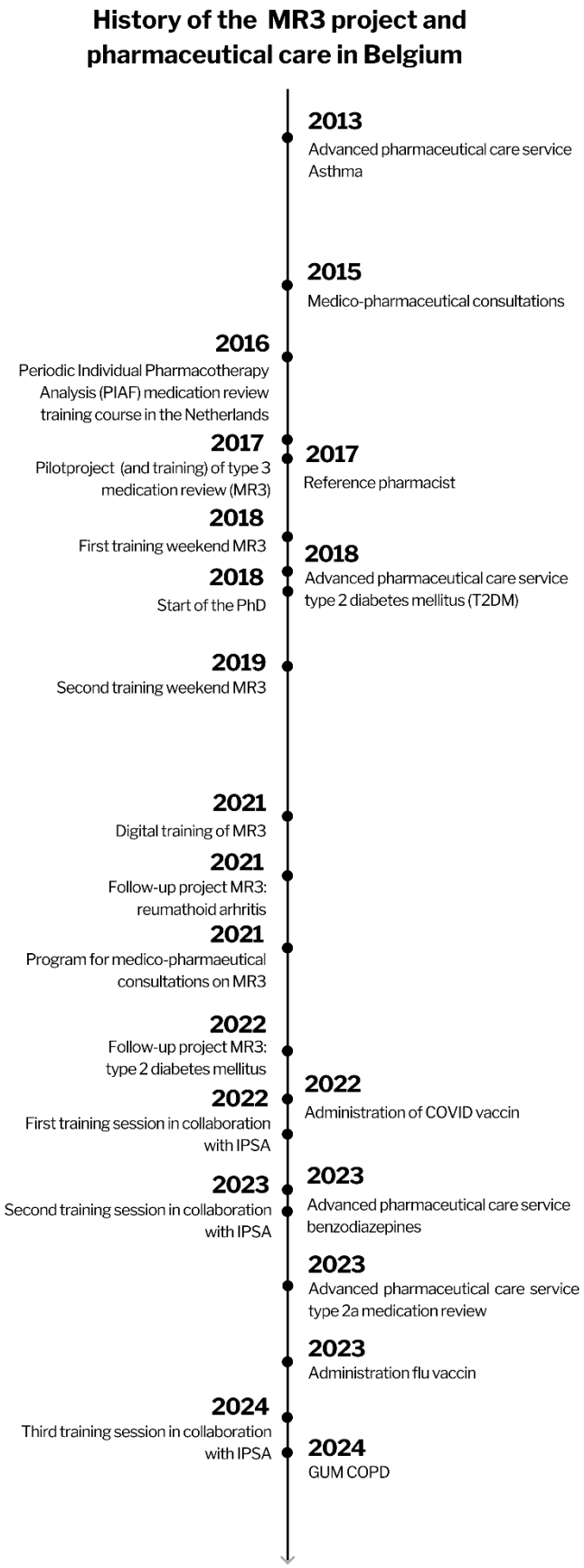

Figure 1.2: The timeline depicts the PhD project's history on the left and the evolution of advanced pharmaceutical care in Belgium on the right.

1.11 Pharmaceutical care in Belgium

Steps have been implemented to strengthen the role of pharmacists and reorient their remuneration, reducing susceptibility to fluctuations arising from changes in pharmaceutical prices.

Belgium differentiates between basic pharmaceutical care and advanced pharmaceutical care. At the heart of basic pharmaceutical care lies pharmacists' pivotal role during dispensing, encompassing patient education, medication guidance, monitoring, referrals, and electronic patient record documentation (122). In Belgium, the concept of pharmaceutical care was introduced in the modified Royal Decree of the 1st of May 2006 and further elaborated in 2009 by the Good Pharmaceutical Practice guidelines (107, 123).

All advanced pharmaceutical care services eligible for reimbursement are outlined in Table 1.4 (124-135). The first advanced pharmaceutical care service qualifying for reimbursement was introduced in Belgium in 2013 and tailored to new asthma patients, focusing specifically on providing guidance for the use of inhalation corticosteroids, referred to as Good Use of Medicines (GUM) Asthma, as shown in Table 1.4 (113). Furthermore, multidisciplinary collaboration between physicians and pharmacists has been actively promoted through the financing of medico-pharmaceutical consultations, which commenced in 2015 (106, 136). In 2017, services related to asthma were expanded to cover chronic patients. Additionally, since October 2017, individuals with a chronic disease have the option to designate a family pharmacist responsible for creating and updating the patient's medication schedule, ensuring its accessibility to other healthcare providers (125, 137).

Starting in 2018, a new remunerated pharmaceutical care service was introduced for pharmacists overseeing patients with type 2 diabetes, focusing on medication adherence (138). Even though it has many advantages, the necessity for a prescription from a physician impedes extensive use of this service (139). Effective January 2024, there is a renewed implementation of this service (135, 140). During the COVID epidemic, pharmacists were permitted to perform rapid antigen tests from November 1, 2021, to June 30, 2023 (132). Additionally, since 2022, pharmacists have been authorized to administer COVID vaccines, and as of 2023, they have gained permission to administer flu vaccines (141).

In February 2023, a pilot initiative to gradually discontinue benzodiazepines was initiated, initially planned for one year but scheduled for extension (127). As a component of this project, patients, in collaboration with their primary care provider and community pharmacist, commence a systematic taper of benzodiazepine utilization. The expenses incurred for compounding medications during the tapering process are fully reimbursed by the NIHDI, eliminating any financial burden on the patient.

Starting from April 1, 2023, Belgium introduced a reimbursed service related to medication review type 2a (131). This service can be initiated by the community pharmacist, patient, or GP. The goal of this MR is to evaluate whether the patient's medication regimen is still suitable and aligned with the individual's needs. It also aims to determine if any adjustments to the treatment plan are required (e.g., to minimize potential drug interactions) and to explore the possibility of phasing out or discontinuing certain medications (131). The pharmacist involved in the review will then inform the patient's GP about the proposed interventions to optimize the medication use. This service is primarily intended for outpatients taking at least five chronic reimbursed drugs who require personalized counselling. These patients typically fall into the category of older adults or individuals with limited health literacy. Patients must provide informed consent (eHealth Consent) for the sharing of their health data and ongoing pharmaceutical care. A similar specific pathway will be established for patients residing in residential care homes in the future (131).

Based on the patients' medication history and a focused initial discussion, the pharmacist will thoroughly assess their medication use. Following the conversation, the pharmacist will analyse all collected data and, using a structured method, identify any potential drug-related issues. An action plan will then be developed, outlining potential interventions to optimize medication use. This plan will initially be presented to the GP before being shared with the patient during a second consultation. If necessary, the

GP will adjust the medication schedule accordingly. This medication review service is fully reimbursed by the healthcare system. Exceptionally, additional medication reviews can be conducted if prescribed by the physician based on a specific need of the patient (131, 142).

There is often a long delay between the initial design phase and the final completion and successful implementation of a new service. This is not unique to Belgium or to pharmaceutical services. It is a common characteristic of project development in many countries and organizations.

Introduced as the latest initiative, Belgium launched an upgraded pharmaceutical care program on April 1, 2024, eligible for reimbursement for individuals with COPD. This program is precisely designed to provide guidance on the appropriate use of inhalation medications, referred to as Good Use of Medicines (GUM) COPD, as outlined in Table 1.4 (143).

Table 1.4: Different remunerated advanced pharmaceutical care services in Belgium

Service	Target group	Purpose	Initiator	Remuneration for community pharmacist (1/1/2024 incl. BTW)
GUM asthma	• Start-up asthma patient: 2 interviews: within 7 days of 1st episode and 3-6 weeks afterwards or Asthma insufficiently controlled: on delivery GM and finding inadequate control of asthma • Outpatient	Improving outcomes in patients with asthma by focusing on good adherence and inhalation technique	Community pharmacist, patient or physician	25.10 euros per conversation
Family pharmacists	Chronic patient taking at least 5 different reimbursed drugs (including 1 chronic, defined daily doses (DDD) > 160)	Keep the patient's medication schedule up-to-date and make it accessible to the other healthcare providers with whom he has a therapeutic relationship.	Community pharmacist, patient or physician	An annual fee of 37.86 euros.
GUM type 2 diabetes	• Every patient with type 2 diabetes, irrespective of age and risk factors, who have shared medical records and are not included in the diabetes care programme or a convention. • Outpatient	Motivate patient for proper use of their medicines and education session on medication adherence. Pharmacists are required to complete two hours of refresher training each year.	On physician's prescription	27.19 euros per individual conversation; 17 euros for a group session (max 10 patients)
GUM discontinue benzodiazepines	• Patient with minimum 3 months single benzodiazepine intake once daily • The pharmacist is the family pharmacist of this patient • Patient follows entire phasing-out programme in the same pharmacy of his/her choice; does not use any benzodiazepine (or Z-drug) other than that prescribed as part of the phasing-out programme • Outpatient	Tapering off benzodiazepine use Only entitled to reimbursement for one programme per year	On physician's prescription and form	Initiation call: 25.10 euros, magistral preparation of the medicines: 16.01 euros
GUM type 2a MR	• Patient with ≥ 5 chronic reimbursed drugs (> 160 DDD per drug) • The pharmacist is the family pharmacist of this patient • Patient is in need for personalised counselling or follow-up • Outpatient	Improving the use of medicines Can be repeated every 2 years	Community pharmacist, patient or physician	101.17 euros
COVID antigen test	*Adults and children > 6 years; within testing guidelines of Sciensano*	*Managing the COVID-19 pandemic (from November 1, 2021, to June 30, 2023)*	*Community pharmacist, patient or physician*	*21.72 euros*
COVID vaccination	Adults and children > 12 years, focusing on high-risk patients	Increase vaccination rates	Community pharmacist, patient or physician	Preparation COVID-19 vaccine: 3.22 euros Administration of COVID-19 vaccine: 15.5 euros
Flu vaccination	Adults and children > 12 years, focusing on high-risk patients	Increase vaccination rates	Community pharmacist, patient or physician	Administration of flu vaccine: 15.5 euros
GUM COPD	• Patients ≥ 50 years who take reimbursed COPD medications: 2 interviews. If prescribed by a physician, the age criterion is waived. The patients require personalized guidance from their pharmacist. • Outpatient	Improving outcomes in patients with COPD by focusing on good adherence and inhalation technique Can be repeated every year.	Community pharmacist, patient or physician	25.10 euros

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Chapter 2: Outline and objectives

The primary objective of this PhD project was to thoroughly investigate and provide substantial guidance for implementing a MR3 intervention in Belgium. Building upon the literature review presented in the introduction, this research focused on identifying barriers and potential pathways for integrating MR3 into the Belgian healthcare landscape. Recognizing the potential benefits of MR3, our goal was to contribute to its implementation in a manner that is both high-quality and sustainable. To achieve this aim, we evaluated the feasibility of MR3 in Belgium, gathered insights from key stakeholders (community pharmacists, general practitioners (GPs) and patients) and developed a tool to facilitate its implementation and assess the quality of the MR3s.

More specifically, this PhD aimed to find an answer to the following research questions:

1. Is it feasible to initiate the integration of MR3 into the day-to-day operations of community pharmacists in Belgium? (**Chapter 3-6**)

2. What are the perspectives and opinions about MR3 of the pharmacists and general practitioners who participated in a pilot project? (**Chapter 3**)

3. What are the perspectives of the patients involved in a pilot project? (**Chapter 4**)

4. What elements do a diverse group of pharmacists consider crucial in a MR3? (**Chapter 5**)

5. Is it possible to develop quality assessment procedures as part of the implementation of MR3s? To what extent do the MR3 reports from participating pharmacists exhibit quality? Can the tool developed for reviewing these reports evaluate the quality of MR3s? (**Chapter 6**)

Chapter 3: Qualitative study of medication review in Flanders, Belgium among community pharmacists and general practitioners

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3.1 Abstract

Background: A pilot project on advanced type 3 medication review, which is new in Flanders (Belgium), was launched by the Royal Pharmacists Association of Antwerp.

Objective: Examining the implementation barriers and facilitators of this service as provided by Belgian community pharmacists in collaboration with general practitioners.

Setting: Community pharmacies in Flanders.

Method: Qualitative study through interviews of pharmacists and general practitioners.

Main outcome measure: Opinions and experiences of pharmacists and general practitioners about type 3 medication review.

Results: Sixteen community pharmacists and thirteen general practitioners were interviewed and generally gave a positive assessment of the project. The general practitioners saw the pharmaceutical and pharmacotherapeutic recommendations of the pharmacists as an added value for the patients. The pharmacists indicated that performing a medication review was time-consuming, but that it improved their professional relationship with general practitioners and patients. They reported obstacles in obtaining information: cumbersome access to individual patient data (laboratory values) and difficulties in finding and choosing adequate medical information sources. Moreover, pharmacists indicated that there is a need for adequate reimbursement and additional training to make the implementation sustainable.

Conclusion: Both pharmacists and general practitioners were enthusiastic about medication reviews. The implementation improved the interprofessional collaboration. However, important barriers remain, such as the considerable investment of time and the difficulty in gathering all the necessary information. The sustainable implementation of type 3 medication review in Belgium requires adequate reimbursement and additional training.

Keywords

Medication review, community pharmacy services, pharmaceutical services, pharmacists, general practitioners, qualitative research, Belgium.

Impact of findings on practice

- The implementation of type 3 medication reviews made general practitioners more aware of the expertise of community pharmacists in optimizing the patient's medication.
- Both pharmacists and general practitioners were of the opinion that patients would benefit from the implementation of type 3 medication reviews in Belgium.
- Cooperation between pharmacists and general practitioners was suboptimal, this project showed that both groups were open to improvements.
- There is unanimity that an adequate remuneration, in accordance with the time investment, is an important precondition for the continued implementation of type 3 medication review in Belgium.

3.2 Introduction

In community pharmacies globally there is a trend towards more patient-oriented pharmaceutical care and pharmacist-led cognitive services (1, 2). Offering these services can potentially improve the clinical outcomes for the patient by reducing drug-related problems and increasing medication adherence (3-5).

A medication review (MR) is a structured evaluation of patient's medication with the aim of optimizing medicines use and improving health outcomes. This includes detecting drug-related problems and recommending interventions (6, 7). The Pharmaceutical Care Network Europe (PCNE) classifies medication reviews into three types: simple (type 1), intermediate (type 2) and advanced (type 3) medication reviews (6). In a basic MR (type 1), only the medication history in the pharmacy is consulted and this is part of the routine dispensing (2). In an intermediate MR (type 2), a patient is interviewed (type 2a) or clinical data (type 2b) are consulted together with the medication history. Clinically positive effects have been reported for a type 2 MR, with impacts on low-density lipoprotein, blood pressure and medication adherence (2, 8). Moreover, economic analysis showed a consistent positive cost/benefit ratio (9). Other studies indicated that medication review has a positive influence on pharmacotherapy (9), for example by tackling polypharmacy i.e., the use of five or more chronic medications, and by improving medication knowledge and adherence (10).

Advanced or clinical MR (type 3) starts from a complete medication history, adds medical data and includes an extensive interview with the patient and feedback from the physician (6). Meta-analysis of type 3 MR demonstrated reduced hospitalization rates, without a proven reduction in mortality (2, 5, 8).

MR has been implemented in nineteen out of the thirty-four European countries (2). In three of these countries, namely the Netherlands, Austria and Germany, type 3 MR is implemented and routinely reimbursed in community pharmacies (1, 2). In Finland, pharmacists were reported to provide type 3 MR, but without remuneration by the government or health insurance. In Slovenia and England, clinical pharmacists perform type 3 MR outside the community pharmacy (2).

In Belgium, pharmacy practice is also becoming more patient-oriented and is gradually introducing elements of pharmaceutical care (11, 12). The first reimbursed pharmaceutical care service was introduced in 2014 and aimed at the rational and appropriate use of inhaled corticoids for the treatment of asthma. The protocol-based intervention allows the pharmacist to assess asthma control and medication adherence (11). A more recently introduced service (2017), known as ‘home pharmacist’, allows ambulatory and poly-medicated chronic patients to choose a community pharmacist as their reference pharmacy (11, 13). The most important part of this service is to provide an up-to-date medication schedule, i.e. a detailed intake plan of all medications. In addition, the pharmacist is expected to assess the medication adherence of the chronic pharmacotherapy. The pharmacist receives an annual fee for this service (13). MRs or other forms of medication assessment are currently not reimbursed in Belgium.

In September 2017, the Royal Pharmacists Association of Antwerp (KAVA) launched a pilot project implementing type 3 MR because, as a professional association, it is strongly committed to further strengthening the patient-oriented role of the pharmacist(14). In order to scientifically evaluate this project, the University of Antwerp and the Vrije Universiteit Brussel were asked to become partners of this project.

3.3 Aim of the study

The objective of this study was to investigate implementation barriers and facilitators of MR among community pharmacists and general practitioners (GPs) in Belgium. The opinions and experiences of participating healthcare professionals are useful for the further implementation of MR in Belgium.

Ethics approval

In the Belgian setting, an ethics approval was not required because no patients were enrolled in this survey. Participation in the study and interview was voluntary and verbal consent was required.

3.4 Method

A qualitative research approach was used to evaluate the opinions and experiences of participating community pharmacists and GPs (15). Only pharmacists and GPs who had experience with or at least basic understandings of MR were included. We have elaborated the methods used in this qualitative study by applying the Consolidated Criteria for Reporting Qualitative Research (COREQ guidelines) (16).

3.4.1 Sample

This pilot project included pharmacists from twenty pharmacies, fifteen of them were independent pharmacies, the remaining five were chain pharmacies. The pharmacists were highly motivated and volunteered to participate in this project.

3.4.2 Study design

From September 2017 to January 2018, approximately twenty-five pharmacists were trained in type 3 MR. Since the pharmacists registered with their whole team, one or two pharmacists could always be present at the training sessions. The exact number therefore varied for each session. The twenty hours of training included the use of reliable sources and guidelines, the interpretation of laboratory results, a workshop on communication and the practice of MR through case studies.

Subsequently, the pharmacists who followed the training carried out the MRs in practice. They worked together with a GP of their choice. The following patient inclusion criteria, based on the Royal Dutch Society for the Advancement of Pharmacy (KNMP) medication evaluation guideline (17), were used: over 65 years of age, use of more than five chronic medications and, if possible, at least one of the additional criteria, namely decreased renal function, reduced cognition, increased risk of falling (more than once in the last 12 months), signs of impaired medication adherence or recent hospitalization for an acute reason. Various methods can be used to detect and determine reduced therapy adherence: by performing calculations based on the delivery history and/or active survey of patient or his caregivers or attending physician with respect to therapy adherence (17). Patients who met the inclusion criteria were not randomly admitted but chosen by the pharmacists and/or GPs. The GPs were also not randomly included, they were contacted by pharmacists with whom they already had a good professional relationship. To structure the MR, pharmacists used a locally adapted step-by-step approach, based on the Dutch KNMP medication assessment guideline (17).

3.4.3 Design and content validity of the survey

All pharmacists who followed the training and their collaborating GPs were contacted by e-mail and/or telephone in the period of October-November 2018. To guarantee the anonymity of the pharmacists and GPs, they are represented by a specific number in the results list. Sixteen pharmacists and thirteen GPs were interviewed by two female master students pharmaceutical care. Great care was taken to formulate the questions in an unbiased way, so that the interviewees could freely express their opinions, and a well-founded theory-based analysis could be made. The interview guide used during the interviews can be found in the appendix. The interviews of the pharmacists were conducted in their own pharmacy. Two pharmacists were, at their own request, interviewed together and this was analysed as a single interview. Of the thirteen GPs, six agreed to a personal interview in their own practice, three preferred contact by e-mail, and the remaining four preferred an interview by telephone. Participation in the study and the

interview was voluntary and verbal consent was required. The semi-structured interviews were recorded and both the facilitators and the barriers for carrying out the MR were assessed. One of the interviewees specifically asked not to make any audio recordings of the conversation and this interview was analysed using the written notes.

3.4.4 Data consolidation and consensus seeking procedure for the results obtained

Codes were compared and differences in opinions between the researchers were discussed with a third researcher in order to reach a consensus.

3.4.5 Data analysis

The audio recordings were transcribed and coded using Nvivo 12, a program for qualitative data analysis (18). The authors of this study are pharmacists who tried to analyse the interviews as objectively as possible. Our primary goal was to get to grips with issues that hamper or facilitate implementation.

3.5 Results

The thematic analyses of the transcripts revealed the following topics: motivation, time investment, selection criteria and reimbursement. The results were therefore subdivided into seven topics for both pharmacists and GPs. Data saturation coincided with the number of interviewed pharmacists and GPs (19). Examples of pharmacists' and GPs' quotations are referred to with quotations references (for example Q1), which can be found in the appendix.

3.5.1 Pharmacists' responses

Of the twenty different pharmacies, sixteen pharmacists from fifteen different pharmacies agreed to participate in the interview. As mentioned before, there was one shared interview, which we recorded as one number in the analysis. Fourteen pharmacies were located in the province of Antwerp and one in the province of Limburg. The interviews with the pharmacists lasted 36 minutes on average.

The pharmacists carried out the medication reviews between January 2018 and December 2018.

Motivation

All pharmacists considered the MR service as an added value for the patient and saw no disadvantages in the provision of this service. The comprehensive nature of the analysis of the medication use was seen as the biggest advantage (Q1).

The medication review service has increased awareness of the role of the pharmacist. It was also seen as an opportunity to develop interprofessional contacts with the GPs and to improve the relationship with the patient. Furthermore, pharmacists considered MR as a type of pharmacotherapeutic refresher course and as an opportunity to increase their knowledge (Q2).

All pharmacists remained motivated to put MR into practice. Almost all interviewed pharmacists agreed that offering such a pharmaceutical care service is an integral part of the role of the pharmacist (Q3 and Q4).

Time investment

Medication review was perceived to be time-consuming for pharmacists. Contact with the GPs was not always smooth. All pharmacists unanimously stated that they spent most of their time collecting information and consulting reference material, such as the summary of product characteristics (SmPC),

interaction checkers, guidelines and textbooks (Q5). The pharmacists wanted to be very comprehensive because they were concerned that certain drug related problems (DRPs) would be missed or misunderstood. The results also indicate that independent pharmacists had slightly more difficulties in conducting MRs than their colleagues working at chain pharmacies.

Moreover, it was difficult to determine where all the information could be found or to distinguish between relevant and irrelevant sources. Most pharmacists indicated that the preparation took a long time because it was still largely unknown territory. The conversation with the patient was also time consuming (Q6). As a consequence, some pharmacists performed the MRs during off-hours, for example during the lunch break.

Type of medication review

Laboratory values are seen as a prerequisite for type 3 MR. Nine out of the sixteen pharmacists considered type 3 MR to be the best possible form of MR in a community pharmacy (Q7). At the same time, some pharmacists reported that starting with the extended type 3 MR compared to type 1 and 2 MR was a challenge, especially because it was very time-consuming (Q8).

According to the pharmacists, a high-quality MR should also include the following parameters: an interview with the patient and the GP, recent laboratory values, indications, allergies, intolerances and an overview of the medication. In other words, most respondents indicated that the completeness of a type 3 MR is an important characteristic to guarantee quality (Q9).

In addition, pharmacists considered it essential to provide both GPs and patients with their feedback. On the other hand, both care providers need to agree afterwards who will take responsibility for the follow-up of the patient (Q10).

Patient selection criteria

The opinion of pharmacists about the eligibility of patients for a type 3 MR was heterogeneous. A large majority of pharmacists felt that the selection criteria should be extended. There was a consensus on the polypharmacy criterion, but MR can also be of interest to people less than 65 years of age, patients who use a lot of OTC medications or patients who ask for a review themselves (Q11 and Q12).

Cooperation with the GP

For the vast majority of pharmacists, cooperation with GPs went well; for a minority of pharmacists this was however a greater challenge (Q13).

We identified the time investment as a recurring barrier. The transfer of data between GP and pharmacist was partly to blame, because a fast and secure communication solution was not immediately available (Q14 and Q15).

The degree of acceptance of the pharmacist's advice was a small barrier (Q16). Not accepting the suggestions was not seen as a major problem at this initial stage of the introduction of MR. Fourteen pharmacists indicated that the GPs were open to changes or suggestions (Q17 and Q18).

The pharmacists had the impression that GPs were reluctant to adjust medications initiated by other physicians. GPs were not inclined to make changes unless absolutely necessary (Q19).

Results of the medication reviews

The most common drug related problems highlighted during the reviews were under- and overtreatment, such as the high use of benzodiazepines and the under-use of osteoporosis prophylaxis. In addition, there were other problems such as drug-drug interactions, failure to adjust the dose according to kidney function, therapy non-adherence, incorrect medication use and double medication (Q20).

Remuneration

Because of the considerable investment of time, all pharmacists agreed that reimbursement is necessary to perform MRs, but they did not agree on how this should be done (Q21, Q22 and Q23). The majority of pharmacists thought that this would require a fixed fee per MR. Some argued that the pharmacist's entire payment system would have to change, because they are currently paid for each product dispensed and not for the pharmaceutical care they provide (Q24). The majority want this service to be reimbursed with minimal or no co-pay by the patient.

Optimization of the medication reviews

The aspects that need to be optimized, and which were most frequently cited, were the time investment on the one hand and the difficulties in obtaining the patient's medical data on the other hand (Q25).

3.5.2 Responses from the GPs

A total of 21 GPs were contacted. Thirteen GPs were interviewed in three different ways: six physicians agreed to a personal interview in their own practice, three preferred contact by e-mail, and the remaining four preferred a telephone interview. Two of the GPs were interviewed at the same time because they work in the same practice. Two GPs did not participate, citing lack of time, and in another six cases, the physician was not consulted by the pharmacists to discuss the MR. Accordingly, questioning those GPs would be irrelevant. The GP interviews lasted 27 minutes on average.

Motivation

The motivation of the majority of GPs was to clarify the issues of polypharmacy (Q26). One GP also indicated that MR was a great help for correcting many errors and misunderstandings (Q27).

Time investment

On the one hand, according to some GPs, a lot of time was spent on the implementation of MRs. One of the GPs indicated that this was due to the selection of complex cases. Accordingly, a lot of time was spent on investigating the entire therapy. A second GP responded that this was due to limited experience in performing MRs. A third GP reported that providing laboratory values and medication related info to the pharmacists was cumbersome and therefore it was time-consuming to prepare medical records for the pharmacist.

On the other hand, there were two GPs who did not experience the implementation of MRs as too labour-intensive or time-consuming. One GP explained that if medical records were properly organised, it really does not take too much effort to provide the needed data. For two other GPs, the time spent was not insurmountable in itself, however they did not expect that there would be enough time to carry out such MRs systematically (Q28). Moreover, it was clear that as long as no reimbursement is provided, it is difficult to make time for MRs (Q29).

One GP suggested appointing a pharmacist to carry out reviews in several pharmacies to partly compensate for the lack of time that the pharmacists struggled with.

Patient selection criteria

Most GPs found patients with polypharmacy the most interesting target group for performing a MR. Patients taking few medications were not considered useful and the GPs therefore advised against recording them (Q30).

One physician found the presence of polypharmacy a poor selection criterion. He found it useful for everyone, regardless of the exact number of prescribed medications. It is essential to determine whether the medication was prescribed correctly and to check, among other things, for adverse effects.

Moreover, the majority felt that this should be possible for both older and younger patients (Q31). However, as older patients often have the most complex therapy, this target group was the most eligible for a MR. Two GPs said that younger patients have little need for a MR because they are better with medication management, but it can be useful when they have mental problems (Q32). Another GP thought it would be unnecessary for younger people who are chronically ill.

Opinions about the psychiatric patients were very diverse. For example, one physician found it useful to perform MRs on patients taking psychotropic medications such as benzodiazepines (Q33). There were two GPs who wanted to exclude psychiatric patients in MRs because of the specific nature of their treatment not following general guidelines. Moreover, according to both GPs, extra caution is needed in order not to undermine existing therapeutic relationships in this vulnerable group. Finally, one GP targeted a MR mainly for elderly patients and patients discharged from the hospital.

Cooperation with the pharmacist

All GPs agreed that pharmacists need the patient's medical history (Q34). Moreover, the majority of the GPs interviewed also found that the laboratory values were necessary for performing an adequate MR. Almost all GPs indicated that kidney function and liver values were the most important parameters (Q35).

The opinions regarding the other lab parameters were divided. One GP indicated that the degree of coagulation might be relevant in certain situations. However, another physician wanted to limit this information to kidney function because it is the task of the GPs to interpret the other laboratory values. In addition, two GPs doubted whether pharmacists have the knowledge to correctly interpret laboratory parameters (Q36).

Only two GPs were of the opinion that pharmacists do not need the laboratory values to be able to do their work properly (Q37). Three GPs spontaneously said that pharmacists should be informed of intolerances and allergies that the patient has (Q38).

All GPs experienced the professional relationship with the pharmacist as something very positive (Q39). Some stated that they were open to closer cooperation. Two GPs, on the other hand, noted that there is still some hesitation among pharmacists, especially when it comes to making telephone calls (Q40).

Almost all GPs would like to see the exchange of patient data digitalised in the future (Q41). One GP suggested the Siilo-app, while others mentioned data exchange via eHealth or Vitalink (20). Siilo is a secure online application for healthcare professionals, as a type of replacement for WhatsApp (21). Vitalink is an initiative by the Flemish government that focuses on the sharing of health and medication data to support primary healthcare (20).

GPs expected pharmacists to critically review the patient's medication schedules during a MR. The GPs themselves do not always have enough time and according to them pharmacists are better trained to deal with medication errors and problems (Q42). GPs were confident that pharmacists could make a clear distinction between relevant and minor drug related problems (DRPs). For example, only the clinically relevant DRPs should be discussed with the GPs (Q43).

One physician even emphasized the importance of considering pharmacists as the ones responsible for the final verification of the effectiveness and correctness of the prescriptions made by the GPs. The GPs considered the collaboration with pharmacists as a support (Q44). Both the ability and willingness to complement each other are important factors. Moreover, pharmacists often receive additional information through a thorough conversation with the patient (Q45).

Results of the medication reviews

According to the GPs who participated in this project, comprehensive oversight and fine-tuning of the medication are the most prominent benefits for the patient. They confirmed that performing MRs optimizes the therapy because several DRPs were detected (Q46). As a result, they believe that this leads to fewer side effects, improving the patient's quality of life. Moreover, they suspect that in this way the number of hospital admissions and medical costs may decrease.

Remuneration

Only one GP did not consider it necessary for pharmacists to receive remuneration for doing a MR. An aspect many GPs questioned was whether a MR should be reimbursed in full or whether it is already part of the services provided by the pharmacist (Q47, Q48 and Q49). Three GPs indicated that GPs should also be fully reimbursed for this service.

Optimization of the medication reviews

The majority of GPs indicated that the time spent on a MR is a problem. The GPs found it labour-intensive and that it would be a huge task if the MR would be applied to all patients with polypharmacy. Theoretically, consultation between GPs and pharmacists is a good idea, but, as one of the interviewed GPs said, this proved not always to be workable in practice (Q50).

Another aspect that can be optimized and that has repeatedly been raised as a point of discussion is the exchange of patient data. During the project, this point was not immediately perceived as a major obstacle, but it would run more smoothly if the exchange could take place via an electronic platform such as eHealth.

3.6 Discussion

3.6.1 Interpretation of the findings

Motivation

Our study showed that there is a willingness to perform type 3 medication reviews in Belgium. Participating pharmacists were aware of MR, had voluntarily joined the training and were willing to participate in this project. For most of the GPs, MR was unknown territory and therefore they were informed about this type of review by their local pharmacist.

Type of medication review

The type 3 MR has several interesting features, such as the incorporation of data from medical records (diagnosis, laboratory values, intolerances, allergies) and conversations with patients and GPs. While some pharmacists reported that starting with the extended type 3 MR compared to type 1 and 2 MR was a challenge, especially because it was very time-consuming, most pharmacists experienced MR as innovative. On the other hand, the majority of them considered the medical record to be an essential part of the preparation of a high-quality MR. Kwint et al. (22) confirms that several drug related problems (DRPs) relate to the monitoring of laboratory data, thereby documenting the need for a type 3 MR.

Exchange of data

For the GPs, most of them agreed that pharmacists should have access to the patient's medical records, including the laboratory values. At present, this is not the case. However, a minority of GPs was reluctant to share this data. This may indicate a lack of trust towards pharmacists, as also mentioned by Hatah et al. (23). It should be noted that these values are only meant to be used for monitoring pharmacotherapy and not for diagnostic purposes. This information item was also explicitly emphasized during the pharmacists' training for this project.

Collaboration between GPs and pharmacists

MR improves the interaction between GPs and pharmacists. There is currently no structural cooperation between general practitioners and pharmacists. As a consequence, some pharmacists were somewhat reluctant to address the GPs. They feared a reserved attitude from the GPs. For that reason, most pharmacists worked with GPs with whom they already had a good relationship. The GPs in this inevitably biased sample were very positive about the collaboration with the pharmacists. A study conducted in New Zealand reported that GPs had mixed feeling towards different new services such as type 3 MR (23). On the one hand, the potential strengths were benefits to GPs and patients and pharmacists' medications knowledge. On the other hand, potential weaknesses were mentioned such as privacy issues, conflict with GPs, pharmacists' skills, undermining of the GP's practice and duplication of work. When they discussed conflict and irritation, the GPs mentioned an overload of significant information e.g. clinical irrelevant drug interactions (23). Australian studies reported that the Home Medicines Review (HMR), a type 3 MR, encouraged the GP to review and discuss the patient's medication therapy with the pharmacist (24, 25). Other studies conducted in New Zealand reported that pharmacists were concerned about the lack of skills and confidence to provide the input for a type 3 MR. Pharmacists should have more confidence when discussing patient-related issues with GPs (26, 27). Studies of pharmaceutical care for dementia showed that better communication between the physician, pharmacist and nurses can improve collaboration, and ultimately enhance the quality of medication assessment (28, 29).

Optimalisation of the medication reviews

Therefore, collaboration between pharmacists and GPs needs to be optimized step-by-step. Awareness-raising, targeted communication and interprofessional education of the healthcare providers could provide a good solution for improved collaboration. An Australian study suggested the need to establish systems, including the development of local protocols for collaboration of the HMR (30). The cooperation, which is part of the type 3 MR, takes time, especially in the initial phase. As previously shown by Kennelty et al., time turned out to be the most important obstacle for most pharmacists (31). Some pharmacists performed the MRs during off-hours, which illustrates their commitment and motivation. However, pharmacists emphasized that this is not feasible in daily practice. A possible strategy for overcoming this time barrier is to set up a different reimbursement system (31, 32). Reimbursement of this MR service was deemed necessary by all participants. The lack of reimbursement inevitably limits motivation, according to both pharmacists and GPs. However, the fee in itself cannot be sufficient to implement the MR service, but will help further implementation.

GPs advise to save time by grouping the MR conclusions for several patients and focusing on the action points. The GPs expected that only the clinically relevant DRPs would be presented and assumed that the pharmacists would be able to propose a concrete alternative to these problems. Despite their lack of experience with MR, the action points proposed by pharmacists were generally well received by the GPs. They also preferred a face-to-face to a telephone consultation. Furthermore, some GPs agreed that after the initial investment of time, cooperation could even be timesaving because pharmacists take over part of the work. The pharmacists also thought about the participation of specialists, because GPs are often reluctant to change medication that was not initiated by themselves. A GP suggested appointing a pharmacist to carry out reviews in several pharmacies. Our research also indicates that chain pharmacists had less difficulty in performing MRs compared to their independent colleagues. A possible reason for this was that the latter group of pharmacists received more structured support, such as the monthly round table among colleagues and a flexible work schedule. The independent pharmacists are not used to collaborate in such a systematic way. They had the possibility to address their questions both towards the project coordinator and each other, but that made the threshold even higher.

Furthermore, the GPs and pharmacists interviewed indicated that the execution of the type 3 MR service took a great deal of time and effort. On the one hand because of the complexity of polypharmacy, on the other hand due to the lack of experience. A strategy that can be applied to overcome this obstacle is to refrain to start with a very complex patient and rather start with, for example, limited complex diabetes patients or hypertension patients. Some pharmacists also reported that the time investment decreased the more MRs were performed. The literature also shows that the time investment can be reduced by two-thirds with good external support (33). This support consisted of different levels, both with organizing and planning the services, as well as with all technical and administrative tasks. Finally, the mentoring pharmacist was also able to provide pharmacotherapeutic support (33).

Inclusion criteria

The opinions on the appropriateness of the inclusion criteria differed widely. On the one hand, most pharmacists and GPs found the age criteria too restrictive and wanted to include younger patients with complex needs. On the other hand, according to some other healthcare providers, patients with too complex therapies, psychiatric problems or limited awareness are better not included. In case of polymorbidity, patients often see several specialists in addition to the GP and all pharmacists thought that it would be interesting to also involve them in the MR. There only was one pharmacist who expressed doubts about this, because specialists are not always easy to approach. Some pharmacists proposed contacting only the specialists in undecided cases in order to obtain a second opinion. For some other participants, it was important not to include patients based on quantitative criteria, such as the number of medications, but on the basis of qualitative criteria, such as the level of care needed. In European countries where type 3 MR is available, the most overlapping selection criteria are patients taking more than five long-term medicines. In addition, the selection is sometimes based on financial aspects, such as in a German project, where the selection depends on the insurance of the patient (2).

Interaction with the patients

The pharmacists were very positive about the interactions with patients and no barriers were perceived. This interview provided an opportunity to determine what the patient was interested in; it was also considered important to identify relevant DRPs. A follow-up interview was necessary in order to reach agreement on pharmacotherapy between the patient, GP and pharmacist. The only barrier mentioned by pharmacists was time management: it was difficult to keep the focus on the pharmacotherapy of the patient and not deviate to less important topics.

Quality of the medication reviews

It is known that the quality of a MR varies (22). A detailed report is a prerequisite for a high quality MR service. Further research is needed to develop a monitoring system to ensure quality.

Electronic exchange

Finally, facilitating the electronic exchange of patient data could improve cooperation. All the care providers interviewed indicated the lack of shared experience or the lack of a convenient digital platform as a bottleneck. Due to the privacy legislation, such as the General Data Protection Regulation (GDPR), patient data cannot be sent by unsecured electronic mail. This data has to be exchanged in person or sent by postal mail, which slows down the process. Technology optimization will lead to time savings. In recent years, the possibilities for exchanging patient data have increased, but there is still a long way to go in terms of user-friendliness (34).

3.6.2 Strengths and weaknesses of the study

Because of the qualitative nature of this study, we only investigated the opinions of a relatively small number of motivated pharmacists and GPs. Both care providers were not chosen at random. The

pharmacists were highly motivated and volunteered; the GPs were contacted by pharmacists with whom they already had a good professional relationship. The patients were not selected at random, they had to meet the inclusion criteria, but were otherwise chosen freely by the pharmacists and/or GPs. Finally, the authors of the study are pharmacists, who have described the data as objectively as possible.

3.6.3 Similarities and differences in relation to other studies

In Belgium, research has already been carried out into the implementation of MUR in community pharmacies (35). The pharmacists surveyed in this study considered MUR to be a satisfactory activity. However, prior to the actual implementation, several adjustments had to be made, such as the reorganisation of the internal workload of the pharmacy and the additional support such as wide-ranging media campaigns and adapted software (12). The complete MR was only studied as a pilot project in the hospital environment and was performed by a clinical pharmacist (36). On the other hand, our study describes the first investigation of type 3 MR in community pharmacies in Belgium. At present, type 3 MR is a routine service reimbursed in community pharmacies in the Netherlands, Austria and Germany (1, 2). There are some international studies describing the opinions of both GPs and pharmacists about collaboration on new medication management services (23, 31, 37). In Australia, GPs took a positive view of the Home Medicines Review (HMR) to reduce polypharmacy and to play an important role in the education of both GPs and pharmacists (38). The new services provide novel opportunities, such as improved communication and better collaboration and integration with the GPs' practice (38). Apparent threats were the GPs' perception of a related, and non-remunerated increase in the GPs' workload, and the perception of a limited benefit for the patients (23). Weaknesses focused on potential confusion and harm for the patient, conflicts and irritation to GPs' practice, and the possibility of fragmenting care for the patient (23).

3.6.4 Open questions and future research

During this study, new questions were raised for further research. Firstly, we do not know which target group would benefit most from the type 3 MR (39). Secondly, the healthcare providers also emphasized that implementation would be difficult without reimbursement. Moreover, if the reimbursement were to be granted, careful consideration should be given to how this would be organised in Belgium (39). Thirdly, there was the barrier around time investment. It remains to be determined how the workload could be reduced.

Few studies have examined the opinions of patients (40-43). That is remarkable because with this service we mainly want to improve patient care. Moreover, there is currently no method available for guaranteeing the quality of the MR. As a high quality MR is of the utmost importance, this should continue to be a matter of concern (44). Objective quality parameters are also needed to investigate whether a MR improves the clinical outcomes of patients (45). In addition, pharmacists need to know how GPs deal with the pharmacists' suggestions (46, 47). Finally, the opinion and role of other stakeholders and potential payers (insurance, private insurers, etc.) should be examined as well (39).

3.7 Conclusion

This pilot project seems to indicate that there is a willingness to perform a type 3 MR in Belgium. It was a positive experience for all GPs and pharmacists that participated in this study. According to the healthcare providers involved, MR will not have negative consequences for the patient. Although this pilot project was well received by this specific group of pharmacists and GPs, important steps still need to be taken to

achieve a successful general implementation of MR in Belgian community pharmacies. Further research and action is needed on how to deal with the main barriers such as the considerable time investment and the lack of reimbursement. In addition, quality control of the MR process is needed, which includes, amongst others, proper training of healthcare providers. Finally, the implementation of MR can likely be improved by facilitating the electronic exchange of patient data.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to this study.

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3.9 Appendices

Appendix 3.1 Examples of pharmacists' quotations

Classification	Quotations references	Quotations
Motivation	Q1	*"Everyone has a piece of information, collected from their own perspective. If you then start piecing all the bits of information together, then you can do a lot more for that patient." (Pharmacist 6)*
	Q2	*"Why I'm so enthusiastic about MR? Medication review in itself is interesting but is also very important for the future of our profession. Actually, it is the core of our profession and is integral for collaboration with the GPs. The fact that there are some pharmacists who don't perceive MR as an asset … I really don't understand that opinion." … (Pharmacist 2)*
	Q3	*"I think it is important to keep growing, so that's why it [MR] is a real added value for our profession. No doubt about it. The past couple of years I feel like we're moving in the right direction, but MR is definitely something to be carried out in the community pharmacy." (Pharmacist 3)*
	Q4	"*Because it [MR] brings us back to our key task, it is the core business of the pharmacy. That's what it is all about." (Pharmacist 9)*
Time investment	Q5	*"You need to check the guidelines for each pathology. When guideline adherence is high, everything is fine, and no intervention is required. But, often, those directives were not followed properly. If that's the case, then you can't always find the exact reason, despite researching various sources. So, even after consulting ten sources, the answer is still unclear" (Pharmacist 6)*
	Q6	*"The conversation takes at least an hour, but it gives you a lot of information and this also includes things that patients typically wouldn't share with their GP." (Pharmacist 13)*
Type of medication review	Q7	*"Without the medical data provided by the physician, pharmacotherapy cannot be properly evaluated. Having that information is the most crucial part and thus the strength of this project." (Pharmacist 15)*
	Q8	*"I think a comprehensive review is good, but it may be a bit ahead of its time" (Pharmacist 4)*
	Q9	*"A more extensive MR is obviously better. The quality of the review increases when more people are involved, such as specialists and other care providers. But that does not mean that a basic review is not useful. On the contrary, it should be an*

		impetus to not postpone things that you can resolve quickly." (Pharmacist 8)
	Q10	*"The medication review is not a one-off thing, it's an ongoing effort. It should not just stop at some point, there needs to be a follow-up. Once initiated, the medication review needs to be updated just like a personal medication schedule." (Pharmacist 6)*
Patient selection criteria	Q11	*"For patients with a chronic illness, I would advocate [a MR] as soon as possible. There are younger people for whom it may even be more beneficial than for example an 80-year-old woman. For a younger person, it might pay off more while for an octogenarian changing things may not be useful. (Pharmacist 15)*
	Q12	*"I would not dissuade anyone [from MR], as changing things is not mandatory, changes are only proposed, and you try to substantiate these." (Pharmacist 8)*
Cooperation with the GP	Q13	*"So far, we've had one conversation with a GP to discuss a whole group of patients at once and that went really well, he was really supportive about everything. Before the actual meeting, we had a quick phone call and he told me that he really looked forward to it." (Pharmacist 15)*
	Q14	*"In some instances, you need to prompt and remind them [the GPs], and that is not pleasant, but it has to be done." (Pharmacist 4)*
	Q15	*"In the beginning, all information was sent by email, but because of the GDPR[1] legislation this was suddenly no longer permitted. That was a bit annoying, because we then always had to collect that data ourselves and that was more time consuming." (Pharmacist 12)*
	Q16	*"One patient's GP didn't want to change anything. That patient then went to the nephrologist, who confirmed what I told her before. With that information she went back to her GP. (...) Physicians shouldn't consider this as an offense, but rather as a way to cooperate. This has to be emphasized." (Pharmacist 3)*
	Q17	*"The cooperation with the GPs was a real success, they happily revealed that they were learning a lot and subsequently we have been holding meetings every month." (Pharmacist 12)*
	Q18	*"The GP was very helpful and very amenable, but in the end, she always thought she got it right. But then again, it's a start! " (Pharmacist 9)*
	Q19	*"I would like to contact the specialists, because GPs are often not willing to adjust medications initiated by the specialist. This*

[1]In the past, there was already a restriction on the sending of confidential information by e-mail but the introduction of the General Data Protection Regulation (GDPR) legislation has increased awareness of these issues.

		would then allow us to provide more information to the GPs." (Pharmacist 9)
Results of the medication reviews	Q20	*"That's why we do this, isn't it? For the benefit of the patient. You don't do this for yourself, nor for the GP, it's about helping the patient in the first place. When he tells you that his kidney function has improved, and that he doesn't have to go to predialysis any longer, then that's a life changing experience…. Then you can think: "Mission accomplished!". (...) This keeps you motivated to continue." (Pharmacist 6)*
Remuneration	Q21	*"I wouldn't be too modest about it but the bar should be raised high. When doing the review, this is your only focus, so that time must be paid for. There is competitive pressure amongst pharmacists and you can make a difference by offering quality. I think we are far too accommodating and too afraid to request remuneration for this service. In every other place advice must be paid for, so why should it be any different for us?" (Pharmacist 1)*
	Q22	*"Working with the patient in a personal way means that you are actually involved in a type of consultation, so it should be paid for as such. " (Pharmacist 3)*
	Q23	*"In my opinion there is some need for a protocol. Payment should only happen after submitting an appropriate report, and an extra fee is needed for follow-up interviews. So, in fact remuneration should be compartmentalized." (Pharmacist 1)*
	Q24	*"Being a pharmacist, it's sometimes difficult not to shoot yourself in the foot by providing the patient with your advice. (…) You look things up, you phone the GP and in the end the patient may leave without purchasing anything. Pharmacists that don't check things carefully, may just say "take this" and they will then have been remunerated for their service. That's the tricky thing about it, this type of advice should be remunerated." (Pharmacist 8)*
Optimalisation of the medication reviews	Q25	*"Lack of time is a real obstacle for us. The review is an extra task that comes on top of the everyday work. Because, in contrast to the GP, there is currently no possibility of a pharmacist planned consultation. Maybe we should aim for that: creating two sources of revenue, one for OTC medicines and a second one for the remaining aspects." (Pharmacist 5)*

Appendix 3.2 Examples of general practitioners' quotations

Classification	Quotations references	Quotations
Motivation	Q26	*"There is no hard scientific evidence that patients benefit from MR, but it's so obvious that it needs no proof." (Physician 5)*
	Q27	*"As a physician, you don't always know the exact list of medications that the patient is taking, so re-assessment is*

		sometimes necessary. You're more likely to do so when there is a second opinion." (Physician 1)
Time investment	Q28	*"It is good to have this pilot project, however, putting this into practice would be too labour-intensive. We took part because it is a study project and we aim for higher quality, but it is unsustainable. Most of my colleagues will abstain, certainly in its current form." (Physician 7)*
	Q29	*"The work is not reimbursed, so it's really something that you should be willing to take on as an extra." (Physician 6)*
Patient selection criteria	Q30	*"You have to set priorities, because you cannot organise [MR] consultations for every patient. Vulnerable patients in particular, such as the polymedicated ones, require most of our attention." (Physician 6)*
	Q31	*"It can sometimes also be useful for younger patients, such as for patients suffering from cystic fibrosis." (Physician 1)*
	Q32	*"I don't think that younger patients are an important target group [for MR]. Except when they have mental problems, then that's something to consider." (Physician 7)*
	Q33	*"Medication adjustment usually requires a big effort so when finalised, patients often get really attached to these medicines. In my view, there is no need to drastically change them. When you decide to do so, it's absolutely necessary to discuss this first with the treating specialist, if the patient has one." (Physician 4)*
Cooperation with the pharmacist	Q34	*"When a pharmacist gets a physicians' prescription and it is not clear to the pharmacist why the patient has been prescribed those medicines, then I can imagine that this must be very frustrating." (Physician 1)*
	Q35	*"It is very useful to provide the laboratory values, particularly values for kidney function. There is no need to communicate every small detail, but the more pharmacists know, the better they can advise their patients. It would be helpful if the prescription would indicate whether the patient suffers from renal insufficiency." (Physician 8)*
	Q36	*"I think there are some shortcomings in the training. You can only act on what you know. There is still a long way to go, as this should really be taught as a new course." (Physician 7)*
	Q37	*"A pharmacist is not a physician. I think that many pharmacists want to take over our role, which creates a big risk. (...) Lab values must be interpreted, this falls outside the scope of the pharmacists' competency." (Physician 6)*
	Q38	*"When a patient experienced an adverse drug reaction, then we must make that known [to the pharmacist]. (...) For example, the use of a certain antibiotic could trigger certain allergies, also*

		impacting the safe use of other antibiotics. Then the pharmacist will also be able to act on such information." (Physician 8)
	Q39	*"It's easy for me to cooperate with pharmacists because they know a lot more about medications than I do." (Physician 11)*
	Q40	*"I notice that many pharmacists are afraid of conducting a telephone conversation with GPs and that there is a type of hierarchy, presuming that the physician is the boss and that the pharmacist should only execute what the physician has instructed. This is disappointing and I think that this is an outdated way of collaborating." (Physician 12)*
	Q41	*"The [electronic] exchange of [patient] data is still not optimal. The government makes out that it is, but practice shows the opposite. They always launch new ideas and products, even when they are far from perfect." (Physician 8)*
	Q42	*"The pharmacist knows much more about medicines and everything that has to do with it in comparison to the average physician." (Physician 5)*
	Q43	*"It would be a real added value if pharmacists would focus on all our patients' chronic medication lists, on the identification of clinically relevant interactions and on making suggestions for optimization." (Physician 12)*
	Q44	*"They [the pharmacists] actually take over a part of our task and that's a good thing, because eventually a medication can suddenly change or can be taken in a different way by the patient, we do not always know about that." (Physician 8)*
	Q45	*"It's a real team effort in which, from a medication-oriented point of view, pharmacists usually get closer to patients than GPs do." (Physician 8)*
Results of the medication reviews	Q46	*"It is for the benefit of the patient's health that we conduct more checks regarding the medication and that we evaluate the chronic medication more closely, which one usually prescribes too readily. Both pharmacists and physicians have a role to play here, and with physicians I do not only mean GPs but all the other specialists as well." (Physician 8)*
Remuneration	Q47	*"I would absolutely find it [a remuneration] normal, because in the end the pharmacist does more than just selling pills. For a part, we outsource this and that is absolutely worth it, because as a physician we sometimes aren't aware of the mistakes that are made. I'm in favour of this review and there should definitely be a budget for that." (Physician 8)*
	Q48	*"I think that in the future a different remuneration is needed for GPs and maybe also for pharmacists. It would not be a bad idea to disconnect the pharmacist's income from the amount of medicines that are sold, that system is really incomprehensible to me. The more a pharmacist sells and the more expensive the*

		products are, the more he earns. That is aberrant and vice versa, when a pharmacist makes the effort to also confer with the doctor, he will not get paid for this. Rather, in some cases he has to dissuade patients from taking certain medications, his income will suffer from that advice. If you ask me, pharmacists should not be part of the consumer society any longer; they need to get away from that pressure. He [the pharmacist] should not be rewarded for stimulating this consumption cycle but he just needs to get compensated for his high quality advice and medical work, just like GPs should." (Physician 6)
	Q49	*"I think compensation [for MR] is justified because it takes a lot of time. You can compare it with the global medical file we handle and for which we also receive a reimbursement per patient. All the money that the NIHDI (National Institute for Health and Disability Insurance) saves with this service should go to the pharmacists. That would be better for everyone. " (Physician 11)*
Optimization of the medication reviews	Q50	*"It takes a lot of time for us to help patients with stopping the use of their medication. It would be a lot easier if we could collaborate with the pharmacists to accomplish this. If he informs the patient about which medication needs to be stopped, it would reduce our workload in discussing this with the patient. I really think that this is a super project!" (Physician 11)*

Appendix 3.3 Pharmacists' interview guide (translated version)

1. What is your motivation to perform medication reviews? In other words, what do you think are the advantages?
2. How much work did it take to complete all different components?
3. What is your opinion about the type of medication review you performed?
4. What was it like to recruit patients?
5. For what kind of patients do you think it would be useful to perform a medication review for? When would you rather discourage it?
6. How did the interaction go with the patients?
7. At what place the conversation has been held and did it take place during working hours or outside?
8. What was it like to recruit doctors?
9. What is your opinion about the collaboration with the doctors?
10. Which specialists would you like to see involved in the process of medication review?
11. How would you describe the exchange of patient data between yourself and the GPs?
12. How would you prospect the future exchange of patient data?
13. What was the impact of the medication reviews?
14. How does the patient's follow-up go after the review?
15. In which way the medication reviews have been implemented by the whole team?
16. According to you, which part of the entire process could even be optimized?
17. How did the pharmacotherapeutic analysis go?
18. What kind of information sources did you consult?
19. After having carried out some first medication reviews, how easily did they become for you?
20. How this part of the pharmaceutical care should be reimbursed?

21. What characteristics a medication review needs to have in order to be of high quality?
22. What suggestions do you have for other general practitioners and pharmacists when performing medication reviews?

Appendix 3.4 Pharmacists' interview guide (original version)

1. Wat was uw motivatie om medicatie reviews uit te voeren?
2. Hoeveel werk kroop er in het uitvoeren van de verschillende onderdelen? Hiermee bedoelen we de selectie van de patiënten, de voorbereiding, het gesprek met de patiënt, het gesprek met de arts en de terugkoppeling naar de patiënt.
3. Zoals u misschien wel weet bestaan er verschillende soorten medicatie reviews. Wat vond u van het type dat u heeft uitgevoerd?
4. Hoe ging het om patiënten te rekruteren?
5. Bij welk soort patiënten is het volgens u zinvol om een medicatie review uit te voeren? Wanneer zou u het eerder afraden?
6. Wat vond u van de interactie met de patiënt?
7. Wanneer vond het gesprek met de patiënt plaats en waar?
8. Hoe ging het om artsen te rekruteren?
9. Wat vond u van de samenwerking met de arts?
10. Welke gespecialiseerde artsen zou u nog willen betrekken bij het proces van medicatie review?
11. Hoe verliep de uitwisseling van de patiëntengegevens tussen u en de huisarts? Hoe zou u dit graag in de toekomst zien gebeuren?
12. Welke soort veranderingen waren het gevolg van de medicatie reviews?
13. What was de impact van de medication reviews?
14. Hoe verloopt de opvolging met de patiënt nadat de review werd uitgevoerd?
15. Op welke manier heeft u in teamverband de medicatie reviews uitgevoerd?
16. Wat zijn volgens u de positieve aspecten van een medicatie review en waar is er volgens u nog een mogelijkheid tot optimalisering?
17. Hoe verliep het verwerken van de patiëntengegevens? (Verkoopshistoriek, medicatieschema, labowaarden,…)
18. Welke soort informatiebronnen heeft u geraadpleegd?
19. Hoe evolueerde de uitvoering qua vlotheid na reeds enkele medicatie reviews te hebben gedaan?
20. Op welke manier moet dit onderdeel van de farmaceutische zorg vergoed worden naar uw mening?
21. Welke eigenschappen moet een medicatie review zeker hebben om kwalitatief goed te zijn?
22. Welke tips heeft u voor andere huisartsen en apothekers bij het uitvoeren van medicatie reviews?

Appendix 3.5 General practitioners' interview guide (translated version)

1. What made you first hear about medication review?
2. What motivates you to participate in medication reviews? In other words, what are the advantages?
3. How much work did you put into the performance for you as a doctor?
4. What are the advantages and/or disadvantages for the patient?
5. For what kind of patients do you think it is useful to perform a medication review? When would you rather discourage it?
6. In your opinion, what medical data should the pharmacist have in order to carry out a proper medication review?

7. How would you describe your relationship with the pharmacists?
8. How did the exchange of patient data go between yourself and the pharmacists?
9. How would you prospect the future exchange of patient data?
10. How did the discussion of the report with the pharmacists go?
11. How does the patient's follow-up go after the review?
12. What exactly do you expect from the pharmacists during a medication review?
13. According to you, which part of the entire process could even be optimized?
14. How would you react if you heard that pharmacists will be compensated for this in the future?
15. Which suggestions do you have for other general practitioners (and pharmacists) when performing medication reviews?

Appendix 3.6 General practitioners' interview guide (original version)

1. Via welke weg hoorde u voor het eerst over 'medicatie review'?
2. Wat motiveert u om mee te werken aan medicatie reviews?
3. Hoeveel werk kroop er in de uitvoering voor u als arts?
4. Wat zijn volgens u de voor- en/of nadelen voor de patiënt?
5. Bij welk soort patiënten is het volgens u zinvol om een medicatie review uit te voeren? Wanneer zou u het eerder afraden?
6. Over welke medische gegevens zou de apotheker volgens u moeten beschikken om een goede medicatie review uit te voeren?
7. Wat vindt u van de verstandhouding met de apotheker?
8. Hoe verliep de uitwisseling van de patiëntengegevens tussen u en de apotheker?
9. Hoe zou u dit graag in de toekomst zien gebeuren?
10. Hoe verliep de bespreking van het verslag met de apotheker?
11. Hoe verliep de opvolging met de patiënt nadat de review werd uitgevoerd?
12. Kan de apotheker een nuttige bijdrage leveren aan het optimaliseren van de medicatie? Wat verwacht u van de apotheker?
13. Wat zijn volgens u de positieve aspecten van een medicatie review en waar is er nog een mogelijkheid tot optimalisering?
14. Wat zou u ervan vinden als apothekers hiervoor in de toekomst een vergoeding krijgen?
15. Welke tips heeft u voor andere huisartsen (en apothekers) bij het uitvoeren van medicatie reviews?

Chapter 4: Patient experiences and opinions on medication review: a qualitative study

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Chapter 4

4.1 Abstract

Background: Medication reviews are a structured critical evaluation of a patient's pharmacotherapy, carried out by a healthcare professional, but are not yet a routine pharmaceutical service in Belgium. A pilot project to initiate an advanced medication review (= type 3 medication review) in community pharmacies was set up by the Royal Pharmacists' Association of Antwerp.

Aim: To investigate the experiences and opinions of patients who participated in this pilot project.

Method: Qualitative study through semi-structured interviews with participating patients.

Results: Seventeen patients from six different pharmacies were interviewed. The medication review process with the pharmacist was perceived as positive and instructive by fifteen interviewees. The extra attention that the patient received was highly appreciated. However, the interviews revealed that patients lacked a complete understanding of the purpose and structure of this new service or were unaware of the subsequent contact and feedback with the general practitioner.

Medication reviews in the home setting put patients more at ease, were highly appreciated, and enabled also to address practical problems such as drug dosing or storage requirements.

Conclusion: This qualitative study analysed patients' experiences during a pilot project on the implementation of type 3 medication review. Although most patients were enthusiastic about this new service, a lack of patients' understanding of the whole process was also observed. Therefore, better communication to patients by pharmacists and general practitioners about the goals and components of this type of medication review is needed, with the added benefit of increased efficiency.

Impact of findings on practice

- Patient satisfaction with medication review type 3 was high, this information can be used to motivate more pharmacists to start providing this new service and convince patients to participate.
- Timely and clear communication with patients is needed to ensure patient understanding of the whole medication review type 3 process.
- Efforts to help patients prepare for the consultation with the pharmacists may improve efficiency.
- Incentives to perform medication reviews at the patient's home are needed.

4.2 Introduction

Medication review (MR) is a structured critical evaluation of a patient's pharmacotherapy, carried out by a healthcare professional. It leads to an evaluation with the patient of his/her treatment, optimizing medication use, minimising medication-related problems and avoiding wastage (1, 2). The Pharmaceutical Care Network Europe (PCNE) classifies medication reviews into three types: simple (type 1), intermediate (type 2) and advanced (type 3) medication reviews (3). Advanced or clinical MR (type 3) starts from a complete medication history, takes medical data into account and includes a 30-60 minutes long consultation, together with reporting to and feedback from the physician (3). A growing number of countries are implementing medication reviews (4, 5). In Belgium, until a few years ago, medication reviews were only sporadically carried out. Therefore, in September 2017, the Royal Pharmacists Association of Antwerp (KAVA) launched a pilot project to identify barriers and facilitators to support the local implementation of the type 3 MR (6).

In our previous qualitative research, we examined the opinions and experiences of general practitioners (GPs) and pharmacists regarding MR. Both types of healthcare providers were enthusiastic about the medication reviews and the implementation promoted interprofessional cooperation. In addition,

important hurdles became evident, such as the considerable investment of time and the difficulty in gathering all the necessary information (6). The experiences and opinions of patients are highly relevant, especially when envisioning a new pharmacy service. Nevertheless, there is a relative scarcity of data on the perceptions of patients about the type 3 MR (7, 8), as illustrated by the fact that we could only identify six such studies (9-14). Four of these studies assessed Home Medicines Review (HMR) services (10-13), Geurts et al. studied patient beliefs in clinical MR, which is also a type 3 MR (14) and Petty et al. assessed a pharmacist-conducted medication review clinic, run in a general practice surgery setting (9).

In these type 3 MR studies describing patients' opinions, different methods were used. Three studies used a qualitative method by organising focus groups to explore patients' opinions (9, 12, 13). The other three studies used a quantitative approach by using a questionnaire to map patients' opinions (10, 11, 14).

Three studies showed that most patients consider MR as a positive service that improved the understanding of their medicines (11, 12, 14). The qualitative study by White et al. showed that patients felt valued and cared for (13). Some patients were concerned that the recommendations of the MR would upset the GP. Other barriers were confidence issues with an unknown pharmacist and the lack of information about the MR itself (13).

The patient's view on medications is an important aspect discussed in the MR process. Shared decision-making with patients is widely accepted as enhancing patients' interest in their treatment and improving treatment effectiveness (14). The importance of the patient consultation during a MR should not be underestimated. One study showed that more than a quarter of all DRPs were identified at the time of the patient consultation and that these DRPs had high clinical relevance (15). If patients are not involved, poor therapy control, nonoptimal medication use, and intentional or unintentional nonadherence may be overlooked (16).

Not much qualitative research is yet available on the type 3 MR, especially regarding patients' experiences and opinions during an implementation phase of a new service. In the present study, we used interviews to determine the opinions and expectations of the patients who participated in the MRs within this pilot project.

4.3 Aim of the study

Our study examined the experiences and opinions of elderly patients and receiving more than five medications, who participated in this pilot project, about medication review (type 3), in order to further guide the implementation of this service in Flanders, Belgium.

Ethics approval

Ethical approval was granted by the UZA/University of Antwerp medical ethics committee in February 2019 with authorization number B300201939368.

4.4 Method

4.4.1 Study design

A qualitative research approach with individual interviews was chosen to evaluate the opinions and experiences of the patients (17). The Consolidated Criteria for Reporting Qualitative Research (COREQ guidelines) were used to guide the reporting of the study findings (18). In this paper the word consultation is used for the conversation between pharmacist and patient and the word interview is used for the conversation between researcher and patient.

4.4.2 Sample

From January until October 2018, twenty-five pharmacists were trained to conduct MRs organized by KAVA. Out of these trained pharmacists, thirteen (52%) effectively carried out MRs. A sample of eight pharmacists was contacted for this study by telephone, as a convenience sample starting with the pharmacies within easy reach of the research team. They were asked if we could contact their patients and six pharmacies agreed. Patients were selected by the pharmacists and their coordinates were communicated to the research team. Patients were then contacted by a final year undergraduate female pharmacy student (L.V.L.) to make an appointment. There was no need to contact any additional patients as data saturation was achieved (see below). The research interviews were conducted in March and April 2019.

4.4.3 Design and content validity of the study

To guarantee the anonymity of the patients, they were represented by a specific number in the results list. Three researchers took great care to formulate the interview guide in an unbiased way, so that the interviewees could freely express their opinions. We used the same grounded-theory approach as in our previous research (6). Specific problems or proposed changes to the pharmacotherapy, discussed between the pharmacist and patient, were explicitly not questioned during the research interviews and were absent from the interview guide, which can be found in the supplementary material.

The research interviews were conducted in the pharmacy or at the patient's home. Participation in the study and the interview was voluntary and informed consent was required. The semi-structured interviews were recorded.

4.4.4 Data analysis

The audio recordings were transcribed and coded using Nvivo 12, a program for qualitative data analysis (19). Thematic analysis was used (20) and contained the following phases: familiarisation with the data, generation of initial codes, search for the themes, review of the themes, defining and naming the themes, and production of the report including a selection of illustrative data and quotes from patients (20). Several approaches were used to increase the trustworthiness of our qualitative approach: i) we used the same methods as in previous research (6), ii) patients were preferably interviewed without the presence of the pharmacist that performed the MR, iii) there were multiple debriefing sessions with the researcher doing the interviews, iv) we used existing literature to frame the findings and v) we recognize the limitations of the study (21).

4.4.5 Data consolidation and consensus seeking procedure for the results obtained

Codes were compared and differences in opinions between the researchers L.V.L. and A.R. were discussed with a third researcher H.D.L. to reach a consensus.

4.5 Results

A total of 17 research interviews were conducted with patients from six different pharmacies. The average age of the participating patients was 73 years. The youngest patient was 60, the oldest 85. Nine male and eight female patients participated. Three interviews were conducted with two patients at the same time, as they were each other's partners. The patient characteristics are represented in Table 4.1.

Table 4.1: Patient characteristics

Patient number	Gender	Age at the interview (years)	Note
1	M	68	
2	F	79	Interview was conducted in presence of local pharmacist
3	M	72	Interview was conducted with his wife (patient 4)
4	V	71	Interview was conducted with her husband (patient 3)
5	M	81	
6	M	69	
7	V	85	
8	V	77	
9	M	68	
10	M	74	Interview was conducted with his wife (patient 11)
11	V	64	Interview was conducted with her husband (patient 10)
12	M	73	Interview was conducted with his wife (patient 13)
13	V	70	Interview was conducted with her husband (patient 12)
14	M	74	
15	M	60	
16	V	75	
17	V	83	

Two of the seventeen interviews were conducted in a private consultation room in the pharmacy, at the request of the pharmacist. All the other interviews were conducted at the patient's home. At the patient's request, the pharmacist was also present during one of the interviews. The interviews lasted 31 minutes on average.

Data saturation was achieved as the last three interviews did not bring about new themes notwithstanding the fact that each patient evidently told their own unique story. The thematic analyses of the transcripts revealed the following topics: (i) general experience, (ii) preparation of the medication review, (iii) patient recruitment, (iv), data sharing, (v) consultation, (vi) cooperation with the GP, (vii) changes after the MR, (viii) frequency of the MR, (ix) patients' perception of the caregivers, (x) remuneration, and (xi) recommendations and tips from patients. The results will be discussed according to these topics. Examples of patients' quotations are referred in the text and additional quotes can be found in the supplementary material.

4.5.1 General experience

Patients reported very positive experiences with their pharmacists regarding the consultation about their medications. Because the patients received more than five medications, obtaining additional information about their medication was of interest to them. Over the years, medication is often taken out of habit. The

MR type 3 assisted patients in updating their knowledge of their medications, as shown by the interviews. The extra interest that the pharmacists showed for their patients by conducting the MR was appreciated by nearly all the patients.

> *"I appreciated the pharmacist's attention and care. The pharmacist is welcome to do this again, but I understand that there are more urgent matters." (Patient 2)*

Only two patients had a less favourable experience with the new service. The first patient took part out of curiosity, but the usefulness of a MR was not entirely clear to him. The second patient was displeased with the fact that the review outcome only contained negative elements.

4.5.2 Preparation of the medication review

A total of thirteen patients were unprepared for their consultation. Most assumed that the pharmacist would already have all the necessary information about their medication. Two patients mentioned they had not been informed in advance about the purpose of the consultation.

> *“If I had known in advance what they wanted to discuss with me, I think my interaction would have been more productive, and maybe even more productive for him.” (Patient 5)*

Only four patients had checked their medication at home. Two of them were also asked to make a list of the medications they were currently taking.

4.5.3 Patient recruitment

Fifteen patients were approached by their pharmacist about the MR. Of the other two patients, one was selected by both their pharmacist and GP; the other patient reported having taken the initiative themselves. From the fifteen patients, one believed the selection was agreed upon with the GP. Although patients readily agreed to participate, many felt a little overwhelmed by the invitation and some were a little apprehensive about why specifically they were chosen.

> *“Initially, I was surprised by the pharmacist's invitation, and I was wondering on what basis they had selected people. Perhaps they selected people who take a lot of medications, or of different ages..." (Patient 16)*

The interviews further revealed that not all patients understood the purpose of the MR. For example, five patients saw themselves primarily as helpers to the pharmacist and his/her trainee rather than as beneficiaries of a new service. One person initially found it terrifying. Others took participation for granted and did not hesitate. However, there were also patients who attached little importance to their participation.

4.5.4 Data sharing

Fourteen patients thought data sharing between GPs and pharmacists was normal to very good, with one patient being concerned that the data should definitely not be misused.

> *“Data sharing is not a bad thing. In emergencies, for instance, it can be extremely useful. However, it should not be used inappropriately." (Patient 15)*

Two patients had mixed feelings about the data sharing and one patient had no opinion about this.

> *“It's difficult to tell. It's not clear to me if there's an added advantage. My GP doesn't see it either." (Patient 1)*

Upon further questioning about being informed of data sharing, just over half of the patients were unsure. The patients who knew about the data exchange, thought that was mainly about medication. Some

patients believed that the pharmacist and the physician additionally shared data on blood values and kidney function and appreciated that.

4.5.5 Consultation

Sixteen patients reported that they clearly understood the context of the consultation. In case of questions or ambiguities, there was enough room for clarification.

> *"The pharmacist knows a lot and is able to explain everything without being too academic." (Patient 3)*

Three patients expressed themselves as being highly educated or having experience in the medical field. Four consultations with the pharmacist took place at the patients' home, three took place in the pharmacist's consultation room and ten consultations were held in a separate room of the pharmacy. All patients were satisfied with the length of the consultation.

> *"I don't remember exactly how long it took, but I think it took three quarters of an hour to an hour. They made time for it, as I expected." (Patient 1)*

They reported that it felt like a calm conversation, and they liked that the pharmacist took time for them. One patient could not quite remember how long the conversation lasted, and another patient wound down the conversation themselves.

Twelve patients knew the names of their own medications. For four patients this was not the case, mostly because their partner or family prepared their medication weekly. One patient could not remember the names of her medications, but thought that she knew the indication.

There were no additional aspects to consider for thirteen patients. They were satisfied with the consultation the way it went. These patients indicated that the consultation was exclusively about their medication use. For a patient with depression, the conversation with the pharmacist took place in a relaxed manner. The patient was given the space to talk about things that sometimes caused them difficulties. Two patients stated that additional information would have been helpful. One patient diagnosed with diabetes regretted that the use of their medical device was not discussed during the consultation. Similarly, another patient wanted to discuss their kidney disease more and it was unclear to the patient why this was not discussed. Two other patients were not able to recall any additional aspects.

4.5.6 Cooperation with the GP

It turned out that some patients, depending on the pharmacist, were much better informed or remembered more about the structure and components of the MR than others. One patient thought there had been no meeting between both healthcare providers. Fifteen patients did not attend the meeting between their GP and pharmacist. This was due to their confidence in their healthcare providers or their discomfort with not being able to contribute anything to this discussion. The other two patients were eager to attend out of interest.

> *"Yes, I would find that interesting. Just to know what they think about it. I don't think it's a necessity, but I would find that interesting. I will let them know." (Patient 16)*

4.5.7 Changes after the medication review

Significant medication changes occurred in two patients. Eight patients experienced a change in their medication use, of which two were uncertain whether this was really because of the review.

> *"I needed to go to the toilet every night due to a certain medication. The pharmacist told me to take it at another time, and that problem was fixed. So, I have already experienced more benefits than drawbacks." (Patient 9)*

In the last seven patients, medication had been changed since the medication review, but this was due to a new diagnosis, for example. During the consultation with the pharmacist, the timing and manner of taking the medication were also discussed.

Most patients trust their GP and don't want to have doubts about their prescriptions. The reasons for the various medication changes were clearly explained by the pharmacist during the consultation, which was appreciated.

> *"I could see the value of it. As someone who doesn't take any medications, unless it's necessary and clearly explained to me why I need to take them...." (Patient 7)*

4.5.8 Frequency of the medication review

Six patients believed that such a MR was a single one-time service, four other patients had no idea about the frequency.

> *"Whenever I visit the pharmacy, I get an opportunity to ask a question. I usually receive a helpful answer. Therefore, a repeat is not necessary for me." (Patient 2)*

For one patient the review lowered the threshold for asking questions to the pharmacist, for example about minor medication changes. Therefore, a repeat consultation was not required. Three patients would like to see it repeated every year, two felt it could be repeated if there were several changes to their medication, and two patients felt a repeat would be useful if the pharmacist or GP thought that it was necessary.

> *"Repeating a medication review seems useful to me if there would be an adjustment within the medication, such as adding one which is known to have the potential to cause problems." (Patient 15)*

4.5.9 Patients' perception of the caregivers

The patients' perceptions toward their GPs were unchanged in fourteen patients after the MR. Most of them had a long running trust relationship with their GP. The patients were very pleased with the way their pharmacist worked and described having the same excellent relationship as with their GP.

> *"Similarly to our family physician, our relationship was good from the start. The pharmacist is very spontaneous and helpful. Any help that she can provide is greatly appreciated. That's the reason why I participated." (Patient 3)*

Twelve patients did not perceive the pharmacist in a different way than before the consultation. However, three patients indicated that they felt less like customers. The MR gave them the opportunity to get to know their care providers better.

> *"It was nice to learn a little bit more about the pharmacists at my pharmacy. They were familiar to me, but now after that consultation, they address me in a more personalised way." (Patient 2)*

Opinions were divided on the patients' views of the GP-pharmacist collaboration as a team. Five patients indicated that they were not aware what this collaboration entailed. There were also eight patients who assumed that the cooperation between the two professions had improved partly as a result of carrying out the MR. One patient felt that nothing had changed, and three patients did not answer the question.

> *"I always felt that both the pharmacist and GP were a bit out of touch with their patients. That they were elevated to a higher status. But that seems to have improved now and they are now a lot more in touch with their patients." (Patient 5)*

4.5.10 Remuneration

There was an equally divided opinion about reimbursement. On the one hand, performing a MR was seen as an additional service for which compensation should be given. On the other hand, patients saw it as part of the pharmacist's duties and did not consider it necessary to provide compensation for each performance. Seven patients did not find reimbursement necessary. While one patient stated that reimbursement was unethical, the others thought it was unnecessary because it should be part of their job or should be provided as a free service. One patient categorically refused to even take into consideration that they should pay for this service.

> *"If you ask me whether the doctor or the pharmacist should be reimbursed by the government or another organisation, then I would answer 'no' across the board." (Patient 15)*

The remaining half of patients considered the new service worthy of remuneration. The question was whether remuneration should be provided for the GP and/or pharmacist. Most of the answers focused on the pharmacist. Less was said about remuneration for the GP. A MR was an extra time commitment, an extra service for which remuneration may be provided. The opinions were again equally divided on the willingness to pay for this service. Half of the patients felt that they already had to pay enough in health costs. The other half of patients found it no problem to pay for this.

> *"In my opinion, they should be reimbursed for the time they spent on it." (Patient 13)*

4.5.11 Recommendations and tips from patients

Thirteen patients would recommend a medication review to other people, and one patient already did and another mentioned that they would suggest it in the case of polypharmacy. Among the remaining four patients, two would not recommend it as they had not personally benefited, and the other two had a neutral perspective.

> *"Anyone who needs to take medication will find it very useful. It doesn't matter if it is for blood pressure or cholesterol. It's always useful to know what you're taking and what its purpose is. I know several people who also take medications, but they don't realize why they are taking the medication." (Patient 11)*

Patients were asked at the end of the interview about suggestions for any improvements that could be made. Their responses included the desire to be more informed about the whole concept of the MR, to be better prepared and to make the consultation more productive.

> *"An invitation to participate in a MR should provide enough information for the patient about its purpose. As for my pharmacist, he asked me how I felt about the medication. If you don't prepare, it's overwhelming. I've only been told now." (Patient 5)*

Another recommendation was to also include specialist physicians in the process.

4.6 Discussion

4.6.1 Interpretation of the findings

General experience

This qualitative study raised some issues that need to be taken into consideration in future implementations. Patients generally appeared to be very satisfied with the new service, as reported

previously (11, 12, 14, 22, 23), considered this new service to be informative and appreciated the time-investment of the pharmacists, as also previously reported (13, 23). But there were a few dissenting opinions as patients felt that their GP's professionalism and knowledge should not be questioned by the pharmacist.

Preparation of the medication review

The patients were not adequately informed about the whole process of the medication review and for many there was only minimal preparation before the consultation with the pharmacist. We note that the precise language describing and defining the outcomes of a medication review is not fully settled (24) and standardisation my allow help the uniform communication among all involved in this new pharmaceutical service. Our previous research had already suggested that this is an aspect that needs to be improved (6).

Patient recruitment

Patients who agreed to participate in the MR were originally recruited by their pharmacist and this resulted in mixed reactions (6). Some patients found it rather worrisome that they were singled out, but others did not question it further. They participated out of self-interest and curiosity, but sometimes also because they wanted to help their pharmacist indicative of not being adequately informed about the goals of a MR and doing this should avoid unnecessary anxiety (25).

Data sharing

Patients agreed on the necessity and desirability of data exchanges between physicians and pharmacists. Although it was taken for granted by many, some patients questioned this in the context of confidentiality and privacy, as was also previously reported (13). The type of data shared should therefore be clearly communicated to the patient from the outset.

Consultation

The usefulness goals and different steps of a MR were not clear to all patients as also found in other studies which showed that clear communication about the goals of the MR improved trust in the pharmacist's MR (22, 23, 26).

In this pilot project, some consultations with the pharmacist took place at the patient's home, whereas most of the consultations took place in a separate room in the pharmacy. Different studies have shown that a home visit by a pharmacist can produce beneficial results (27-29). In addition, the pharmacist can supervise the storage method immediately when the patient has all their medication within easy reach (28).

The majority of patients were satisfied with their consultation and the willingness of their pharmacist to provide additional explanations to their patients, as has been described previously (22, 23, 26). Depending on factors such as education, interest and age, not all patients appeared to have sufficient knowledge of, for example, the medication names. This could be overcome by asking patients to bring their medication(s) to their consultation as a visual aid.

Changes after the medication review

For some patients, pharmacotherapeutic improvements were suggested as a direct result of the MR. A MR also provides a better understanding of the medication use, which is similar to previous findings (11, 12, 14).

Patients' perception of the caregivers

The pharmacist-GP collaboration was valued by half of the patients who were aware of the collaboration, which is in line with results from Kempen et al. (23). The lack of communication described above reduced the understanding of the GP-pharmacist collaboration in some patients. Previous studies have indicated

that, in general, caregiver cooperation needs to be optimized, but that introducing this new service may actually catalyse that (6).

Remuneration

Opinions on the need for reimbursement were split 'fifty-fifty'. As most patients were addressed by their own pharmacist, who also conducted the consultation, reimbursement for the physician did not immediately came up. Moreover, the healthcare providers themselves did find it necessary to be reimbursed for a MR (6).

Recommendations and tips from patients

Except for receiving additional information about the use of medical devices, such as blood glucose meters few extra suggestions were offered by the patients. The majority of patients would recommend the MR service to other patients, certainly polymedicated patients or those with limited understanding of their medications. However, they thought that the general practitioner or pharmacist should select these specific patients. The patients with a clear outcome from the MR, e.g., discontinuation of a certain medication after the consultation, were full of praise for this new service. Suggestions for optimizing the consultation, or enhancing collaboration, were not raised. However, an interesting suggestion that was made was to involve the physician-specialist as an additional partner, as many patients receive treatment from more than one healthcare provider.

4.6.2 Strengths and limitations of the study

Due to the qualitative nature of this study, only a limited number of patients were interviewed. Any transferability will therefore be tentative. There was a patient sample bias as the pharmacists were very enthusiastic and involved benevolent patients who were eager to learn more about a completely new service. Nevertheless, qualitative research with patients is important as this may improve the quality of a MR by informing the implementation process. Pharmacists were allowed to choose which patients to include in their MR, rather than patients just being chosen at random (6) and this bias was therefore also present in the assessment of the patients' opinions. There was period of approximately one year between the MR and the research interview, which potentially could have introduced some recall bias. Lastly, this study did not focus specifically on the individual pharmacotherapeutic content of the MR, but rather on its process. This is a more difficult topic for patients who are not yet familiar with this new type of service.

4.6.3 Similarities and differences with other studies

The current literature encompasses six studies describing patients' opinions about type 3 MR (9-14). None of these however used individual interviews, as we did in our study, but instead used focus groups (9, 12, 13). One study revealed that patients' opinions about the service varied greatly, as most patients understood the purpose of the review, but some had suspicions about its real objective (9). Another study also showed that experience with MR, and to a lesser extent, prior knowledge of MR, increased willingness to participate in a MR (10). Our study also demonstrated the need for better communication between healthcare providers and patients about this new service. Two quantitative surveys showed that patients had positive opinions about medications and that a MR provided them with increased medication knowledge (11, 14).

4.6.4 Future research

During this study, new questions arose for further research. How can the quality of MR be secured in an objective way (30) and what quality parameters are necessary in this endeavour (31). Another question focuses on how to measure the clinical impact of type 3 MR because of the diversity of the population and the complexity of the intervention (31). Finally, it would be interesting to learn what non-participating healthcare providers think of this new service (32).

4.7 Conclusion

Many patients greatly appreciated the pharmacists' attention and time invested. Nevertheless, some patients were not adequately informed about this, for them, new service. An adequate description and rationalisation of the purpose and goals of the MR type 3, tailored to the individual patient, should therefore be mandatory. For patients, this would also likely counteract any potential anxiety caused by the invitation to participate in a MR and for the additional questions posed about their medication. In conclusion, our results show that patients are overwhelmingly positive about this new service and provide constructive input for its further development and implementation. Better communication to patients by pharmacists and general practitioners about the goals and components of this type of medication review is needed, with the added benefit of increased efficiency.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to this study.

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4.9 Appendices

Appendix 4.1 examples of patients' quotations

Classification	Quotations
General experience	*"The consultation can teach you a lot, can't it? You're prescribed different types of medications, but after a while you can't remember anymore for what they were intended. If that knowledge can be refreshed, that would be great." (Patient 13)*
	"I think that it's good that you can show the specialist [physician] your medication schedule. Before, you had no idea how to explain all that to them. With that in mind, I hope that when I'm prescribed something, that it will be compatible with my other medications. I find this scheme very informative." (Patient 3)
	"I appreciated the pharmacist's attention and care. The pharmacist is welcome to do this again, but I understand that there are more urgent matters." (Patient 2)
	"The pharmacist said that I was doing the wrong thing, contrary to what my doctor said. At that point, I felt 'Does my pharmacist know more than my doctor?' Of course, there's always the possibility of two different perspectives." (Patient 15)
Preparation of the medication review	*"If I had known in advance what they wanted to discuss with me, I think my interaction would have been more productive, and maybe even more productive for him." (Patient 5)*
Patient recruitment	*"As a matter of fact, I requested the medication review myself because I was taking a number of medications that I thought were contradictory." (Patient 15)*
	"Initially, I was surprised by the pharmacist's invitation, and I was wondering on what basis they had selected people. Perhaps they selected people who take a lot of medications, or of different ages..." (Patient 16)
	"I was curious and wanted to participate and make a meaningful contribution." (Patient 1)
	"If we don't take part, then you wouldn't get the information you need. […] It's good to help students. We also have some relatives who are at university." (Patient 14)
	"This invitation sounded like a good opportunity for me to learn. I didn't object to it." (Patient 5)
Data sharing	*"My medication and medication doses are shared between my GP and pharmacist. Also, as I have been diabetic for many years, if my diabetes specialist at the clinic changes anything to my treatment, then this information is provided to my doctor, who then tells my pharmacist. It's great that this happens. Even though I don't have dementia yet, I think that it's important for those who tend to forget things. It's great!" (Patient 8)*

	"We thought data sharing was actually a very good thing. Consequently, we could always ask for advice from one of them." (Patient 11)
	"Data sharing is not a bad thing. In emergencies, for instance, it can be extremely useful. However, it should not be used inappropriately." (Patient 15)
	"It's difficult to tell. It's not clear to me if there's an added advantage. My GP doesn't see it either." (Patient 1)
	"In my opinion, privacy is an illusion. I do not object. I do not believe in privacy." (Patient 5)
	"As a result of the chemotherapy I received, I have poor kidney function. The pharmacist checks that my medication won't harm my kidneys." (Patient 13)
Consultation	*"It was all clear to me. Of course, there were terms that made me ask 'what does that mean exactly?' and then she explained it a bit better, with or without a diagram." (Patient 15)*
	"The pharmacist knows a lot and is able to explain everything without being too academic." (Patient 3)
	"I don't remember exactly how long it took, but I think it took three quarters of an hour to an hour. They made time for it, as I expected." (Patient 1)
	"My feeling was that the conversation turned up more negative than positive things. I started winding it down because it felt a bit negative." (Patient 15)
	"The names of the medications are simply too complex for me. And sometimes the names of the medications change, or new ones are added. To be honest, I don't even try to understand them." (Patient 16)
	"I don't recall the names very well, but I know what they do and why I take them. I see the little pill and I know when to take it. (Patient 4)
	"There were also some things that came up that I wouldn't normally talk about, but I brought up anyway. We did have a personal conversation too. I actually thought that it was okay. We talked about my depression in the past, and what it was like for me at that time ... ." (Patient 16)
	"While I would have liked to do this sometimes, it never came up. I have diabetes and have a lot of hypos. […] I would like to learn to use my device again in a quiet environment, and not in a crowded pharmacist's shop." (Patient 2)
Cooperation with the GP	*"Because we trust both our GP and pharmacist, that's not necessary for us." (Patient 11)*
	"Yes, I would find that interesting. Just to know what they think about it. I don't think it's a necessity, but I would find that interesting. I will let them know." (Patient 16)
Changes after the medication review	*"Because it was bad for my kidneys, I stopped taking medicine X. The GP prescribed it, I took it, and then a blood test proved it was very bad for my kidneys, so it had to be stopped.[…]." (Patient 13)*

	"I needed to go to the toilet every night due to a certain medication. The pharmacist told me to take it at another time, and that problem was fixed. So I have already experienced more benefits than drawbacks." (Patient 9)
	"About the cholesterol medication that I needed to take in the evening, I explained to the pharmacist that I actually have a problem with that as I sometimes forget to take it. She said, "We can easily switch that pill so that you can take it in the morning." There you have it. I can now take everything in the morning. Super easy!" (Patient 7)
	"I wasn't aware that certain medications cannot be taken with grapefruit. I have informed my acquaintances as well to stop using grapefruit with medications." (Patient 7)
	"I could see the value of it. As someone who doesn't take any medications, unless it's necessary and clearly explained to me why I need to take them...." (Patient 7)
Frequency of the medication review	*"Whenever I need to talk to my pharmacist, I go to the pharmacy. So, if there is a problem, my pharmacist is there to help." (Patient 9)*
	"Whenever I visit the pharmacy, I get an opportunity to ask a question. I usually receive a helpful answer. Therefore, a repeat is not necessary for me." (Patient 2)
	"I suggest once a year or every six months, but not more. Whatever it is, if you start to have doubts about something, get in touch with the pharmacist." (Patient 16)
	"Repeating a medication review seems useful to me if there would be an adjustment within the medication, such as adding one which is known to have the potential to cause problems." (Patient 15)
Patients' perception of the caregivers	*"Similarly to our family physician, our relationship was good from the start. The pharmacist is very spontaneous and helpful. Any help that she can provide is greatly appreciated. That's the reason why I participated." (Patient 3)*
	"It was nice to learn a little bit more about the pharmacists at my pharmacy. They were familiar to me, but now after that consultation, they address me in a more personalised way." (Patient 2)
	"Taking my pharmacist's word for it, I believe that the collaboration is much more intense now. In addition, the GP also reports seeing my pharmacist about my medications. Those things are followed up more quickly now. This didn't happen previously. So, I think that's a good thing. I also think that they both prefer it that way." (Patient 7)
	"... in a certain way they [the pharmacist and GP] control each other a bit. Nobody is perfect and someone else can, if necessary, always make readjustments." (Patient 9)
	"I always felt that both the pharmacist and GP were a bit out of touch with their patients. That they were elevated to a higher status. But that seems to have improved now and they are now a lot more in touch with their patients." (Patient 5)

Remuneration	*"If you ask me whether the doctor or the pharmacist should be reimbursed by the government or another organisation, then I would answer 'no' across the board." (Patient 15)*
	"I do believe that pharmacists should also be remunerated. Actually, for the GP this already happens." (Patient 10)
	"In my opinion, they should be reimbursed for the time they spent on it." (Patient 13)
	"This is an extra service that is not part of the job description. Therefore, I think it should be compensated." (Patient 3)
	"It's actually the government's responsibility to take care of this. We already pay contributions for all kinds of things." (Patient 7)
Recommendations and tips from patients	*"Anyone who needs to take medication will find it very useful. It doesn't matter if it is for blood pressure or cholesterol. It's always useful to know what you're taking and what its purpose is. I know several people who also take medications, but they don't realize why they are taking the medication." (Patient 11)*
	"An invitation to participate in a MR should provide enough information for the patient about its purpose. As for my pharmacist, he asked me how I felt about the medication. If you don't prepare, it's overwhelming. I've only been told now." (Patient 5)
	"My only thought is that specialists also prescribe medications. In that case, the pharmacist would also be required to sit together with the specialist and do the same thing." (Patient 3)

Appendix 4.2 Patients' interview guide (translated version)

1. How did you experience the consultation regarding your medication?
2. Did you prepared anything yourself for the consultation? If yes what exactly?
3. How did you feel about being selected for an interview around your medication?
    a. Were you selected by your pharmacist or doctor?
    b. How did your pharmacist/GP address this?
    c. How was your reaction at the time?
    d. Where did the conversation take place?
4. How did you feel about your data being shared between your GP and your (family) pharmacist?
    a. Can you tell me what kind of data was shared?
5. (Format): How did you find the consultation itself?
    a. Could you understand all the terms the pharmacist used?
    b. How were the pharmacist's questions? (rather difficult/easy/...)
    c. In terms of length
    d. Could you understand the conversation well if the names of the drugs were mentioned?
6. (Content): What aspects were not discussed that you would have liked to have seen covered? Which aspects were covered but you did not think they should be discussed with the pharmacist?
7. The findings from the interview were discussed in consultation with your GP and pharmacist. What did you think about that? How would you feel about being present there?
8. What has changed regarding medication after this interview?

   a. What has changed regarding the regularity with which you pick up medication or the regularity of use?
   b. Has anything changed financially?
   c. Has your idea about the usefulness/danger of the medicines changed?
9. How often should such a conversation take place?
10. Do you now look at your GP in a different way ?
11. Do you now look at your pharmacist in a different way?
12. Do you think anything has changed about the way GP and pharmacist work together?
13. Do you have a different perception of the doctor/pharmacist team now?
14. How would you feel if this consultation resulted in remuneration for the pharmacist and doctor? Are you willing to pay for this?
15. Would you recommend the consultation to other people? If yes, to whom? Why yes/no?
16. This is another new concept. What tips do you have for doctor and pharmacist to improve the whole process?

Appendix 4.3 Patients' interview guide (original Dutch version)

1. Hoe heb je het gesprek rond je medicatie ervaren?
2. Had je zelf iets voorbereid voor het gesprek? Indien ja wat juist?
3. Hoe vond je het om geselecteerd te worden voor een gesprek rond je medicatie?
   a. Werd je geselecteerd door je apotheker of arts?
   b. Hoe heeft je apotheker/arts dit aangekaart?
   c. Hoe was je reactie op dat moment?
   d. Waar vond het gesprek plaats?
4. Wat vond je ervan dat je gegevens gedeeld werden tussen je huisarts en je (huis)apotheker?
   a. Kan je me vertellen welke soort gegevens er gedeeld zijn?
5. Vormelijk: Hoe vond je het gesprek zelf?
   a. Kon je alle termen verstaan die de apotheker gebruikte?
   b. Hoe waren de vragen van de apotheker? (eerder moeilijk/makkelijk/…)
   c. Qua lengte
   d. Kon je het gesprek goed volgen als de namen van de geneesmiddelen vermeld werden?
6. Inhoudelijk: Over welke aspecten is er niet gepraat die je aan bod had willen zien komen? Welke aspecten zijn aan bod gekomen maar vond je niet dat ze besproken moesten worden met de apotheker?
7. De bevindingen uit het gesprek werden in overleg met je huisarts en huisapotheker besproken. Wat vond je daarvan? Hoe zou je het ervaren om daar aanwezig te zijn?
8. Wat is er veranderd ivm medicatie na dit gesprek?
   a. Wat is er veranderd ivm de regelmaat waarmee je geneesmiddelen komt ophalen of de regelmaat van gebruik?
   b. Is er financieel iets veranderd?
   c. Is je idee over het nut /gevaar van de geneesmiddelen veranderd?
9. Hoe dikwijls moet zo'n gesprek plaatshebben?
10. Bekijk je je arts nu op een andere manier?
11. Bekijk je je apotheker nu op een andere manier?
12. Denk je dat er iets veranderd is over de manier waarop arts en apotheker samenwerken?
13. Bekijk je het team arts/apotheker nu op een andere manier?

14. Wat zou je ervan vinden als dit gesprek een vergoeding zou opleveren voor de apotheker en arts? Ben je bereid hiervoor te betalen?
15. Zou je het gesprek aanraden aan andere mensen? Indien ja, aan wie? Waarom wel/niet?
16. Dit is nog een nieuw gegeven. Welke tips heb je voor arts en apotheker om het geheel te verbeteren?

Chapter 5

Chapter 5: Key elements in the quality assessment of a type 3 medication review

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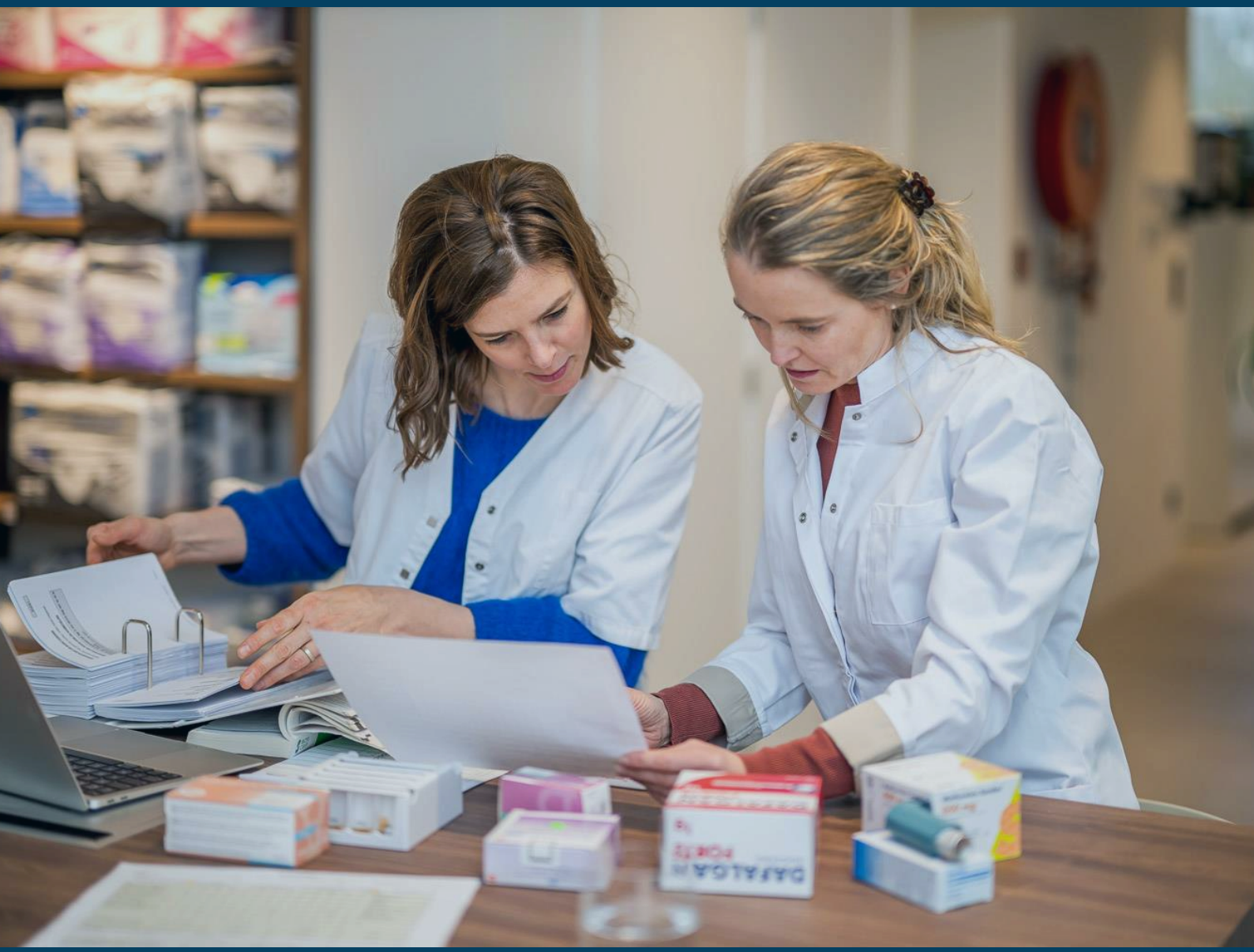

5.1 Abstract

Background: Medication reviews are a structured evaluation of a patient‘s pharmacotherapy with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug related problems and recommending interventions. A high level of quality is essential for the successful implementation of this service in community pharmacies but currently there is no instrument or tool to assess that overall quality.

Aim: This study investigated the development of quality criteria of type 3 medication reviews (MR3s).

Methods: After surveying the literature, an electronic questionnaire was developed to gather information about quality criteria for MR3. This survey, in Dutch, was distributed electronically. Four groups were queried: (i) pharmacists, mainly working in the Netherlands, involved in practice research and contacted through the PRISMA (Practice Research In Collaboration With Pharmacists) foundation, (ii) Belgian pharmacy academics and pharmacists active in professional associations (APA), (iii) Belgian pharmacists trained in medication review (MR) by the Royal Pharmacists Association of Antwerp (KAVA) and (iv) Belgian pharmacy students. The survey included 57 criteria, divided into eight domains, which were ranked according to their importance by the participants. The results were analysed statistically using the nonparametric Kruskal-Wallis test.

Results: The survey was completed by 95 participants, including 42 PRISMA pharmacists, 19 APA pharmacists, 18 KAVA pharmacists and 16 pharmacy students. Opinions from participants from the different groups overlapped significantly. The use of simple and understandable language in the conversation with the patient was considered essential by the majority. Discussing the usefulness and purpose of a MR3 with the patient was also rated highly by all groups. Differences of opinion were present in aspects about laboratory values, the use of specific tools, and reporting to and consultation with the treating physician. The participants themselves formulated a limited number of additional assessment criteria.

Conclusion: There was widespread agreement on the hierarchy of the quality assessment criteria for MR3s. Minor differences were related to the experience of the participants. With these results and a small number of suggested extra criteria, a quality assessment instrument for MR3 can be created.

5.2 Introduction

Following the lead of other countries such as the Netherlands or Australia (1, 2), medication reviews (MRs) are increasingly implemented in primary care in Belgium (3, 4). As for any new service, quality assessment should be an integral part of their implementation (5-9). In 2017, the Royal Pharmacists’ Association of Antwerp (KAVA) started a pilot project in which pharmacists were trained in conducting type 3 MR (MR3) i.e., an advanced or clinical MR. Type 3 MR starts from a complete medication history, adds medical data and includes an extensive interview with the patient as well as feedback from the physician (3, 10).

In recent years, more focus has been placed on the implementation and quality of MRs (5, 7, 9, 11-16). Five studies dealt with Medicines Use Review (MUR) (5, 7, 11, 12, 16), a type 2a MR and two other studies involved type 3 MR (9, 14) whereas the type of MR was not specified in two other studies (13, 15). Only one of the MR3 studies was carried out by pharmacists in primary care (14). The quality of the MR can be affected by the pharmacist's competence, guidelines, comprehensive knowledge of drugs currently in use (including over-the-counter (OTC) drugs), willingness to engage in an extended role, organizational setting of the pharmacy (e.g., time available), financial rewards and peer review (12, 14). Rose et al. analysed pharmacists’ activities during MR across six countries (Australia, Canada, Chile, Germany, United Kingdom

and United States) (9) and found that MRs were not performed in a consistent and standardized way across or within these countries. Activities such as “assess that all medications are optimal” and “follow up with patient”, which are key steps in the patient care process, were not performed in all 6 countries (9). Recent research showed that interprofessional collaboration in MR leads to higher quality MRs (17).

There are various quality improvement initiatives in the wider healthcare setting, such as checklists and tools (6, 18, 19). These tools aim to facilitate implementation research and quality improvement projects (19). Additionally, quality measures for pharmacy practice were recently reported to be lacking in terms of development, standardization, and validation (8). A standardised MR process was also suggested to enable comparisons between process evaluations (20). Quality parameters may help in the development of a quality assessment tool. However, such a tool should be user-friendly and concise, otherwise it may be ignored. Furthermore, criteria should not be readily predictable, as this can lead to ‘gaming’, defined as reactive subversion such as ‘hitting the target and missing the point’ or reducing performance where targets do not apply (21).

5.3 Aim of the study

This study was undertaken to investigate criteria for quality assessment of MR3s, an aspect that has received little attention in the literature so far. The primary research question focused on identifying the key elements for assessing the quality of a MR3. Furthermore, the study compared the perspectives of various participants on several influencing factors, including experience in conducting MR3s and work setting, to investigate whether specific pharmacist’s characteristics influenced their opinions and to gauge the amount of consensus among the different groups. The objective was to discriminate the relative importance of some topics and inquire if there were any topics we had forgotten.

Ethics approval

In the Belgian setting, an ethics approval was not required because the survey was anonymous.

5.4 Materials and methods

5.4.1 Questionnaire design

A comprehensive online survey was prepared after reviewing the literature on the quality assessment of MRs. Literature was consulted until April 2020, when the study was conducted. The questions of the survey were extensively discussed with the researchers M.M., A.R., G.D.M. and H.D.L. All researchers gave feedback on each of the three successive survey drafts. The survey also inquired about the participants' utilization of specific tools, including the Ghent Older People's Prescriptions Community Pharmacy Screening (GheOP^{3}s) tool, the START/STOPP criteria, the Medication Appropriateness Index (MAI), and the Opioid Risk Tool (ORT) (22-25). Subsequently, the feedback of three pharmacists who were not involved in the design of the survey was incorporated in the fourth and final version. The Qualtrics online survey tool was used to conduct the questionnaire (26). A translation of the full survey, statements, and original Dutch questions can be found in the appendix.

5.4.2 Design and content validity of the study

The survey asked participants to rank 57 statements in eight domains for importance, without allowing for ties, showed in table 5.1. Each domain contained five to nine statements that were presented to each

participant in an individually randomized order. The survey started with four general questions to determine the profile of the respondent. After finishing the survey, participants were asked if any statements or criteria were missing from the questionnaire and if they had any other feedback.

Table 5.1: Overall statements within each domain.

	Overall statements
DOMAIN A: General aspects of the MR3.	
A.1	Pharmacists need to use simple and understandable language with their patients.
A.2	There was reporting and consultation with the attending physician.
A.3	Literature consulted and cited was scientific.
A.4	Discussion with the patient took place in a familiar and calm environment.
A.5	Reliable tools for conducting a MR were used. For example, GheOP³S (Ghent Older People's Prescriptions community Pharmacy Screening) (22), START/STOPP criteria (24), MAI (Medication Appropriateness Index) (23), etc.
A.6	Consideration was given to communicating non-pharmacological advice. For example, healthy diet, exercise, smoking cessation, etc.
A.7	Sufficient attention was given to non-drug substances (dietary supplements, herbal medicines and homeopathy) that the patient may be taking.
A.8	Availability of cheaper alternatives for patient and/or National Institute for Health and Disability Insurance (NIHDI) was considered (other drugs, other quantity/packaging).
DOMAIN B: Patient characteristics taking into account living situation, resources and need for MR3.	
B.1	The usefulness and purpose of a MR was discussed with the patient.
B.2	Patient characteristics at risk for poor adherence were considered.
B.3	MR was tailored to the patient's living situation (informal carer).
B.4	Aids used by the patient to perform daily tasks were considered.
B.5	Risk of addiction was considered (e.g., by using a screening tool such as ORT (Opioid Risk Tool)).
DOMAIN C: Patient's ability: ease of taking, opening drugs and storage conditions.	
C.1	The pharmacist paid attention to whether the patient could swallow the drugs.
C.2	Pharmacist paid attention to whether the patient can open and close the drugs (including a box, twist-top and/or child-proof closure).
C.3	Consideration was given to whether the patient gets his/her drugs out of the blister.
C.4	Whether the patient can accurately measure out a liquid was considered.
C.5	Pharmacist paid attention to whether the medication could be put into medication boxes.
C.6	Proper storage conditions for drugs were discussed with the patient (not in a humid room such as kitchen, away from children, ...).
C.7	Patient's attitude towards injections was considered.
DOMAIN D: The patient: follow-up knowledge, instructions and adherence.	
D.1	Which drugs was used for which condition was discussed with the patient.
D.2	Patient was informed about the correct way to take the drug.
D.3	Pharmacist paid attention to whether the patient knows the difference between regular drugs and drugs taken only when needed (prn (pro re nata) drugs).
D.4	Consideration was given to whether the patient could understand the instructions.
D.5	Patient compliance was assessed based on a comprehensive analysis of medication over a sufficient period of time.
D.6	Pharmacist paid attention to whether the patient can read instructions.
D.7	Pharmacist has paid attention to whether the patient knows when his/her drugs are past their expiry date.
DOMAIN E: Current therapy: major drugs, missing drugs, evolution of therapy and vaccination status.	
E.1	A recent and clear medication schedule was created and discussed with the patient.
E.2	Consideration was given to which medicines are particularly important for the treatment of the condition.
E.3	Pharmacist paid attention to medicines that were missing from the treatment for example, the need for stomach protection, laxatives and/or statins).

E.4	Pharmacist paid attention to whether all conditions were treated, if needed for these conditions.
E.5	Changes in previous medication use were critically reviewed (why stopped/adjusted?).
E.6	Appropriate guidelines were always consulted to evaluate treatment.
E.7	Changes to the patient's previous medication regimen were discussed with them.
E.8	Patient's vaccination status was evaluated.
DOMAIN F: Evaluation of medication use: simplification, current drug indications, dose appropriateness, use of lab values and achievement of goals.	
F.1	Pharmacist paid attention to whether all drug indications were still current.
F.2	Drug dose was assessed for appropriateness.
F.3	Efforts were made to simplify medication use.
F.4	All relevant parameters/lab values requested from the (primary) physician were considered.
F.5	A discussion was held with the patient about why certain goals were or were not achieved.
F.6	Attention was paid to tapering off the medications.
DOMAIN G: Causes of adverse drug reactions, intolerances, interactions and their solutions.	
G.1	Patients were given the opportunity to discuss their illness symptoms with the pharmacist.
G.2	The patient was engaged in a discussion regarding the timing of drug intake in relation to nutrition, addressing possible interactions and considerations.
G.3	All drugs and their dose were matched to renal function.
G.4	During a thorough analysis of the symptoms cited, it was considered whether they could have been caused by the chronic or acute drugs.
G.5	Contraindications associated with the condition were identified and evaluated.
G.6	Relevant drug-drug interactions between all chronic and temporary drugs were checked and a concrete solution sought whenever necessary.
G.7	Pharmacist paid attention to the presence of drugs with central anticholinergic properties.
G.8	Patient allergies/intolerances were considered.
G.9	Pharmacist paid attention to the presence of QT-prolonging drugs.
DOMAIN H: The new treatment plan: factors for drafting, implementation of adjustments and follow-up.	
H.1	The patient's expectations and concerns were taken into account when developing the treatment plan
H.2	New treatment plan was discussed with the patient and the patient agreed to it.
H.3	Clear agreements were made with the patient regarding follow-up.
H.4	Patient was informed in detail which over-the-counter (OTC) drugs should no longer be used due to the presence of contraindications.
H.5	Clear agreements were made with the physician regarding follow-up.
H.6	Priorities in the treatment plan are clear.
H.7	Detailed report contains reasoned arguments per recommended adjustment and was reported in writing to the physician.

5.4.3 Questionnaire distribution

The online questionnaire link was emailed in April 2020 to four different groups: (i) pharmacists involved in practice research and approached through the Dutch PRISMA (Practice Research In Collaboration With Pharmacists) foundation, (ii) pharmacy academics and pharmacists active in professional development as well as in insurance companies in Flanders (APA), (iii) Flemish pharmacists trained in MR3 by KAVA (3) and (iv) last year pharmacy students with a varied amount of real word experience studying at the University of Antwerp, Belgium. Each group received a separate link to the survey. The PRISMA foundation sent the survey to all of its members and the email to students reached all last year pharmacy students at the University of Antwerp. Targeted communication was used for pharmacists in the APA group, while within the KAVA group all pharmacists who had taken a previous MR3 course were contacted. The survey through PRISMA included an additional question to distinguish the nationalities of the participants.

5.4.4 Data analysis

Consensus assessment was analysed through the use of bump charts (27). A statistical evaluation of the results was also performed using the Statistical Package for the Social Sciences (SPSS, version 28.0.1.1, IBM). Differences between groups were evaluated using the nonparametric Kruskall-Wallis test with P values <0.05 pointing toward significant differences of opinion.

5.5 Results

5.5.1 General results

A total of 113 responses were received. Subsequently, the 18 participants who provided only personal demographic data without responding to statements were excluded. Of these 95 participants, 91 completed the survey in full. Table 5.2 presents the demographics of the surveyed population that consisted of 59% Belgian, 40% Dutch and 1% German participants. The majority of participants were 31-60 years old, with 34% aged 20-30 and 8% over 60. The two most prominent participant profiles were pharmacy practice researchers (n=18, 19%) and pharmacy students (n=16, 17%). A majority of 78% had pharmacy experience, mainly for 1-5 or 20-30 years.

Table 5.2: Demographics of the research population (n = 95)

Measure	Item	Count	Percentage (%)
Age (years)	20-30	32	34
	31-40	19	20
	41-50	18	19
	51-60	18	19
	61-70	8	8
	> 70	0	0
Nationality	Belgian (B)	56	59
	Dutch (NL)	38	40
	German (D)	1	1
Group	PRISMA pharmacists (NL + B + D)	42	44
	KAVA pharmacists (B)	18	19
	APA pharmacists (B)	19	20
	Pharmacy students (B)	16	17
Profile	Pharmacy practice researcher	18	19
	Pharmacy student 2nd master	16	17
	Deputy pharmacist (community pharmacy)	12	13
	Practice pharmacist and researcher	9	9
	Head pharmacist (community pharmacy)	8	8
	Academic staff within pharmaceutical care field	8	8
	Researcher in pharmaceutical field	6	6

	Pharmacist involved in professional development of pharmacists	3	3
	Pharmacist stand-in	1	1
	Other	14	15
Years of Pharmacy experiences	None	22	23
	1-5	18	19
	5-10	14	15
	10-15	11	12
	15-20	7	7
	20-30	16	17
	> 30	7	7
Number of MR3 performed by the participants	None	38	40
	< 5	18	19
	5-15	8	8
	16-25	2	2
	>25	29	31

The largest of the four surveyed groups, the PRISMA group encompassing 44% of the participants, displayed considerable heterogeneity, through the inclusion of community pharmacists, researchers and academic teaching staff. Within this group, 39 participants (92%) were Dutch, three (7%) were Belgian, and one participant (2%) held the German nationality. Two groups accounted for respectively 20% and 19% of the participants, namely the APA group and Belgian pharmacists trained in MR3. The fourth group (n=16, 17%) consisted of Belgian pharmacy students.

The participants' experiences with MR3s showed significant variation. Among the participants, 40% had never conducted a MR3, while 31% had completed more than 25 reviews. Notably, the PRISMA group participants exhibited the most extensive experience with MR3. The median time taken to complete the survey was approximately 16 minutes.

Table 5.3 displays the statements deemed, on average, to be the most important ones by all participants. No significant differences were found between the groups. For each group, the interquartile range and median for each statement were computed, as detailed in the Appendix.

Table 5.3: Overall most important statement within each domain.

Most important statements
- A.1: Pharmacists need to use simple and understandable language with their patients. - B.1: The usefulness and purpose of a MR was discussed with the patient. - C.1: The pharmacist paid attention to whether the patient could swallow the drugs. - D.1: Which drugs was used for which condition was discussed with the patient. - E.1: A recent and clear medication schedule was created and discussed with the patient. - F.1: The pharmacist paid attention to whether all drug indications were still current. - G.1: Patients were given the opportunity to discuss their symptoms with the pharmacist. - H.1: The patient's expectations and concerns were taken into account when developing the treatment plan.

5.5.2 Ranking of the statements and differences between the groups

The rankings and their variations among the various groups are detailed below and illustrated in Figure 5.1-9.

5.5.2.1 Domain A: General aspects of the MR3

Participants stressed the importance of using language that is easy to understand when communicating with patients (A.1) (Figure 5.1). There was a significant consensus on this statement, as indicated by a p-value of 0.329. Around 58% of participants placed this statement among their top two rankings. Three out of four groups concurred that the statement pertaining to the availability of cheaper medication alternatives for patients and/or the National Institute for Health and Disability Insurance (NIHDI) (A.8) held the least significance for MR3 with the students' opinions diverging from this (p=0.007).

However, there was considerable variation in opinions regarding the other statements in this domain, as five of them had a p-value below 0.05. A notable difference was observed for statement A.3 that pertained to the use of literature (p<0.001). Participants with less MR3 experience, including KAVA and APA pharmacists and students, deemed it moderately important, while more experienced individuals considered it less important. Another difference between participants with varying levels of MR3 experience was noted for statement A.5 on the use of reliable tools. The student group considered this statement significantly less important (p<0.001), than the other three groups.

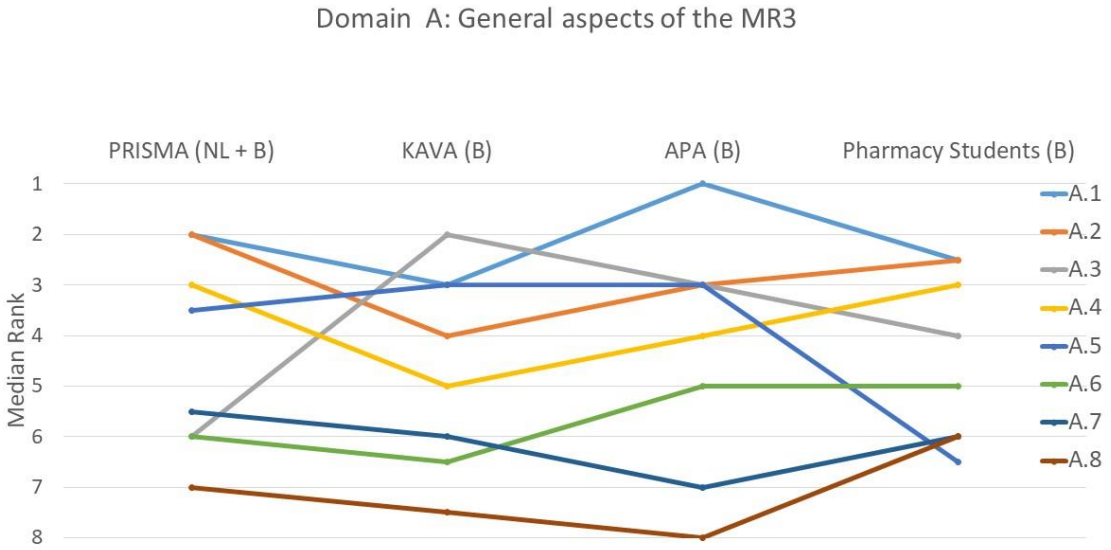

Figure 5.1: Ranking of the statements from domain A.

A.1 Pharmacists need to use simple and understandable language with their patients.
A.2 There was reporting and consultation with the attending physician.
A.3 Literature consulted and cited was scientific.
A.4 Discussion with the patient took place in a familiar and calm environment.
A.5 Reliable tools for conducting a MR were used. For example, GheOP³S (Ghent Older People's Prescriptions community Pharmacy Screening) (22), START/STOPP criteria (24), MAI (Medication Appropriateness Index) (23), etc.
A.6 Consideration was given to communicating non-pharmacological advice. For example, healthy diet, exercise, smoking cessation, etc.

A.7 Sufficient attention was given to non-drug substances (dietary supplements, herbal medicines and homeopathy) that the patient may be taking.

A.8 Availability of cheaper alternatives for patient and/or National Institute for Health and Disability Insurance (NIHDI) was considered (other drugs, other quantity/packaging).

5.5.2.2 Domain B: Consideration of patient characteristics, including living situation, resources and need for MR3

There was a strong consensus in domain B about the importance of statement B.1 (The usefulness and purpose of a MR3 was discussed with the patient), with 56% of participants ranking it first (p=0.427) (Figure 5.2). Similarly, statement B.5 that pertained to the consideration of addiction risk, was deemed less important by all groups (p=0.133) and ranked last by 60% of the individual participants. The remaining three statements all had a p-value greater than 0.05, suggesting a consensus among the participants.

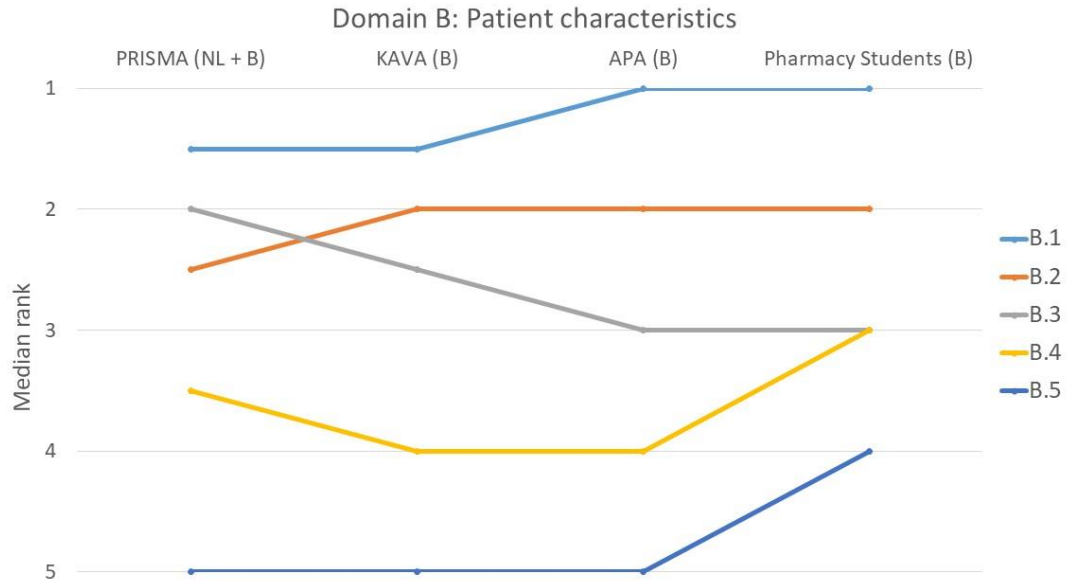

Figure 5.2: Ranking of the statements from domain B.

B.1 The usefulness and purpose of a MR was discussed with the patient.

B.2 Patient characteristics at risk for poor adherence were considered.

B.3 MR was tailored to the patient's living situation (informal carer).

B.4 Aids used by the patient to perform daily tasks were considered.

B.5 Risk of addiction was considered (e.g., by using a screening tool such as ORT (Opioid Risk Tool)).

5.5.2.3 Domain C: The patient's ability to easily take medication, open drug boxes and store medication under appropriate conditions

In this domain, 55% of participants rated statement C.1 addressing the pharmacist's consideration of the patient's ability to swallow medication as most important (p=0.103), while 51% regarded statement C.7 that addressed the patient's attitude towards injections as the least important (Figure 5.3). However, students partially dissented about this last statement and ranked it significantly higher than the other three groups (p=0.007). Regarding four other statements (C.2, C.3, C.5 and C.6), there was a consensus among the groups. These statements covered topics such as the ease of opening medication boxes, measuring out liquids, the use of medication boxes and the proper storage of patients' medicines.

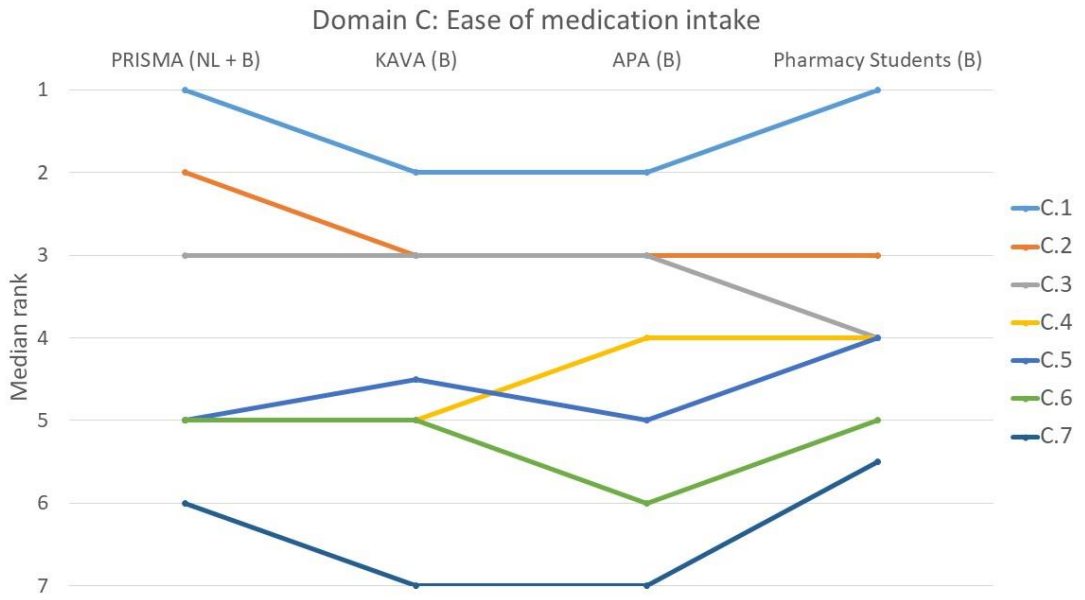

Figure 5.3: Ranking of the statements from domain C.

C.1 The pharmacist paid attention to whether the patient could swallow the drugs.
C.2 Pharmacist paid attention to whether the patient can open and close the drugs (including a box, twist-top and/or child-proof closure).
C.3 Consideration was given to whether the patient gets his/her drugs out of the blister.
C.4 Whether the patient can accurately measure out a liquid was considered.
C.5 Pharmacist paid attention to whether the medication could be put into medication boxes.
C.6 Proper storage conditions for drugs were discussed with the patient (not in a humid room such as kitchen, away from children, ...).
C.7 Patient's attitude towards injections was considered.

5.5.2.4 Domain D: The patient: follow-up, knowledge, instructions and adherence to therapy

When examining the aspects of follow-up, knowledge, instructions and adherence to therapy, statement D.1 that focused on discussing with the patient which drug was used for which condition, was ranked at the top by 44% of the participants (p=0.222) (Figure 5.4). Informing the patient about the correct way to take the drug (D.2) was also deemed important by the participants, with 45% ranking it as the most or second most important statement (p=0.210). All groups unanimously agreed that statement D.7, on whether the pharmacist ensured that the patient was aware of the expiration dates of their medications, was the least important (p=0.707). This was indicated by 76% of the participants. A borderline significant difference between groups was only observed for statement D.4 (p=0.048) that focused on the pharmacist's assessment of the patient's ability to understand instructions where PRISMA pharmacists, on average, ranked this slightly higher. Despite the presence of divergences, these were not substantial, as illustrated in the Figure.

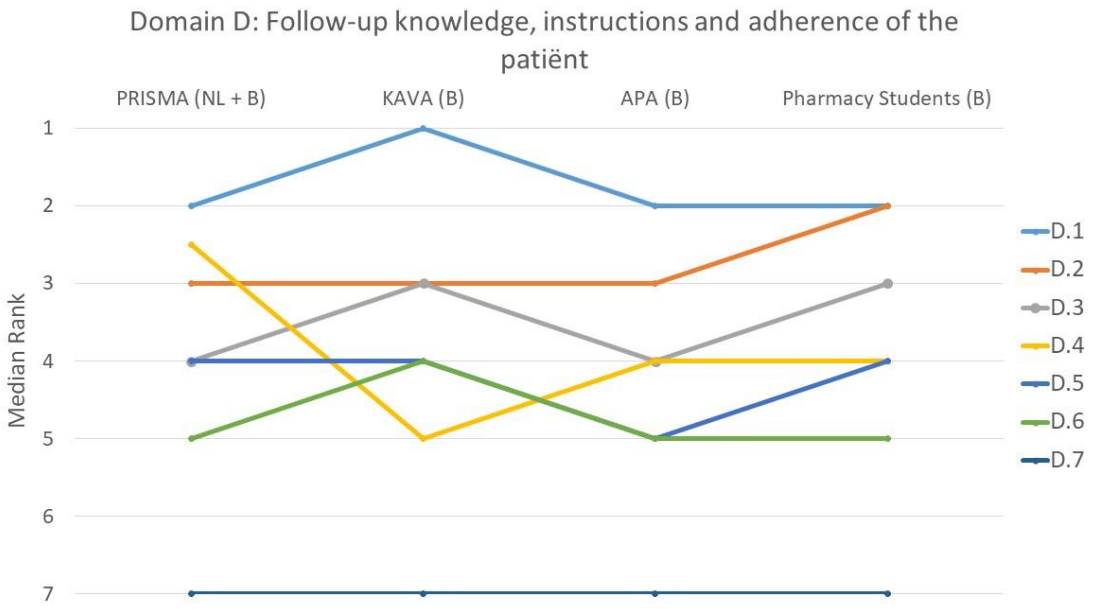

Figure 5.4: Ranking of the statements from domain D.

D.1 Which drugs was used for which condition was discussed with the patient.
D.2 Patient was informed about the correct way to take the drug.
D.3 Pharmacist paid attention to whether the patient knows the difference between regular drugs and drugs taken only when needed (prn (pro re nata) drugs).
D.4 Consideration was given to whether the patient could understand the instructions.
D.5 Patient compliance was assessed based on a comprehensive analysis of medication over a sufficient period of time.
D.6 Pharmacist paid attention to whether the patient can read instructions.
D.7 Pharmacist has paid attention to whether the patient knows when his/her drugs are past their expiry date.

5.5.2.5 Domain E: Current therapy: major drugs, missing drugs, evolution of therapy and vaccination status

The creation of an up-to-date and easily understandable medication schedule that was discussed with the patient (E.1), was deemed important by all four groups (p=0.075), with 54% of the participants ranking it as the most important statement within this domain (Figure 5.5). Statement E.8, on the evaluation of the patient's vaccination status, was considered the least important by 61% of the participants. However, students once again had a different opinion and considered this statement more important than the other three groups (p<0.001). There was also significant variation on whether the pharmacist paid attention to treating all conditions whenever necessary (E.4) with KAVA pharmacists perceiving this statement as relatively less important (p<0.001). Conversely, for statement E.7 that involved discussing changes to the patient's previous medication regimen with the patient, KAVA pharmacists rated this as more important than the other groups (p<0.001).

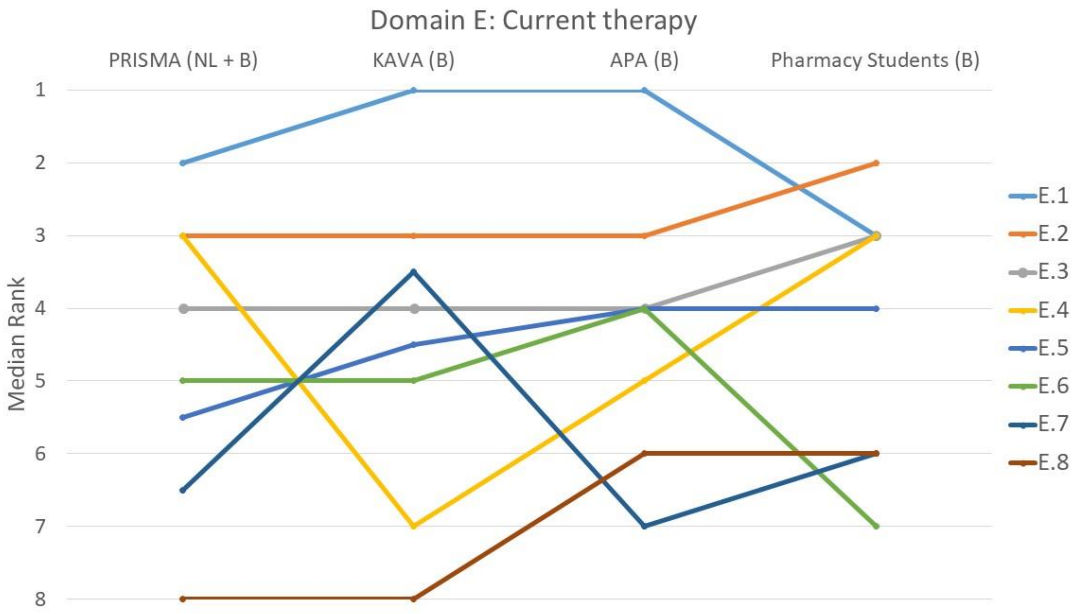

Figure 5.5: Ranking of the statements from domain E.

E.1 A recent and clear medication schedule was created and discussed with the patient.
E.2 Consideration was given to which medicines are particularly important for the treatment of the condition.
E.3 Pharmacist paid attention to medicines that were missing from the treatment for example, the need for stomach protection, laxatives and/or statins).
E.4 Pharmacist paid attention to whether all conditions were treated, if needed for these conditions.
E.5 Changes in previous medication use were critically reviewed (why stopped/adjusted?).
E.6 Appropriate guidelines were always consulted to evaluate treatment.
E.7 Changes to the patient's previous medication regimen were discussed with them.
E.8 Patient's vaccination status was evaluated.

5.5.2.6 Domain F: Assessment of medication use, including simplification, verification of current drug indications, evaluation of dose appropriateness, consideration of lab values and determination of goal achievement.

With consensus among the groups (p=0.835), 49% of participants considered statement F.1 that focused on the pharmacist's attention to the current relevance of all drug indications, to be the most important (Figure 5.6). Statement F.6 that focused on the gradual reduction of medications, was ranked lower by all groups (p=0.123). Statistically significant differences were observed among the four groups for three other statements. The student group ranked statement F.2 that pertained to the drug dosing appropriateness, higher compared to the other groups. In contrast, PRISMA pharmacists indicated that they considered this statement least important during a MR3 (p<0.001). Statement F.4 that involved considering all relevant parameters or lab values obtained from the (primary) physician, was regarded as less important by the students compared to the other groups (p=0.004). Furthermore, the discussion with the patient about why certain goals were or were not achieved (F.5) was deemed much more important by PRISMA pharmacists (p=0.032).

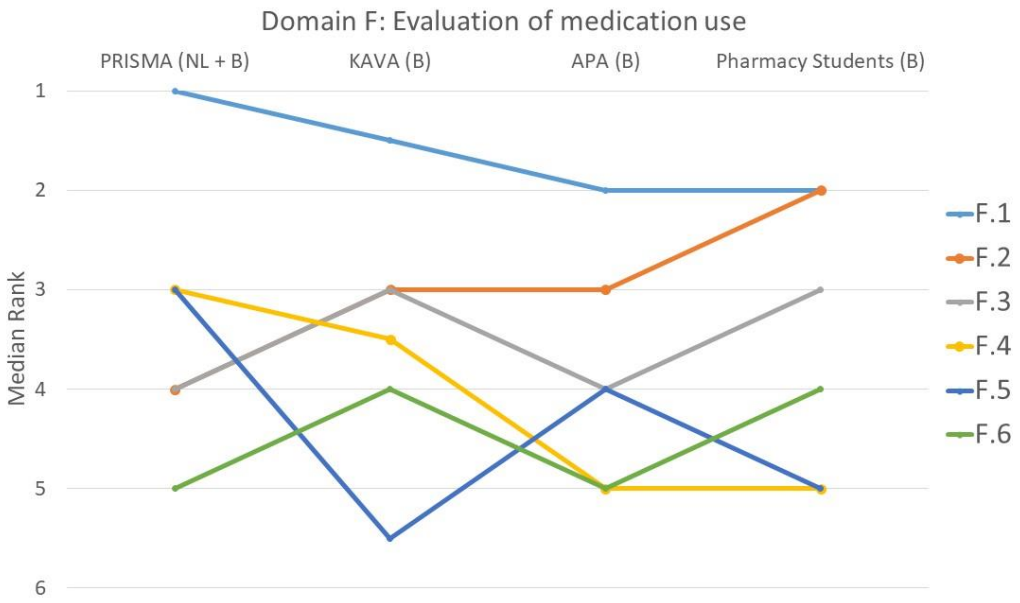

Figure 5.6: Ranking of the statements from domain F.

F.1 Pharmacist paid attention to whether all drug indications were still current.
F.2 Drug dose was assessed for appropriateness.
F.3 Efforts were made to simplify medication use.
F.4 All relevant parameters/lab values requested from the (primary) physician were considered.
F.5 A discussion was held with the patient about why certain goals were or were not achieved.
F.6 Attention was paid to tapering off the medications.

5.5.2.7 Domain G: Causes of adverse drug reactions, intolerances, interactions and their solutions

In domain G, the opportunity for patients to discuss their symptoms (G.1) with the pharmacist was ranked as top priority by 39% of participants (p=0.530) (Figure 5.7). On the other hand, the statement on whether the pharmacist handled QT-prolonging drugs was deemed the least important in domain G (G.9, p=0.150). One third of participants ranked this statement last or second-to-last. Significant differences between the groups were also observed in statement G.2 that involved the intake of drugs in relation to meals (p<0.001), and statement G.4 that addressed whether the symptoms mentioned by the patients could have been caused by the chronic or temporary use of drugs (p=0.002). PRISMA pharmacists considered G.2 to be less important, while ranking G.4 as more important compared to the other groups.

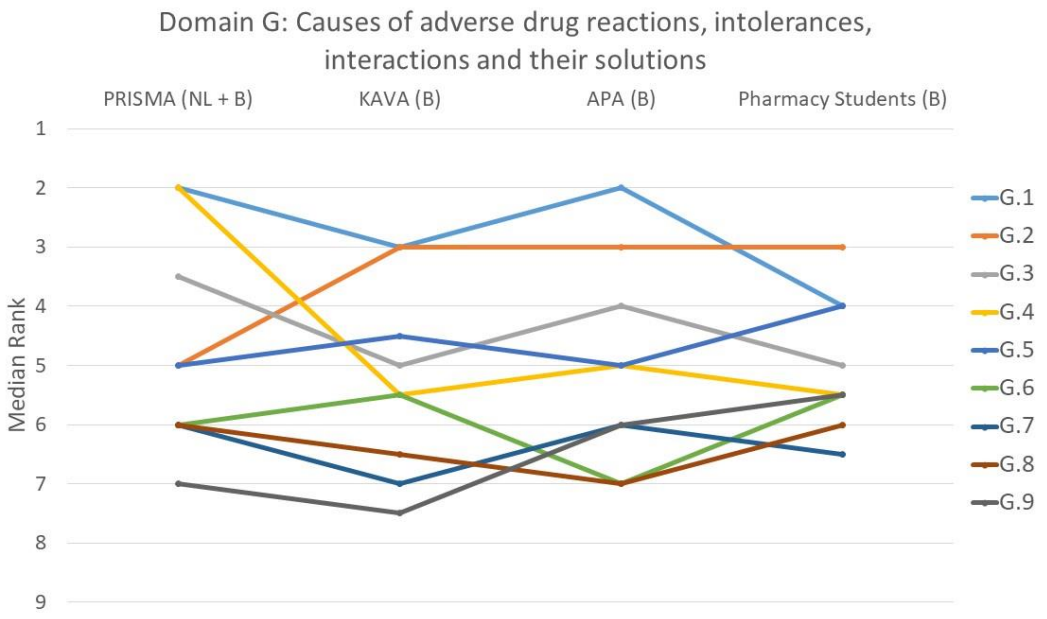

Figure 5.7: Ranking of the statements from domain G.

G.1 Patients were given the opportunity to discuss their illness symptoms with the pharmacist.
G.2 The patient was engaged in a discussion regarding the timing of drug intake in relation to nutrition, addressing possible interactions and considerations.
G.3 All drugs and their dose were matched to renal function.
G.4 During a thorough analysis of the symptoms cited, it was considered whether they could have been caused by the chronic or acute drugs.
G.5 Contraindications associated with the condition were identified and evaluated.
G.6 Relevant drug-drug interactions between all chronic and temporary drugs were checked and a concrete solution sought whenever necessary.
G.7 Pharmacist paid attention to the presence of drugs with central anticholinergic properties.
G.8 Patient allergies/intolerances were considered.
G.9 Pharmacist paid attention to the presence of QT-prolonging drugs.

5.5.2.8 Domain H: The new treatment plan: factors for drafting, implementation of adjustments and follow-up

The statement regarding whether patient expectations/concerns were considered during the development of the treatment plan (H.1) was deemed most important by 31% of participants (Figure 5.8). Notably, PRISMA pharmacists and pharmacy students demonstrated a tendency to perceive this statement as more important in comparison to the other two groups, although this difference did not reach statistical significance (p=0.388). On the other hand, the least important statement in this domain was H.7 (A detailed report contains reasoned arguments per recommended adjustment and was reported in writing to the physician), with 29% of participants ranking it at the lowest position (p=0.287). This opinion was mainly expressed by the student group with 57% of them ranking this statement last. Regarding statement H.4, on informing the patient in detail about which over-the-counter (OTC) drugs should no longer be used, there was a striking difference between the groups (p<0.001). PRISMA pharmacists considered it the least relevant topic, while KAVA pharmacists scored it a top priority. The other two groups ranked it somewhere in the middle.

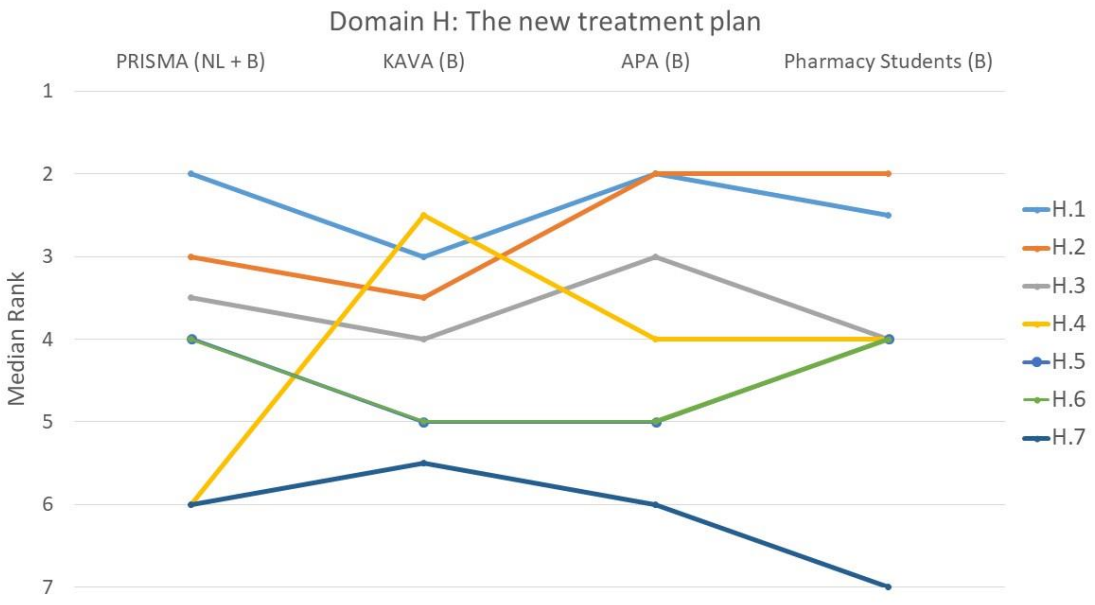

Figure 5.8: Ranking of the statements from domain H.

H.1 The patient's expectations and concerns were taken into account when developing the treatment plan
H.2 New treatment plan was discussed with the patient and the patient agreed to it.
H.3 Clear agreements were made with the patient regarding follow-up.
H.4 Patient was informed in detail which over-the-counter (OTC) drugs should no longer be used due to the presence of contraindications.
H.5 Clear agreements were made with the physician regarding follow-up.
H.6 Priorities in the treatment plan are clear.
H.7 Detailed report contains reasoned arguments per recommended adjustment and was reported in writing to the physician.

5.5.3 Global ranking: which of the domains covered do you think is most essential for evaluating a MR3?

When assessing the relative importance of the different domains, participants predominantly selected domain F (follow-up knowledge, instructions and adherence) as the most important (p=0.466): 42% ranked this domain within the top two (Figure 5.9). In contrast, domains G (causes of adverse drug reactions, intolerances and their solutions) and H (the new treatment plan) were considered the least important by participants. Around 54% of participants ranked domain H last or second-to-last (p=0.011), while for domain G this was 43% (p=0.148). In addition to domain H, domain A (general aspects of the medication review) also exhibited a statistically significant difference between the groups (p=0.011). KAVA pharmacists considered domain A to be much more important compared to the other participants. The remaining three domains, namely C (ease of medication intake), D (follow-up knowledge, instructions and adherence), and E (current therapy), received an average score in the rankings.

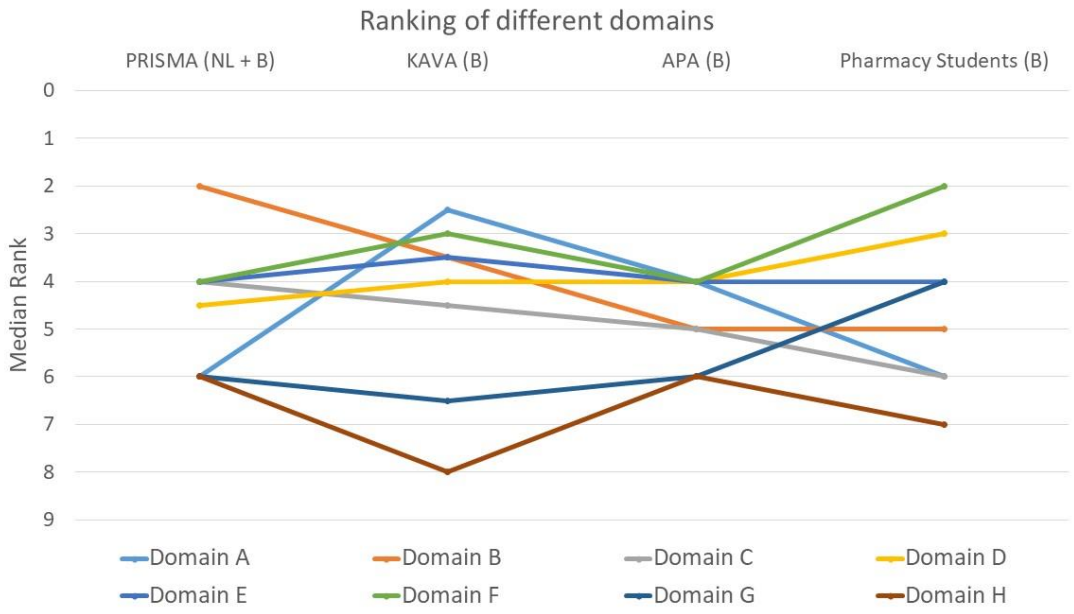

Figure 5.9: Ranking of the eight different domains.
Domain A: General aspects of the MR3
Domain B: Patient characteristics taking into account living situation, resources and need for MR3.
Domain C: Patient's ability: ease of taking, opening drugs and storage conditions.
Domain D: The patient: follow-up knowledge, instructions and adherence.
Domain E: Current therapy: major drugs, missing drugs, evolution of therapy and vaccination status.
Domain F: Evaluation of medication use: simplification, current drug indications, dose appropriateness, use of lab values and achievement of goals.
Domain G: Causes of adverse drug reactions, intolerances, interactions and their solutions.
Domain H: The new treatment plan: factors for drafting, implementation of adjustments and follow-up.

5.5.4 Feedback

A number of participants (11%) raised concerns about the ranking method employed, expressing a desire for statements to be grouped together and given equal importance in certain instances.

> *"The survey was very comprehensive but it was challenging to rank the items because everything appears to be significant in a medication review."*

> *"My overall feedback on this survey is that it is quite complicated (and seemingly unnuanced) in its design. I'm not sure how useful it is to make a qualitative distinction between many of these statements. I also feel that the format pushed me in a certain direction, so I couldn't answer honestly or clearly."*

Additional feedback highlighted the components that should be included during each drug dispensing and medication review (MR3). In this context, participants mentioned an ideal scenario where aspects such as adherence and challenges with swallowing are assessed during each pharmacy visit, and a review is conducted to determine if there is still a valid indication for each medication.

> *"I think certain basic matters such as drug-drug interactions should already have been checked when a medicine is newly dispensed. That's why I ranked these types of checks relatively lower. However, that doesn't mean they are not important."*

A recurring theme in the comments was the importance of engaging in a conversation with the patient and valuing their input. Four participants emphasized that this dialogue and the patient's expressed goals should serve as the foundation for the quality of a MR3.

> *"The pharmacotherapy anamnesis with the patient serves as the cornerstone of every MR, as well as for subsequent analysis and treatment planning."*
>
> *"In a MR, it is important to prioritize the patient's personal goals as much as possible. "*

Additionally, there were inquiries regarding time allocation and remuneration.

> *"Time (and remuneration for it) is not mentioned anywhere, but if anything, it is one of the most decisive factors for doing a MR or not."*

Finally, a participant from the APA group highlighted the significance of the pharmacist's overall knowledge when conducting a MR3.

> *"I believe that a good MR is built on the foundation of a pharmacist's sound basic knowledge. Tools can provide support, but they have little value if the pharmacist lacks understanding what it is all about. In a conversation with physicians, such a lack of knowledge by pharmacists is readily uncovered."*

5.5.5 Missing statements

Participants highlighted several crucial factors related to MR3 that were missing. Primarily, there were lingering uncertainties about the appropriate method of patient selection, specifically on how to select patients for whom MR3 is most pertinent. Furthermore, there was a comment to identify patients' needs concerning MR3, as well as a request to also address aspects of evaluation and monitoring of MR3s, how changes are managed and who is responsible for the evaluation.

> *"I am missing the comprehensive assessment of the patient's needs to be the subject of a MR."*
>
> *"Evaluation and monitoring, how are the changes going? Who is evaluating this? Does anything need to be adjusted in the treatment plan? Evaluate drugs that may not be effective for certain symptoms? Etc"*

5.6 Discussion

5.6.1 Main findings

The objective of this work was to provide a basis for the key elements of a quality assessment of a MR3. Despite the challenges faced by some participants in ranking the statements (see Feedback and missing statements from the participants), there was a remarkable consensus among the various participant groups in general. This consensus enabled us to identify a statement for each domain that was either partially or fully ranked as the most important across all groups. In 7 out of the 8 (A.1-H.1) statements considered to be of utmost importance, no significant differences were observed between the groups. However, there was one notable exception with divergent opinions about statement C.1 that addressed whether the pharmacist paid attention to whether the patient swallowed the drugs. Even for the statements with the lowest scores, there were substantial similarities between the groups, as 5 out of the 8 statements (A.8, B.5, C.7, D.7, E.8, F.6, G.9 and H.7) did not show any statistically significant difference. Notably, significant differences emerged among the groups for three specific statements: whether patients were asked about the availability of a cheaper alternative (A.8), whether their attitude toward injections was taken into account (C.7), and whether the patient's vaccination status was evaluated (E.8).

Participants gave high ratings to statements that emphasized the significance of ensuring that patients can easily understand medication reviews. This involved using straightforward and easy-to-understand

language when talking to patients (A.1), as well as giving clear, personalized explanations about the benefits and goals of MR3s (B.1). Past investigations have revealed that patients are not always properly informed about the goals or procedures of MR3 (28). This situation is acknowledged by most respondents, endorsing the approach used to determine crucial elements that demand attention in the continued implementation and quality monitoring of this pharmaceutical care service.

Differences in opinion between groups

Some divergences were detected in the opinions expressed by the different groups of participants, specifically, PRISMA pharmacists and students demonstrated contrasting rankings on six statements, while KAVA pharmacists showed differences on three statements. However, no significant outliers were identified among APA pharmacists.

Students versus other groups

The importance of using tools was given less significance by the students compared to the other groups (A.5). It is possible that this group either lacks sufficient experience with these tools or, conversely, believes that they possess enough knowledge, making their use redundant. However, none of the groups made the use of these tools a priority as they do not guarantee quality and can lead to differing outcomes, be outdated, or be used incorrectly (29). When it comes to ranking, the students gave significantly lower ratings to the report and communication with the physician compared to the other groups (statement H.7). It should be noted that the average student has limited practical experience with MR3s, which may hinder their understanding of the entire process.

The students also assigned a lower ranking to statement (F.4) regarding laboratory values and other parameters provided by the primary physician. The greater availability of data in the Netherlands (Koster et al., 2016) compared to Belgium easily explains the higher ranking given by Dutch pharmacists.

PRISMA pharmacists versus other groups

The importance of discussing the timing of drug intake in relation to nutrition, including drug-food interactions, (G.2), was ranked lower by the PRISMA pharmacists. Feedback revealed that Dutch pharmacists may consider this to be part of regular dispensing rather than something specific to MR3s. PRISMA pharmacists, in contrast to all their Belgian counterparts, gave less weight to the importance of OTC drug use (H.4). PRISMA pharmacists have less data available on the use of OTC drugs by their patients, as these are also available outside pharmacies in the Netherlands (30) in contrast to Belgium, and where there is a centralized database that includes OTC drugs (31).

In addition, the PRISMA group also prioritized addressing their patients' needs more than other groups. This focus on patient-centred care was reflected in their higher rankings for statements such as assessing the patient's understanding of instructions (D.4), and emphasis on the importance of personal goals (F.5), quality of life, and addressing individualised health problems in the medication management process. (32, 33). Finally, PRISMA pharmacists gave a higher ranking to statement G.4 that involved performing a thorough analysis of the patient's reported symptoms and assessing the likelihood that they were caused by medication use.

Feedback and missing statements from the participants

Several participants expressed difficulties with the ranking form, citing an inability to assign different statements with the same level of importance. While we understand and empathize with these emotions and worries, in our quest for an overarching ranking, these individual divisions hold no substantial importance. There are antecedents in the literature of the methodological advantages of enforcing a strict ranking without allowing for ties (34-36).

Moreover, the substance of specific statements also met with some opposition. Four participants believed that certain statements, for example about drug-drug interactions, should be implemented and assessed during each pharmacy visit, rather than being discussed specifically within the context of a MR3. Nonetheless, these statements were included in the questionnaire, as there may be situations where specific aspects are overlooked for a range of reasons such as the occurrence of multiple prescribers, frequent hospital visits or dispensing in multiple pharmacies. Overall, the ranking may therefore reflect the participants' opinion on the benefits of additional monitoring of the patient's pharmacotherapy during the MR3 process.

Some additional criteria were provided by the participants. One suggestion involved adding a statement about follow-up interviews with the patients. Although this concept was partially covered by statements H.5 and H.6, the explicit mention of conducting follow-up interviews and follow-up adjustments of the treatment plan was absent. Another participant highlighted the importance of relevant patient selection, emphasizing the need for pharmacists to assess and document whether a patient truly requires a MR3 before initiating the process.

Furthermore, participants raised important points regarding the necessity of comprehensive knowledge about pharmacotherapy, the attentiveness to the personal goals of the patients, and the patient's readiness to participate in the MR3. These factors were also deemed crucial in ensuring the quality of MR3s.

5.6.2 Similarities and differences in relationship to other studies

There are a small number of studies within the current literature that focus on the quality of MR (5, 7, 9, 11-16, 37). We observed a recent increase that coincided with the timing of our survey administration. However, our literature analysis identified divergent interpretations and definitions of MR, making it challenging to compare and synthesize findings across studies, as previously observed by others (8, 20).

Only one study focused on the implementation of MRs by pharmacists in primary care (Mestres Gonzalvo et al., 2014). The objective of this specific study was to determine pertinent covariates, conducted by a research group comprising 49 participants with expertise in MR. These covariates were rated on a 10-point scale. Our study, which reviewed 57 statements, expanded on Mestres Gonzalvo's methods and participant selection, providing a broader and more detailed perspective on MR components. This comprehensive analysis provided an even broader and more detailed perspective on the various components involved in a MR.

5.6.3 Strengths and limitations of the study

One strength of this study is that despite the diverse backgrounds of the participants, there was a high level of agreement on what are the key elements that define the quality of a MR3. While some differences emerged, they could readily be explained by the participants' varying backgrounds and local contexts. Moreover, the small number of additional topics recommended for inclusion in the list of criteria serves as validation for the questionnaire's design process. The study also gained from employing a drag-and-drop

method for statement ranking, which yielded unambiguous rankings even though it posed a challenge for some participants.

This study also had some limitations, such as the relatively small sample sizes of the four participant groups and its narrow geographic scope, which may impact the generalizability of the findings. As highlighted by certain participants, this study did not encompass aspects of patient selection methods, medication review costs nor its reimbursement, while aspects regarding the MR3 follow-up process may have been evaluated too superficially. Another bias may stem from the differences in professional experience with MRs between the different groups, which could imply that those with more experience have a more practical and realistic view on the subject. Finally, there may have been an apparent bias among those without an interest in MRs because they would have been less inclined to participate in our survey.

Additionally, some of the key elements deemed important to evaluate quality of a MR3 may pose implementation challenges. Statement A1, emphasizing the importance of pharmacist-patient communication, is widely considered crucial, but the implementation of assessing it poses significant challenges. Furthermore, a list of key quality evaluation criteria necessitates ongoing maintenance and regular updates to keep pace with evolving knowledge and practices.

5.6.4 Open questions and future research

The quantitatively ranked statements from this study can function as key elements of MR3 quality standards and be tested and implemented in diverse settings like self-assessment, peer evaluation, or external audit. Instead of using the full list of criteria for auditing, which can be time-consuming, this study suggests an alternative approach where a random subset of criteria is used, with their frequency weighted according to the rankings from the survey. This approach could improve the efficiency of the auditing process while preventing reactive subversion.

5.7 Conclusion

This study revealed a broad consensus regarding the key elements for assessing the quality of a MR3. There was substantial agreement among the four participant groups about the statements deemed most important within each domain. Eight key statements emerged as essential components that should be included in a comprehensive MR3. These statements encompassed aspects such as [1] using understandable language, [2] explaining the purpose of the review to the patient, [3] addressing the patient's ability to take medications correctly, [4] discussing the appropriate use of each drug for specific conditions, [5] creating and reviewing a recent and clear medication schedule with the patient, [6] evaluating the ongoing relevance of all drug indications, [7] providing an opportunity for patients to discuss their symptoms with the pharmacist, and [8] considering the patient's expectations and concerns when developing the treatment plan. Some minor differences were observed, related to the participants' level of experience. In light of the study’s findings and the additional criteria proposed by the participants, the next step is to develop a quality instrument for medication reviews that is both efficient and effective.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

A.R., G.R.Y.D.M. and H.D.L. designed the experiment, M.M. carried out the survey and preliminary data analysis. A.R. carried out the final data analysis and wrote the manuscript with support from H.D.L., S.S. and G.R.Y.D.M.

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Data Availability Statement

The datasets generated for this study can be found in the [figshare] repository with the identifier [DOI https://doi.org/10.6084/m9.figshare.23681166].

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5.9 Appendix

Appendix 5.1 Online survey (translated version)

Personal questions

- What is your age?
- What is your nationality?
- What is your job title?
- How many years of pharmacy experience do you have?
- How many medication reviews type 3 have you conducted in practice?

Ranking questions: rank the statements by domain.

Domain A. Ranking of the statements from domain A by the four groups.

A.1 Pharmacists need to use simple and understandable language with their patients.
A.2 There was reporting and consultation with the attending physician.
A.3 Literature consulted and cited was scientific.
A.4 Discussion with the patient took place in a familiar and calm environment.
A.5 Reliable tools for conducting a MR were used. For example, GheOP³S (Ghent Older People's Prescriptions community Pharmacy Screening), START/STOPP criteria, MAI (Medication Appropriateness Index), etc. (22-24)
A.6 Consideration was given to communicating non-pharmacological advice. For example, healthy diet, exercise, smoking cessation, etc.
A.7 Sufficient attention was given to non-drug substances (dietary supplements, herbal medicines and homeopathy) that the patient may be taking.
A.8 Availability of cheaper alternatives for patient and/or National Institute for Health and Disability Insurance (NIHDI) was considered (other drugs, other quantity/packaging).

Domain B. Ranking of the statements from domain B by the four groups.

B.1 The usefulness and purpose of a MR was discussed with the patient.
B.2 Patient characteristics at risk for poor adherence were considered.
B.3 MR was tailored to the patient's living situation (informal carer).
B.4 Aids used by the patient to perform daily tasks were considered.
B.5 Risk of addiction was considered (e.g., by using a screening tool such as ORT (Opioid Risk Tool)).

Domain C. Ranking of the statements from domain C by the four groups.

C.1 The pharmacist paid attention to whether the patient could swallow the drugs.
C.2 Pharmacist paid attention to whether the patient can open and close the drugs (including a box, twist-top and/or child-proof closure).
C.3 Consideration was given to whether the patient gets his/her drugs out of the blister.
C.4 Whether the patient can accurately measure out a liquid was considered.
C.5 Pharmacist paid attention to whether the medication could be put into medication boxes.
C.6 Proper storage conditions for drugs were discussed with the patient (not in a humid room such as kitchen, away from children, ...).
C.7 Patient's attitude towards injections was considered.

Domain D. Ranking of the statements from domain D by the four groups.

D.1 Which drugs was used for which condition was discussed with the patient.
D.2 Patient was informed about the correct way to take the drug.
D.3 Pharmacist paid attention to whether the patient knows the difference between regular drugs and drugs taken only when needed (prn (pro re nata) drugs).
D.4 Consideration was given to whether the patient could understand the instructions.

D.5 Patient compliance was assessed based on a comprehensive analysis of medication over a sufficient period of time.
D.6 Pharmacist paid attention to whether the patient can read instructions.
D.7 Pharmacist has paid attention to whether the patient knows when his/her drugs are past their expiry date.

Domain E. Ranking of the statements from domain E by the four groups.
E.1 A recent and clear medication schedule was created and discussed with the patient.
E.2 Consideration was given to which medicines are particularly important for the treatment of the condition.
E.3 Pharmacist paid attention to medicines that were missing from the treatment for example, the need for stomach protection, laxatives and/or statins).
E.4 Pharmacist paid attention to whether all conditions were treated, if needed for these conditions.
E.5 Changes in previous medication use were critically reviewed (why stopped/adjusted?).
E.6 Appropriate guidelines were always consulted to evaluate treatment.
E.7 Changes to the patient's previous medication regimen were discussed with them.
E.8 Patient's vaccination status was evaluated.

Domain F. Ranking of the statements from domain F by the four groups.
F.1 Pharmacist paid attention to whether all drug indications were still current.
F.2 Drug dose was assessed for appropriateness.
F.3 Efforts were made to simplify medication use.
F.4 All relevant parameters/lab values requested from the (primary) physician were considered.
F.5 A discussion was held with the patient about why certain goals were or were not achieved.
F.6 Attention was paid to tapering off the medications.

Domain G. Ranking of the statements from domain G by the four groups.
G.1 Patients were given the opportunity to discuss their illness symptoms with the pharmacist.
G.2 The patient was engaged in a discussion regarding the timing of drug intake in relation to nutrition, addressing possible interactions and considerations.
G.3 All drugs and their dose were matched to renal function.
G.4 During a thorough analysis of the symptoms cited, it was considered whether they could have been caused by the chronic or acute drugs.
G.5 Contraindications associated with the condition were identified and evaluated.
G.6 Relevant drug-drug interactions between all chronic and temporary drugs were checked and a concrete solution sought whenever necessary.
G.7 Pharmacist paid attention to the presence of drugs with central anticholinergic properties.
G.8 Patient allergies/intolerances were considered.
G.9 Pharmacist paid attention to the presence of QT-prolonging drugs.

Domain H. Ranking of the statements from domain H by the four groups.
H.1 The patient's expectations and concerns were taken into account when developing the treatment plan
H.2 New treatment plan was discussed with the patient and the patient agreed to it.
H.3 Clear agreements were made with the patient regarding follow-up.
H.4 Patient was informed in detail which over-the-counter (OTC) drugs should no longer be used due to the presence of contraindications.
H.5 Clear agreements were made with the physician regarding follow-up.
H.6 Priorities in the treatment plan are clear.
H.7 Detailed report contains reasoned arguments per recommended adjustment and was reported in writing to the physician.

Global ranking: Ranking of the eight different domains by the four groups.
Domain A: General aspects of the MR3

Domain B: Patient characteristics taking into account living situation, resources and need for MR3.
Domain C: Patient's ability: ease of taking, opening drugs and storage conditions.
Domain D: The patient: follow-up knowledge, instructions and adherence.
Domain E: Current therapy: major drugs, missing drugs, evolution of therapy and vaccination status.
Domain F: Evaluation of medication use: simplification, current drug indications, dose appropriateness, use of lab values and achievement of goals.
Domain G: Causes of adverse drug reactions, intolerances, interactions and their solutions.
Domain H: The new treatment plan: factors for drafting, implementation of adjustments and follow-up.

Final questions

- Do you have any essential questions or statements you did not find in this questionnaire?
- Do you have any comments or suggestions?

Appendix 5.2 Online survey (original version)

Persoonlijke gegevens

- Wat is uw leeftijd?
- Wat is uw nationaliteit?
- Wat is uw functie?
- Hoeveel jaren ervaring heeft u in de apotheek?
- Hoeveel medication reviews type 3 hebt u al in de praktijk uitgevoerd?

Rangschikkingsvragen: rangschik de stellingen per onderdeel.

Onderdeel 1: Algemene aspecten van de MR: voorbereiding, taalgebruik, aandacht voor niet-farmacologische middelen, advies en rapportering

Stelling 1.1 De apotheker gebruikt eenvoudige en begrijpbare taal met de patiënt.
Stelling 1.2 Er was rapportering en overleg met de behandelende arts.
Stelling 1.3 De geraadpleegde en geciteerde literatuur was wetenschappelijk.
Stelling 1.4 Het gesprek met de patiënt vond plaats in een vertrouwde en rustige omgeving.
Stelling 1.5 Er werd gebruik gemaakt van betrouwbare tools voor het uitvoeren van een MR. Bijvoorbeeld GheOP³S, START/STOPP-criteria, MAI, etc.
Stelling 1.6 Er werd voldoende aandacht geschonken aan niet-geneesmiddelen (voedingssupplementen, kruidengeneesmiddelen en homeopathie) die de patiënt mogelijks gebruikt.
Stelling 1.7 De beschikbaarheid van goedkopere alternatieven voor patiënt en/of RIZIV werd bekeken (Ander GM, andere hoeveelheid/verpakking).
Stelling 1.8 Er werd aandacht besteed aan het communiceren van niet-farmacologisch advies. Bijvoorbeeld gezonde voeding, lichaamsbeweging, rookstop etc.

Onderdeel 2: De patiënteigenschappen rekening houdend met de leefsituatie, hulpmiddelen en de nood aan een MR.

Stelling 2.1 De MR werd afgestemd op de leefsituatie (mantelzorger) van de patiënt.
Stelling 2.2 Er werd gekeken welke hulpmiddelen voor het uitvoeren van dagdagelijkse taken de patiënt gebruikt.
Stelling 2.3 Er is met de patiënt gesproken over het nut en doel van een MR.
Stelling 2.4 Er werd rekening gehouden met het risico op verslaving (bijvoorbeeld door gebruik van een screeningtool zoals ORT).
Stelling 2.5 Er werd rekening gehouden met de patiënteigenschappen die een risico vormen voor gebrekkige therapietrouw.

Onderdeel 3: Het kunnen van de patiënt: het gemak van inname, openen van medicatie en bewaarcondities

Stelling 3.1 De apotheker heeft erop gelet of de patiënt de medicatie kan openen en sluiten. (o.a een doos, draaidop en/of kindveilige sluiting)
Stelling 3.2 De apotheker heeft erop gelet of de patiënt de medicatie kan slikken.
Stelling 3.3 Er werd rekening mee gehouden of de patiënt zijn/haar medicatie uit de blister krijgt.
Stelling 3.4 Er werd rekening mee gehouden of de patiënt nauwkeurig een vloeistof kan afmeten.
Stelling 3.5 De apotheker heeft gelet of de medicatie in medicatiedoosjes gestopt kan worden.
Stelling 3.6 De juiste bewaarcondities voor geneesmiddelen werden samen met de patiënt besproken. (Niet in een vochtige kamer zoals keuken, weg van kinderen, …)
Stelling 3.7 Er werd rekening gehouden met hoe de patiënt tegenover injecties staat.

Onderdeel 4: De patiënt: opvolging kennis, instructies en therapietrouw

Stelling 4.1 De apotheker heeft erop gelet of de patiënt weet wanneer zijn/haar medicatie de vervaldatum overschrijdt.
Stelling 4.2 De apotheker heeft erop gelet of de patiënt de instructies kan lezen.
Stelling 4.3 Er werd rekening gehouden of de patiënt de instructies kan begrijpen.
Stelling 4.4 De apotheker heeft gelet of de patiënt het verschil kent tussen gewone medicatie en medicatie enkel genomen bij nood (prn medicatie).
Stelling 4.5 De therapietrouw van de patiënt werd beoordeeld ahv een uitgebreide analyse van de medicatie over een voldoende lange periode.
Stelling 4.6 Er is met de patiënt overlopen welk geneesmiddel voor welke aandoening gebruikt wordt.
Stelling 4.7 De patiënt werd ingelicht over de juiste innamewijze van de medicatie.

Onderdeel 5: De huidige therapie: belangrijke geneesmiddelen, ontbrekende geneesmiddelen, evolutie van de therapie en vaccinatiestatus.

Stelling 5.1 De apotheker heeft gelet of alle aandoeningen behandeld worden, indien het voor deze aandoeningen nodig is.
Stelling 5.2 Er werden steeds gepaste richtlijnen geraadpleegd voor de behandeling te evalueren.
Stelling 5.3 De wijzigingen in voorgaand geneesmiddelengebruik werden kritisch bekeken. (Waarom gestopt/aangepast?)
Stelling 5.4 Er werd een recent en overzichtelijk medicatieschema aangemaakt en besproken met de patiënt.
Stelling 5.5 Er werd rekening gehouden met welke geneesmiddelen zeer belangrijk zijn voor de behandeling van de aandoening.
Stelling 5.6 De apotheker heeft gelet op geneesmiddelen die ontbraken in de behandeling. (Bijvoorbeeld de nood aan maagbescherming, laxativa en/of statines.)
Stelling 5.7 Het vaccinatiestatus van de patiënt werd geëvalueerd.
Stelling 5.8 Veranderingen in de therapie in het verleden werden besproken met de patiënt.

Onderdeel 6: Evaluatie geneesmiddelgebruik: vereenvoudiging, actuele geneesmiddelindicaties, dosiscontrole, het gebruik van labo-waarden en het bereiken van doelstellingen

Stelling 6.1 De apotheker heeft gelet of alle geneesmiddelindicaties nog actueel zijn.
Stelling 6.2 Er werd gelet op het afbouwen van de geneesmiddelen.
Stelling 6.3 Er werden inspanningen geleverd om het medicatiegebruik te vereenvoudigen.
Stelling 6.4 De dosis van de verschillende geneesmiddelen werd gecontroleerd.
Stelling 6.5 Er werd rekening gehouden met alle relevante parameters/labo-waarden die werden opgevraagd bij de (huis)arts.
Stelling 6.6 Met de patiënt werd een gesprek gevoerd over waarom bepaalde doelen wel of niet bereikt werden.

Onderdeel 7: Oorzaken van adverse drug reactions, intoleranties, interacties en hun oplossingen

Stelling 7.1 De patiënt kreeg de kans zijn ziekteklachten te bespreken met de apotheker.

Stelling 7.2 Tijdens een grondige analyse van de aangehaalde symptomen, werd er bekeken of deze veroorzaakt kunnen zijn door de chronische of tijdelijke medicatie.
Stelling 7.3 Er werd gecontroleerd op relevante GM-GM-interacties tussen alle chronische en tijdelijke medicatie en gezocht naar een concrete oplossing.
Stelling 7.4 Het innamemoment van medicatie ten opzichte van voeding werd besproken met de patiënt. (Met of zonder voeding, interacties etc.)
Stelling 7.5 Alle GM en hun dosis werden naar de nierfunctie afgestemd.
Stelling 7.6 De contra-indicaties geassocieerd met de aandoening werden geïdentificeerd en geëvalueerd.
Stelling 7.7 De apotheker heeft gelet op de aanwezigheid van qt-verlengende geneesmiddelen.
Stelling 7.8 De apotheker heeft gelet op de aanwezigheid van geneesmiddelen met centraal anticholinerge eigenschappen.
Stelling 7.9 Er werd rekening gehouden met allergieën/intoleranties van de patiënt.

Onderdeel 8: Het nieuwe behandelplan: factoren voor het opstellen, het uitvoeren van de aanpassingen en de opvolging.

Stelling 8.1 Bij het opstellen van het plan werd er rekening gehouden met de verwachtingen/bekommernissen van de patiënt.
Stelling 8.2 De patiënt werd gedetailleerd ingelicht over welke GM-klassen deze niet meer (OTC) mag gebruiken door de aanwezigheid van contra-indicaties.
Stelling 8.3 Het gedetailleerd verslag bevat onderbouwde argumenten per aanbevolen aanpassing en werd schriftelijk gerapporteerd naar de arts.
Stelling 8.4 Er werden duidelijke afspraken gemaakt met de arts ivm de opvolging hiervan.
Stelling 8.5 Er werden duidelijke afspraken gemaakt met de patiënt ivm de opvolging hiervan.
Stelling 8.6 In het behandelplan zijn de prioriteiten duidelijk aanwezig.
Stelling 8.7 Het nieuwe behandelplan werd met de patiënt besproken en deze gaat hiermee akkoord.

Onderdeel 9: Welk van de gebruikte onderdelen vindt u het meest essentieel voor de evaluatie van de MR?

Deel 1: Algemene aspecten van de MR: voorbereiding, taalgebruik, aandacht voor niet-farmacologische middelen, advies en rapportering
Deel 2: De patiënteigenschappen rekening houdend met de leefsituatie, hulpmiddelen en de nood van een MR.
Deel 3: Het kunnen van de patiënt: het gemak van inname, openen van medicatie en bewaarcondities.
Deel 4: De patiënt: opvolging kennis, instructies en therapietrouw
Deel 5: De huidige therapie: belangrijke geneesmiddelen, ontbrekende geneesmiddelen, evolutie van de therapie en vaccinatiestatus.
Deel 6: Evaluatie geneesmiddelgebruik: vereenvoudiging, actuele geneesmiddelindicaties, dosiscontrole, het gebruik van labo-waarden en het bereiken van doelstellingen
Deel 7: Oorzaken van adverse drug reactions, intoleranties, interacties en hun oplossingen
Deel 8: Het nieuwe behandelplan: factoren voor het opstellen, het uitvoeren van de aanpassingen en de opvolging.

Finale vragen

- Hebt u nog essentiële vragen of stellingen die u niet terugvond in deze vragenlijst?
- Heeft u nog opmerkingen of suggesties?

Appendix 5.3 Interquartile range and median for each statement for each group

	PRISMA (NL + B)		KAVA (B)		APA (B)		Pharmacy students (B)	
	Median	Interquartile Range	Median	Interquartile Range	Median	Interquartile Range	Median	Interquartile Range
A.1	2	2	3	2	1	3	2.5	3
A.2	2	2	4	4	3	2	3	3
A.3	6	3	2	3	3	4	4	5
A.4	3	3	5	4	4	5	3	4
A.5	3.5	3	3	3	3	3	6.5	1
A.6	6	1	6.5	2	5	2	5	2
A.7	5.5	3	6	2	7	1	6	4
A.8	7	1	7.5	3	8	2	6	2
B.1	1.5	2	1.5	2	1	1	1.5	3
B.2	2.5	1	2	1	2	1	2	2
B.3	2	3	2.5	2	3	1	3	2
B.4	3.5	1	4	1	4	2	3	3

B.5	5	1	5	2	5	1	4	2
C.1	1	1	2	2	2	2	1	1
C.2	2	2	3	2	3	4	3	4
C.3	3	2	3	2	3	2	4	3
C.4	5	2	5	2	4	3	4	2
C.5	5	2	4.5	3	5	3	5.5	4
C.6	5	2	5	4	6	4	5	3
C.7	6	2	7	0	7	2	5.5	2
D.1	2	2	1	2	2	3	2	1
D.2	3	3	2.5	2	3	1	2	2
D.3	4	2	3	3	4	2	3.5	4
D.4	2.5	3	4.5	2	4	4	4	3
D.5	4	2	5	3	5	2	4	3
D.6	5	2	4.5	2	5	3	5	2
D.7	7	0	7	1	7	0	7	1

E.1	2	4	1	1	1	2	3	5
E.2	3	1	3	3	3	2	2	3
E.3	4	2	4	4	4	2	3	2
E.4	3	2	7	4	5	4	3.5	4
E.5	5.5	2	4.5	3	4	5	4	3
E.6	5	3	5	4	4	4	6.5	3
E.7	6.5	2	3.5	3	7	2	6	3
E.8	8	0	8	1	6	3	6	3
F.1	1	2	1.5	2	2	2	2	2
F.2	4	3	3	2	3	1	2	2
F.3	4	3	3	3	4	2	3	2
F.4	3	2	3.5	4	5	2	5	2
F.5	3	3	5.5	5	4	4	5.5	2
F.6	5	3	4	1	5	2	4	1

G.1	2	5	3	4	2	7	4	4
G.2	5	3	3	4	3	2	3	2
G.3	3.5	3	5	4	4	4	5	5
G.4	2	2	5.5	5	5	5	5.5	3
G.5	5	4	4.5	6	5	4	4	7
G.6	6	5	5.5	6	7	6	5.5	4
G.7	6	3	7	4	6	2	6.5	3
G.8	6	4	6.5	4	7	5	6	5
G.9	7	2	7.5	6	6	2	5.5	4
H.1	2	2	3	3	2	3	2.5	3
H.2	3	4	3.5	4	2	2	2	4
H.3	3.5	3	4	2	3	3	4	3
H.4	6	3	2.5	2	4	2	4	3
H.5	4	2	5	4	5	2	4	2
H.6	4	3	5	3	5	4	4	3
H.7	6	3	5.5	4	6	4	7	2

DOMAIN A	6	5	2.5	4	4	5	6	4
DOMAIN B	2	4	3.5	3	5	4	5	6
DOMAIN C	4	3	4.5	2	5	4	6	4
DOMAIN D	4.5	2	4	3	4	3	3	3
DOMAIN E	4	4	3.5	3	4	3	4	2
DOMAIN F	4	3	3	4	4	5	2	3
DOMAIN G	6	4	6.5	3	6	4	4	3
DOMAIN H	6	6	8	1	6	5	7	2

Chapter 6: Use of BRANT-MERQS scoring table for the quality assessment of type 3 medication review in patients with rheumatoid arthritis and those with type 2 diabetes mellitus

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Submitted at Frontiers of pharmacology

6.1 Abstract

Background: A type 3 medication review (MR3) is a patient-centred medication service primarily provided by pharmacists and is presently employed routinely in several countries. In this process, pharmacists interview patients and collaborate with the treating physician to optimize the patient's pharmacotherapy, taking into account the patient's medication history and other medical data including laboratory values. The need to maintain the quality of such interventions during and after their initial implementation cannot be overstated.

Aim: The objective of this study was to refine and assess a scoring table to evaluate the quality of MR3.

Methods: The comprehensive quality of MR3s was assessed by scoring its various components using a previously developed scoring table, called BRANT-MERQS, Brussels Antwerp Medication Review Quality Score. MR3s were analysed from an implementation study with patients suffering from rheumatoid arthritis (RA, subproject 1) and type 2 diabetes mellitus (T2DM, subproject 2). Additional information was obtained during a telephone call with a subset of participating pharmacists.

Results: In subproject 1, a total of 21 MR3s of patients with RA were examined. The assessment showed favourable scores for elements such as a well-organized medication schedule, treatment adherence, and the elaboration of specific interventions. However, certain other quality criteria posed challenges in the evaluation, for example the use of simple and understandable language. Pharmacists faced time constraints, and elderly general practitioners (GPs) displayed limited enthusiasm, which were notable barriers observed for this subproject.

In the context of subproject 2 that investigated 41 MR3s in patients with T2DM, the quality criteria of interaction between pharmacist and GP and used sources and tools received high scores. However, there was still room for improvement, especially in areas such as accurate dosing, handling kidney function, QT prolongation, correctly associating laboratory values with relevant drugs and medical conditions, and optimization of medication schedules for patients.

Conclusion: This study demonstrated the feasibility of MR3 quality assessment through a scoring system. However, it also unveiled the tool's current imperfections and highlighted the ongoing need for refinement, something expected of a new service in an implementation phase.

6.2 Introduction

Quality assurance plays a crucial role in ensuring the long-term success and effectiveness of a newly implemented service. By implementing robust quality assurance measures, organizations can proactively identify and address many potential issues or shortcomings, thus enhancing the overall quality and reliability of the service. This not only instils confidence in both service providers and health insurance companies but also helps to establish a solid foundation for continuous improvement and innovation, while improving patient safety. By upholding high standards through quality assurance, organizations can strive for excellence and deliver a service that meets or exceeds expectations, fostering positive patient experience and satisfaction, and the long-term sustainability of the service (1). Already in 1969, a guideline from the Committee for National Health Insurance of the United States of America, stated that the national health insurance program should encompass provisions aimed at ensuring the quantity, quality, effectiveness, continuity, and cost-efficiency of the family healthcare services it supported (2). More recently, the Interactive Systems Framework for Dissemination and Implementation (ISF) acknowledges the critical role of quality assessment in widespread innovation success (3).

Since 2017, the Royal Pharmacists Association of Antwerp (KAVA) has overseen initiatives related to type 3 medication review (MR3) in Belgium. Type 3 medication review involves a thorough assessment of a

patient's medication, starting with a comprehensive medication history, incorporating medical data, and involving an extensive patient interview along with feedback from the general practitioner (4, 5). The objective is to optimize the patient's pharmacotherapy while minimizing potential medication errors, reduce waste, and enhance medication adherence (4). KAVA's initiatives involved training pharmacists for MR3 and guiding them to implement it effectively in their community pharmacies (5). Responding to requests from participating pharmacists in the pilot initiative, additional courses were introduced in 2021 and 2022. These courses, tailored to pharmacists with prior MR3 training, focused on specific patient populations, with the 2021 course addressing rheumatoid arthritis (RA, subproject 1) and the 2022 course centring on patients with T2DM (subproject 2).

Rheumatoid arthritis is a chronic, systemic, inflammatory autoimmune disorder. The condition is linked to substantial morbidity and mortality risks (6). While scientific research on medication review (MR) in patients with RA is limited, some existing studies centre around medication adherence, drug-related problems (DRPs) and pharmaceutical interventions within this patient group (7-10). The clinical significance of pharmaceutical interventions during MRs was examined in 2018 in the rheumatology department of a French hospital (8). Using MR type 2b, i.e. starting from clinical data but without active patient input (4), the study uncovered a considerable number of DRPs of substantial clinical relevance. Effective collaboration between pharmacists and physicians led to the necessary pharmaceutical interventions (8).

Another major chronic condition is T2DM. Despite its potential for various complications, adherence to pharmacological treatment for T2DM is often suboptimal (11). Moreover, effective lifestyle modifications are frequently lacking. Despite the crucial role of pharmacists in primary care, they are not consistently involved in the follow-up care of patients with T2DM (12). Nonetheless, research has demonstrated the significant impact of pharmacists in providing advanced care for patients with multiple chronic diseases (13, 14).

Various studies have demonstrated that MR positively impacts glycaemic control, quality of life, medication adherence, lifestyle adjustments, disease understanding, and the rate of DRPs (12, 14-17). Common DRPs include poor adherence, inappropriate drug selection, contraindications and side effects. Additionally, enhanced understanding of conditions and improved adherence have been linked to better glycaemic control (12, 14, 17).

In recent years, a limited but growing emphasis on the quality dimension of MRs can be recognized (18-21). Standards and evidence-based guidelines must guide MRs. This is crucial for assisting pharmacists and the broader clinical pharmacy team in achieving optimal results for both patients and the healthcare system (22). In Canada, a study outlined that community pharmacists, when implementing a reimbursed MR program, prioritized strategies emphasizing service efficiency and quantity rather than quality (23). With regard to prioritizing quality, our previous research identified eight key elements in assessing MR3 quality (24). These components involve using clear language, explaining the review's purpose, addressing medication adherence, discussing specific drug use, creating and reviewing a comprehensible medication schedule with the patient, assessing ongoing relevance of all drug indications, providing an opportunity for patients to discuss their symptoms with the pharmacist, and considering patient expectations and concerns in treatment planning (24). The current study has incorporated these findings, yet the primary objective is not to replace future Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs) but rather to conduct a quality assessment of the content within MR3 reports.

Ethical approval was granted by the UZA/University of Antwerp medical ethics committee in September 2020 with authorization number 20470 20200921 DGA UZA.

6.3 Aim of the study

The objective was to further develop and evaluate a scoring table to assess the quality of MR3, focusing on its application in patients with RA and T2DM (24).

6.4 Materials and methods

6.4.1 Data collection

This study consisted of two subprojects: one focused on patients with RA (subproject 1) and the other on patients with T2DM (subproject 2). Pharmacists who participated in prior MR3 training sessions were invited by email. The participating pharmacists were permitted to enroll patients with either RA or T2DM and using more than five chronic medications. There were no age restrictions. The outcomes were processed on a per-pharmacy basis, considering that pharmacists were sometimes collaboratively conducting MR3s within the same pharmacy. Subproject 1 was conducted between September 2020 and June 2021, while subproject 2 took place from March 2022 to April 2023. At the beginning of each subproject, pharmacists were provided with customized supplementary materials, including a locally adapted step-by-step medication assessment guideline based on the one developed by the Royal Dutch Society for the Advancement of Pharmacy (KNMP), instructions for calculating medication adherence, model letters for general practitioners (GPs) and patients, a prototype for obtaining informed consent from patients, and a review report template (25). Furthermore, participating pharmacists underwent specific training and received ongoing support and guidance from the research team (A.R. and H.D.L.) throughout the project's duration (26).

Pharmacists who provided anonymised MR reports to the research team were given a minor financial reward, as MR3s were not yet reimbursed in Belgium during that period. These reports were used to assess the MR3 quality. Participants in subproject 1 could employ either a Word template or a Google Forms to generate their reports. Subproject 2 adopted a consistent reporting method and used only the Google Forms, reflecting the preference of 71% of those involved in subproject 1. The Google Forms utilized for both projects was identical, except for the questions about the particular project (RA or T2DM). All templates can be found in the appendix.

6.4.2 Design of the study

The evaluation of MR3 quality assessment was conducted and documented using a scoring table, called BRANT-MERQS Brussels Antwerp Medication Review Quality Score, as showed in Table 6.1. To reduce bias, researchers independently evaluated predetermined quality criteria without disclosing the scoring table's content to the pharmacists. The table was created using quality criteria derived from prior research (24), which identified broad consensus-based key elements for assessing MR3 quality. In addition, the hierarchy of quality assessment criteria for MR3s was also widely agreed upon (24). The scoring table was therefore structured into six themes[2]: (1) general aspects, (2) drug assessment, (3) treatment evaluation, (4) consultation between pharmacist and GP, (5) sources and tools, and (6) in-depth analysis of RA or T2DM.

In the context of subproject 1, a comprehensive assessment of 46 quality criteria was undertaken, with one criterion tailored specifically for RA. In the subsequent subproject, minor adjustments were applied to the quality criteria utilized in the first subproject, encompassing an additional four criteria tailored for

[2] The examination encompassed an extensive review of the current methods pharmacists employ to submit reports to physicians. Integrating this information with the study on the quality assessment of MR3, we identified six themes for the scoring table.

T2DM. Consequently, the second subproject involved the assessment of a combined total of 49 quality criteria.

During subproject 1, pharmacists who finalised their first MR3 were contacted by phone offering support during this early implementation phase between March and April 2021. Furthermore, they were reminded about any incomplete data and were asked some general questions to inform the overall subproject implementation. This was not the case for subproject 2.

Table 6.1: The BRANT-MERQS scoring table used for the two subprojects.

SCORING TABLE BRANT-MERQS		**Included in total score**
GENERAL QUALITY CRITERIA	Explanation benefit and purpose of MR	No
	General characteristics (birth date, gender)	Yes
	Allergies and intolerances	Yes
	Lab values	Yes
	Current conditions	Yes
	Simple and comprehensible language	No
	Familiar and quiet environment	No
QUALITY CRITERIA OF THE DRUG TREATMENT	Overview chronic medication	Yes
	Overview self-care medication	Yes
	Indications known by patient	No
	Medication schedule recent	Yes
	Indications still topical	No
	Effectiveness	Yes
	Side effects	Yes
	Drugs treating side effects	No
	Interactions with other drugs/ food	Yes
	Relevance of interactions	Yes
	Correct dose	Yes
	Vaccination status	Yes
	User-friendly administration form	Yes
	Control of storage of medication	No
QUALITY CRITERIA OF THE CURRENT OVERALL TREATMENT	Treatment construction	No
	Treatment choice as a function of comorbidities	No
	Drug changes + motivation	No
	Nonmedical measures	No
	Undertreatment	Yes
	Overtreatment	Yes
	Tapering of medication	No
	Addiction risk	No
	Adherence	Yes
	Motivation control by healthcare providers (HCP)	Yes
	Interpretation lab values	Yes
	Lab values linked to conditions and drugs	Yes
	Tools: medication schedule, medication box, ...	Yes
QUALITY CRITERIA OF THE INTERACTION BETWEEN PHARMACIST AND GP	Report to GP	Yes
	Elaboration of specific interventions	Yes
	Interventions sufficiently reasoned	Yes
	Intervention plan discussed with patient	No

	Actions without consulting GP (non-medicinal)	No
	Actions after consultation of GP	No
	Follow-up interview with the patient	No
QUALITY CRITERIA OF THE USED SOURCES AND TOOLS	Availability of lower cost alternatives	No
	Use of reliable tools	Yes
	Bibliography	Yes
	Reliable literature	Yes
PROJECT SPECIFIC QUALITY CRITERIA	Accurately estimate osteoporosis risk using the Fracture Risk Assessment (FRAX) tool and interpret the results correctly	Subproject 1
	HbA1c	Subproject 2
	HbA1c target known?	Subproject 2
	Is the patient part of a care program?	Subproject 2

6.4.3 Data analysis

The same scoring table was employed to assess each aspect of the MR3 report for patients with RA or T2DM and consisted of the following ratings: very good (3), good (2), insufficient (1), and not present in the report (0). As an illustration, a score of 0 was assigned when no laboratory values were included in the report. In instances with incomplete values, such as a missing important parameter, a score of 1 was given. A score of 2 was attributed to a rather comprehensive list of laboratory values with room for improvement for example the missing of a less important laboratory value, while a score of 3 was assigned when no further enhancements were deemed necessary. The total score was obtained by adding up the individual scores from all assessable statements. The total score comprised only the quality criteria that were quantifiable. The highest possible total score for subproject 1 was 84, and for subproject 2, it was 90. To enhance interpretability, the results were transformed into percentages. Other quality criteria were not measurable as they could not be evaluated solely through a written report, like, for instance, elucidating the benefits and purpose of MR.

In subproject 1, K.S. conducted the data analysis, and in situations where uncertainties arose, she reached out to A.R. and H.D.L. For subproject 2, L.P. and M.P. were responsible for the data analysis. Similarly, in case of any uncertainties, they consulted A.R. and H.D.L. for assistance.

6.5 Results

Using the scoring table, an aggregate score was determined by summing up individual scores for each measurable quality criterion. General criteria with insufficient reporting or non-measurable aspects were excluded from the total score calculation, accounting for 18 criteria in both subprojects. The distribution of the scores can be found in the attachment.

6.5.1 General results subproject 1: patients with RA

52 pharmacists who previously participated in trainings around MR3, were invited to participate in the first subproject and garnered participation from fifteen pharmacies. Out of these eight (53%) individual pharmacies ultimately conducted at least one MR3, as detailed in Table 6.2. All pharmacies were located in the province of Antwerp and a total of 21 MR3s were collected. The quality assessment of these MR3s was analysed and described using the score table provided in the appendix. The average total score was 65 (77%). The highest score of the 21 MR3 in this subproject was 81 (96%) and the lowest score was 44 (52%), as illustrated in Figure 6.1.

Table 6.2: General characteristics of the two subprojects.

	Subproject 1: RA	**Subproject 2: T2DM**
Timing	September 2020 – June 2021	March 2022 – April 2023
Participating pharmacies who submitted at least one MR3	8	7
Location of the pharmacies	8 (100%) Antwerp	4 (57%) Antwerp 1 (14%) Flemish Brabant 1 (14%) Limburg 1 (14%) East Flanders
Total MR3 reports	21	41
Patients' characteristics	29% male patients, age between 69 and 85; median = 76 71% female patients, age between 32 and 90; median = 64	54% male patients, age between 56 and 91; median = 69.5 46% female patients, age between 49 and 89; median = 70
Average score of the MR3 reports (%)	77%	67%
Highest score of the MR3 reports (%)	96%	86%
Lowest score of the MR3 reports (%)	52%	40%

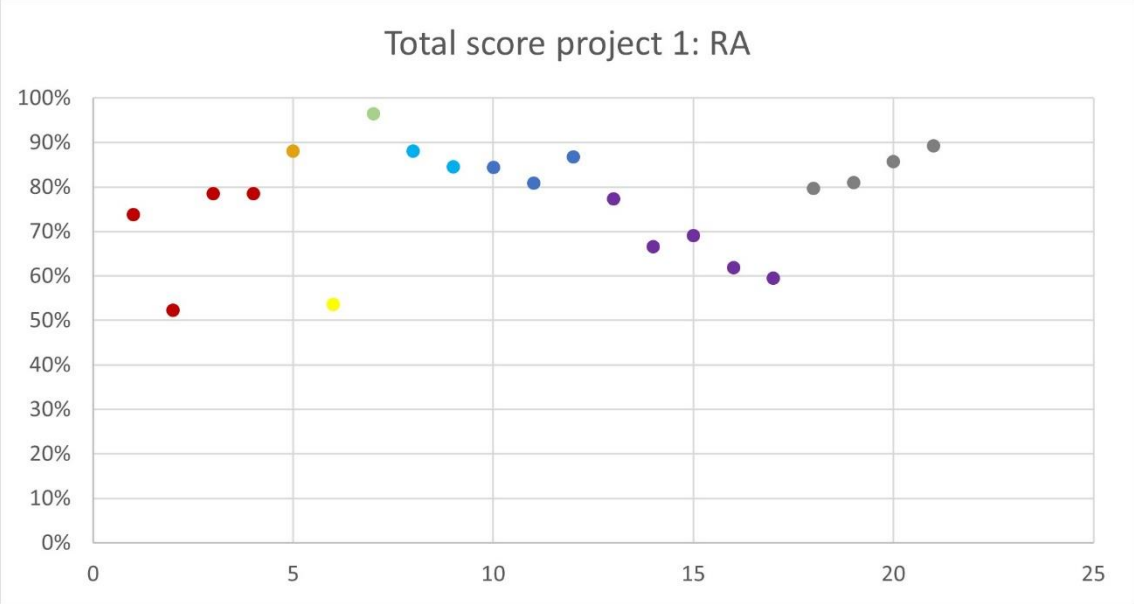

Figure. 6.1: The overall quality assessment scores (in %) for each MR3 report of subproject 1 carried out by the same pharmacy team are shown in the same colour. Different colours represent different pharmacy teams.

6.5.2 General results subproject 2: patients with T2DM

Subproject 2 extended invitations to 114 pharmacists who had undergone prior training on MR3. Eighteen pharmacies participated in the T2DM subproject. Eventually, seven pharmacies (38%) performed at least one MR3. These pharmacies were located all over Flanders; four were located in the province of Antwerp, one in Flemish Brabant, one in Limburg and one in East Flanders. Together, 41 MR3 reports were completed and could be analysed.

The quality assessment of these reports was evaluated using the scoring table that was slightly adapted to the context of T2DM (see Table 6.1). According to the medical history obtained from the GP, the patients suffered from three chronic conditions on average, including T2DM.

The total score per MR3 is shown in Figure 6.2. The average total score of the 41 reports was 61 (67%). The highest score given to a MR3 in this subproject was 77 (86%), as shown in Figure 6.2. The lowest score was 36 (40%). The total score of some, but not all, pharmacies improved as they performed more MR3s. Several pharmacies showed strong variability and no obvious trend. Two pharmacies, displayed in dark blue and orange, performed two and one MR3(s), respectively but scored remarkably high.

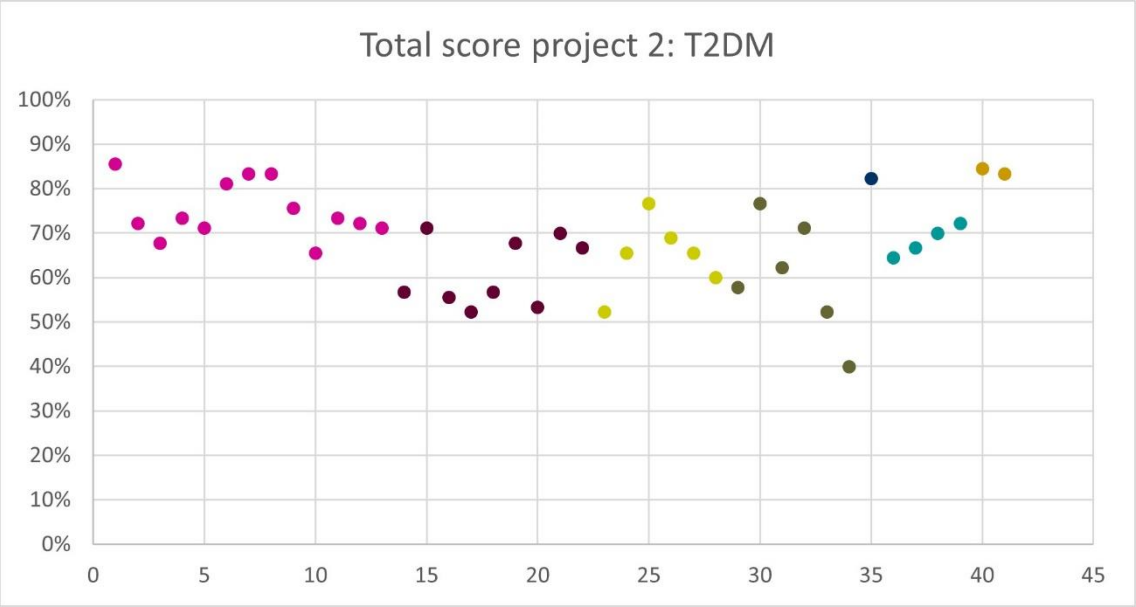

Figure. 6.2: The overall quality assessment scores (in %) for each MR3 report of subproject 2 carried out by the same pharmacy team are shown in the same colour. Different colours represent different pharmacy teams.

6.5.3 Scoring table BRANT-MERQS

Table 6.3 presents the quality criteria of BRANT-MERQS that consistently achieved the highest scores in both subprojects.

Table 6.3: Quality criteria for subproject 1 and 2 with the highest scores.

Quality criteria	**Quality criteria in tool**
Patient's general characteristics were carefully documented.	General characteristics (birth date, gender)
The pharmacist conducted a comprehensive review of the patient's chronic medication.	Overview chronic medication
A recent and well-structured medication schedule was included.	Medication schedule recent
Side effects were taken into consideration.	Side effects
Overtreatment was thoroughly examined.	Overtreatment
Patient medication adherence was diligently assessed by the pharmacist, using a table provided for calculations.	Adherence
The use of tools or devices such as medication schedules, medication boxes, and pill cutters was inquired about.	Tools: medication schedule, medication box, ...
Use of reliable tools such as START – STOPP criteria and GheOP³s tool (27, 28).	Use of reliable tools
Use of reliable literature such as local and international guidelines.	Reliable literature

6.5.3.1 General quality criteria

Out of the seven quality criteria that constituted the first theme, four could be determined directly from the report: the patient's general characteristics (date of birth, gender), allergies or intolerances, presence of laboratory values, and current conditions, as presented in Table 6.1. The remaining three quality criteria include the explanation of MR3s purpose and usefulness to the patient, the use of simple and understandable language with the patient and ensuring a familiar and calm environment during the consultation.

The patient's general characteristics was consistently reported by all pharmacists and scored ‘very good’ across all reports, as shown in Figure 6.3.a. Similarly, the collection of data such as laboratory values and current conditions scored well, with most reports describing this aspect as ‘good’ or 'very good'. In subproject 1, 91% received a score of ‘good’ or ‘very good’ for this aspect, while in subproject 2, the corresponding percentage was 73%. However, in a few MR3s, these elements were either overlooked or lacked sufficient data. For example, in subproject 2, twelve MR3 reports (29%) received an 'insufficient' score regarding current conditions as more than half of the drugs in the medication schedule were not linked to a current condition provided by the GP. This occurred because the pharmacist initially prepared the medication schedules without knowledge of the actual conditions and no optimization of the regimens took place after having gained insights in the patient's conditions following the MR3s. Notably, the inquiry about allergies or intolerances was mostly missing from the reports (52% in subproject 1, 85% in subproject 2), although eight MR3s of subproject 1 (38%) addressed it appropriately and received the highest score.

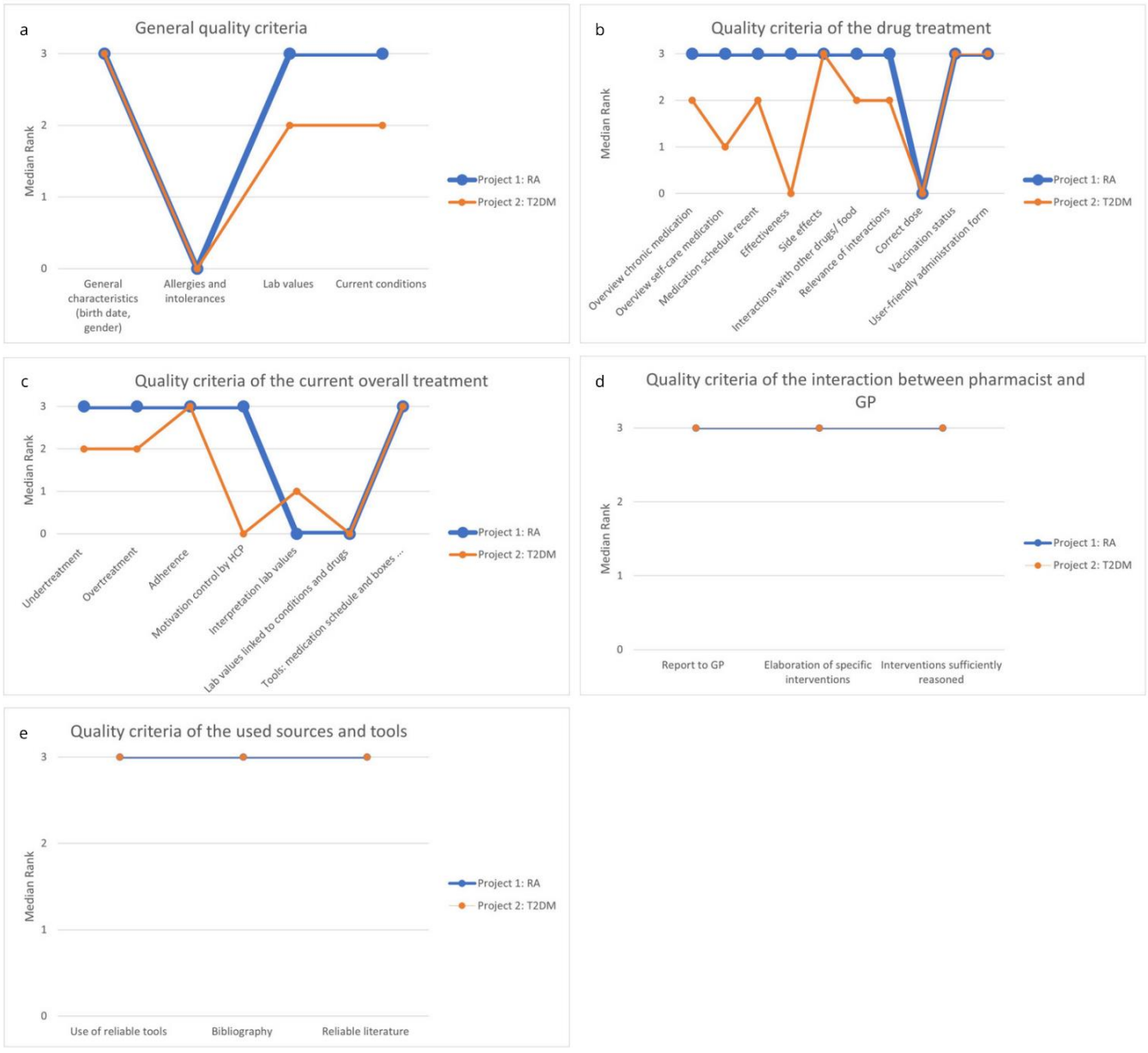

Figure. 6.3: The Figure illustrates the distinctions and similarities between the two projects when examining the five common sections of the scoring table. HCP = healthcare providers.

6.5.3.2 Quality criteria of the drug treatment

The second theme included all quality criteria related to a patient's medications, with various aspects such as an overview of chronic medication, effectiveness, side effects, ease of use and vaccination status. Table 6.1 presents the corresponding fourteen quality criteria. Out of these, ten quality criteria were considered quantifiable from the reports and were integrated into the assessment of the MR3 reports, as illustrated in Figure 6.3.b.

For the quality criteria concerning side effects, vaccination status and user-friendly medication administration, both subprojects, scored 'very good'. Two quality criteria, the overview of chronic medication and its inclusion in a medication schedule, were present in almost all MR3 reports. In subproject 1, every report (100%) received a 'good' or 'very good' score for the overview of chronic medication and its inclusion in the medication schedule. However, in subproject 2, the corresponding percentages were 76% for the overview of chronic medication and 81% for inclusion in the medication schedule. The lower score in subproject 2 was attributed to incomplete information.

Concerning drug interactions and their importance to the patient, the majority of MR3 reports garnered favourable ratings of 'good' or 'very good.' In subproject 1, 76% received a score of 'good' or 'very good' for interactions with other drugs or food, and 81% of the reports were rated 'good' or 'very good' regarding the relevance of the interactions. In subproject 2, these percentages were 68% and 61%, respectively.

The evaluation of self-care medications, dietary supplements and homeopathy received mostly positive scores in subproject 1 but scored less well in subproject 2. In subproject 1, 86% of the reports were rated 'good' or 'very good', whereas in subproject 2, this was only 46%.

Pharmacotherapeutic effectiveness reporting was not included in six reports (29%) from subproject 1 and in 31 reports (76%) from subproject 2. However, in subproject 1, the remaining 15 reports (71%) effectively addressed this aspect and received the highest score, while this was only the case for 5 reports (12%) in subproject 2. The verification of the patient's drug dosage was infrequently reported in both subprojects.

Furthermore, specific quality criteria were excluded from the scoring table due to measurement complexity or because the reports did not explicitly address them, leading to insufficient data collection for these criteria. These included verifying whether the patient was informed about the indications for each medication, ascertaining the relevance of these indications, checking for medications used to address side effects, and ensuring the proper storage of medications.

6.5.3.3 Quality criteria of the current overall therapy

The third theme covered thirteen quality criteria pertaining to the patient's specific treatment that included aspects such as therapy appropriateness and choice, under- and over-treatment, therapy adherence, addiction risk, and motivation for regular physician visits. Seven of these criteria were deemed sufficiently measurable and were integrated into the assessment of the MR3 reports, as outlined in Table 6.1 and Figure 6.3.c.

The quality criteria that scored best were related to the tools used for medication management, such as medication schedules, pill cutters and medication boxes, as well as therapy adherence, present in almost every report. For subproject 1, 95% of the reports scored 'good' or 'very good' for the quality criteria regarding tools, medication schedule and medication boxes, and for subproject 2 this was 100%. For adherence, this was 100% for the first subproject and 76% for the second subproject.

In terms of under-treatment and over-treatment, the majority of MR3 reports received favourable ratings of 'good' or 'very good.' For under-treatment, this constituted 81% in subproject 1 and 73% in subproject 2, while for over-treatment, the percentages were 95% in subproject 1 and 78% in subproject 2. However, in subproject 2, nine reports (22%) were assessed as 'insufficient' for not adequately addressing under-treatment and over-treatment.

The quality criteria regarding patient check-ups with various healthcare providers (HCP) resulted in positive scores in subproject 1, with 86% scoring 'very good,' but was mentioned less frequently in subproject 2, where only 32% of MR3 reports scored 'very good.'

Conversely, there was greater variability and a frequent absence of two other quality criteria in the reports. Specifically, the accurate interpretation of laboratory values was absent in 57% of reports in subproject 1 and 49% in subproject 2, and their correlation with drugs or medical conditions was absent in 67% of reports in subproject 1 and 56% in subproject 2.

The quality criteria relating to appropriate therapy choices based on comorbidities, non-drug measures, and addiction risk could not be adequately assessed based on the data provided by the pharmacists. Additionally, several quality criteria within this theme were only found in a limited number of MR3 reports.

6.5.3.4 Quality criteria of the interaction between pharmacist and GP

The fourth theme explored seven components of the pharmacist's interaction with the GP, encompassing the communication with the GP and the validation of interventions. Three quality criteria were considered quantifiable to a satisfactory degree and were incorporated into the analysis of the MR3 reports, as delineated in Table 6.1 and Figure 6.3.d.

All evaluable quality criteria within this theme scored quite high in both subprojects. These criteria encompassed the GP report, the detailed explanation of specific interventions, and the appropriateness of the reasoning for the interventions. In subproject 1, 72% of the reports received a rating of 'good' or 'very good' for the report to the GP, whereas in subproject 2, this percentage was 86%. Regarding the initiation of specific interventions, 95% received a score of 'good' or 'very good' in subproject 1, and 85% in subproject 2. For quality criteria regarding the appropriateness of the reasoning for the interventions, 91% received a score of 'good' or 'very good' in subproject 1, while the corresponding percentage for subproject 2 was 68%.

Unfortunately, the quality criteria concerning the intervention plan developed in collaboration with the patient, the actions taken post-consultation with the GP and the follow-up interviews with the patient could not be evaluated using the scoring table due to an insufficient amount of data from the pharmacists' reports.

6.5.3.5 Quality criteria of the used sources and tools

The fifth theme centred on four quality standards associated with the resources, guidelines, and tools employed by pharmacists during the MR3 process. These standards encompassed the use of reliable tools, the incorporation of a bibliography, the trustworthiness of the cited literature and the identification of cost-effective medication alternatives for patients.

In the overall assessment, the first three criteria factored into the total score, and each of them demonstrated high performance in both subprojects, as presented in Figure 6.3.e. In the first subproject, 19%, 14%, and 19% of the reports, respectively did not include these three quality criteria. In contrast, in the second subproject, all quality criteria related to sources and tools were always present. The second subproject displayed minimal variation in results, with scores predominantly falling within the range of 'good' to 'very good'.

However, the criterion related to the identification of cost-effective alternatives could not be evaluated in both subprojects since it was mentioned in only one report, rendering it impossible to assign a score.

6.5.3.6 In-depth analysis of RA and T2DM

The sixth and final theme centred on the specific conditions of both subprojects. For the RA subproject, the sole component in this theme was to accurately estimate osteoporosis risk using the Fracture Risk Assessment (FRAX) tool. The tool is a valuable resource for estimating an individual's fracture risk (29). and was used in 17 (81%) reports resulting in a ‘good’ or ‘very good’ score.

Regarding the T2DM subproject, only two (5%) MR3 reports did not receive the maximum score of ‘very good’ on the item related to the patient's HbA1c. One report did not mention it at all, while the other MR3 report provided an interpretation of the HbA1c value as 'too high', leading to a score of 'good' since it was based on an interpretation rather than the presence of the precise value. Most MR3 reports scored ‘very good’ on reporting the item 'HbA1c target known', except for two reviews (5%) that failed to mention it. All MR3 reports received a score of 'very good' on the item 'patient in a care program'. Among the 21 patients (51%) enrolled in a care program, eight patients were aware of their target HbA1c value. In

contrast, only 2 out of the 20 patients who were not in a care program knew the appropriate target value for their HbA1c.

6.5.4 Results of the phone conversation regarding subproject 1

The phone conversations with the seven pharmacists who had submitted at least one MR3 between March and April 2021 yielded positive and enthusiastic feedback.

6.5.4.1 Overall appreciation of subproject 1

Feedback on this first subproject was generally positive. The COVID-19 crisis was frequently cited as the primary cause of delays in performing medication reviews. Some pharmacists mentioned challenges in collecting data from the GP and contacting patients. However, they found the model letter for physicians to be a helpful tool. Utilizing a single theme, RA, proved to be an efficient approach for conducting multiple MR3s. However, recurring concerns emerged about the intensive preparation and time-consuming nature of the MR3s. Despite the acknowledged challenges, pharmacists recognized the potential of MR3s to provide significant benefits to patients.

6.5.4.2 Materials used for the reports

Pharmacists were asked about their preferred method of reporting MR3s and a majority opted for the Google Forms. They valued its convenience for updating the report at any time. However, some pharmacists found it more challenging to input complex information, such as medication schedules, laboratory values and adherence tables in the Google Forms.

6.5.4.3 Questions or support needed

When pharmacists were asked about their need for additional support, three of them asked for clarification on the interpretation of laboratory values. They expressed uncertainty about the appropriate course of action based on the results. One pharmacist requested more specific content for the model letters addressed to both the physician and patient, while another proposed providing a concise report for the patient after the consultation. Additionally, several pharmacists repeatedly asked for an extension of the subproject's deadline.

6.5.4.4 Experiences from GPs

Pharmacists mentioned that GPs expressed positive feedback regarding the subproject. Although one GP initially had difficulty grasping the concept, all eventually embraced it. In the majority of instances, discussions with GPs about possible actions resulting from the MR3s proceeded without difficulty. However, according to the pharmacists, a few GPs retained a degree of ambiguity or generality when deliberating about specific follow-up interventions.

6.5.4.5 Time investment

There was a significant variation in the responses regarding the time needed for the preparation of MR3, conducting patient interviews, and processing data. The time spent on preparation ranged from 30 minutes to 15 hours, while patient interviews usually lasted between 30 minutes and 1.5 hours. Data processing

and creating the report could vary from one to eight hours. Pharmacists expressed their anticipation that future reviews could be conducted somewhat more quickly.

6.6 Discussion

To guarantee effective quality assessment and support future implementation, it is imperative to conduct an analysis of the quality of individual MR3 reports. This study explored the feasibility of a specific framework for integrating quality assessment into the design of this complex intervention. Earlier research has underscored the importance of various key elements in ensuring MR3 quality (24), and this study examined the applicability of these findings by testing them in two distinct practice-based projects that were part of an overall implementation initiative (5, 30).

The cumulative scores of individual reviews offer a comprehensive estimate of the MR3s' quality. The ratings generally ranged from ‘good' to 'very good’, although it's noteworthy that both positive and negative outliers existed. However, the decision on the benchmark score for an acceptable quality level of MR3, or the present need for establishing that value, remains to be addressed. Nevertheless, this study allowed to assess the feasibility of developing such a score and to accumulate the experience needed to inform future developments.

The findings of this study indicate that certain pharmacy teams progressed in the quality of their MR3s, likely by establishing a uniform implementation approach and the accumulation of expertise within a subproject. Conversely, some scores modestly declined, potentially linked to variations in pharmacists' proficiency within the team or the intricacies associated with subsequent and potentially more complex cases (5).

The assessment of the reports also varied somewhat depending on the graders involved. In the second subproject, the evaluation process was more stringent compared to the first subproject, underscoring the necessity for a comprehensive scoring manual providing clear guidance. The first subproject's higher scores may be attributed to participants receiving reminders about incomplete data during telephone conversations. Regardless, the objective remained analysing the utility of the scoring table for evaluating the quality of MR3 reports as part of assessing the quality of this pharmaceutical care service.

Within the MR3 reports, certain elements received suboptimal or no scores. Despite the acknowledged importance of these aspects, they were at times inadequately covered or not included in the examined reports (24). The areas where scores were suboptimal or incomplete mainly involved accurate dosing, handling kidney function decline, QT prolongation, and correctly associating laboratory values with the relevant medications and medical conditions. While the participants received training on these topics, it may require more practice or additional training to become adequately experienced in it. These difficulties were not a surprise in the light of a recent study that documented the difficulties in handling QT interval pop-ups in a larger cohort of community pharmacists in Belgium (31). Undoubtedly, these aspects will need to be integrated into future implementation and training programs.

The remaining criteria that lacked sufficient scores or had to be excluded typically pertained to elements that were either not assessed or found in only one of the two report templates. This absence of certain statements in the uploaded reports suggests that there is room for improvement in the design of the report format. Examples of such criteria include discussions about the usefulness and purpose of a MR with the patient, the use of simple and understandable language by the pharmacist during interaction with the patient, awareness of the reason for medication use by the patient, and verification of the necessity of all medications. Previous research has highlighted the significance of these criteria (24). This limitation in the process can only be addressed if there is a willingness to allocate both time and resources for the random surveying of patients (32). Additionally, follow-up is essential, but assessing the quality criteria for the

intervention plan, post-consultation actions with the GP and patient follow-up interviews were hindered by insufficient data in the pharmacists' reports.

The statement about allergies and intolerances was only present in the Word template contributing to the lower score for this criterion in most of the MR3s. Further optimalisation of the report form is therefore required. Striking a balance between the completeness of the report form and its practical feasibility is essential. Effective digital tools, such as an intelligent decision support systems, have the potential to improve the efficiency and quality of MRs (33-35). Additional variation in the reports arises from the fact that variables such as addiction risk, abrupt medication adjustments, medication tapering, and non-drug interventions are not applicable to every patient.

MR3s were not yet a routine procedure and in subproject 1 the pharmacists valued the feedback obtained during the telephone conversations which aided them in enhancing their review quality and adjusting to this novel service. They also frequently cited the COVID-19 crisis causing delays in performing the reviews.

To the best of our knowledge, this study is a first attempt to assess the quality of MR3s using a scoring system offering a transparent view of pharmacists' actions during MR3. However, there is room for further development. A limitation of the first subproject was the availability of two reporting options hampering exhaustive comparison of the scoring. In both subprojects, starting from the anonymized reports, it is not possible to gauge all aspects of the MR3s such as the assessment of plain and comprehensible language with the patient. This points to the need for the potential inclusion of PROMs/PREMs to comprehensively assess the quality of the MR3 process (24).

Another limitation was the possible inconsistency in the researchers' evaluations because in subproject 1 a single researcher conducted the report analysis, consulting senior researchers when uncertainty arose, while in subproject 2, two researchers with the option to seek guidance from senior researchers were involved. A manual that guides a uniform scoring process would be advantageous for future uses.

We could only retrieve a limited number of studies about assessment of MR quality (19-21, 36-42). Nonetheless, there are indications of an uptake in the evaluation of pharmaceutical care quality, particularly in settings like nursing homes (43). Only two studies concentrated on the implementation of MRs by pharmacists in primary care (19, 44). In the first study, a research group comprising 49 participants with expertise in MRs sought to pinpoint relevant covariates influencing the quality of MR. These covariates were subsequently rated on a 10-point scale (19). Our study, in contrast, employed a more comprehensive scoring system to evaluate MR3 reports, providing more detailed results. The second study involved a comparison of the number of DRPs identified in MRs conducted by community pharmacists and expert reviewers (44). A distinctive aspect of our study was the comprehensive analysis, which was slightly broader than the DRPs examined in the previously published study. For instance, we also aimed to take into account elements like the use of medication boxes and the correct application of resources and tools.

The inherent complexity and potential quality issues of interventions like MRs contribute to the lack of clarity in research findings regarding their efficacy and suitability or transferability for various contexts. Therefore, his research may serve as a resource for future quality assessment and control of MR3s facilitating continuous improvement in the quality in addition to effectiveness research of MR3s (24). Additionally, the implementation process involves various factors, demanding time, continuous learning, endorsement from patients and healthcare professionals, and fair remuneration (5, 45, 46).

Additionally, it is essential to devise a method to assess the quality of MR3 elements that were not explicitly addressed in the MR3 report, but were nevertheless deemed important by many in our previous research (24). It’s crucial to differentiate between elements that are often missed, which can be efficiently handled with a checklist or enhanced report templates, and those that are not straightforward to measure of evaluate from the reports. For the latter category incorporating PROMs and PREMs can be used to comprehensively evaluation of MR3 quality (47). Without a doubt, this would require substantial effort and resources, and it’s an area that calls for more detailed scrutiny and dedicated research.

Other open research questions include the impact of the number of completed MR3s on quality, the optimal report template for MR3s, and the additional training needed to improve pharmacists' MR3 performance.

6.7 Conclusion

This study demonstrates the applicability of quality criteria, established in our previous research, in evaluating the quality of MR3s conducted by community pharmacists. It highlights the crucial role of practical considerations in MR3 implementation, such as a structured report template, phone feedback opportunities, and ongoing pharmacist training. The findings of this study pave the way for internal, peer, and external evaluation of MR3s quality. A comprehensive evaluation of MR3 quality is essential to ensure fidelity in implementation and enable large-scale outcome studies of this valuable pharmaceutical care service.

6.8 References

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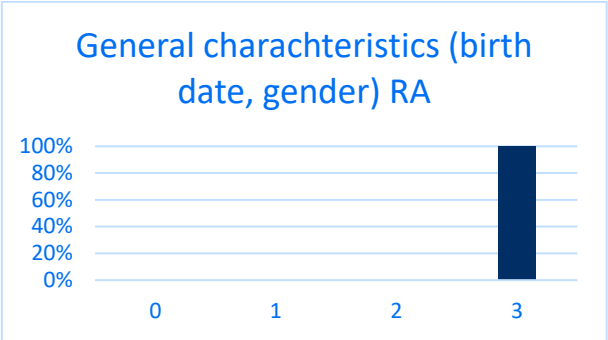
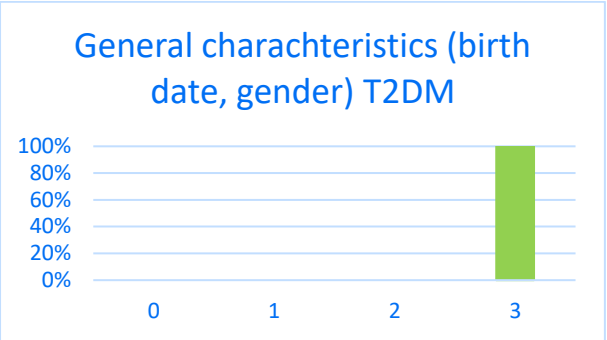
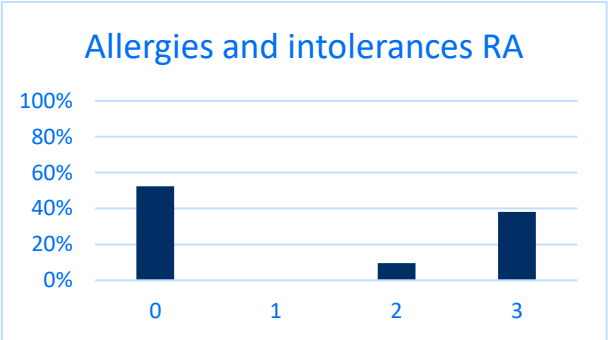
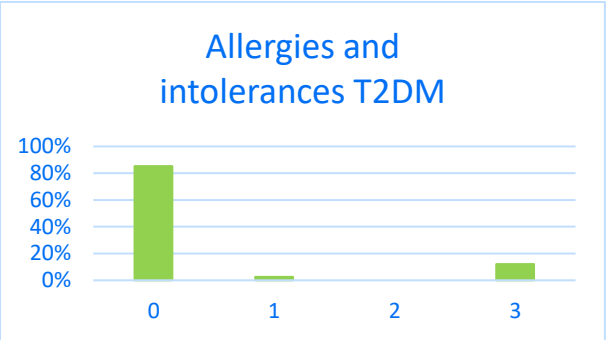
6.9 Appendix

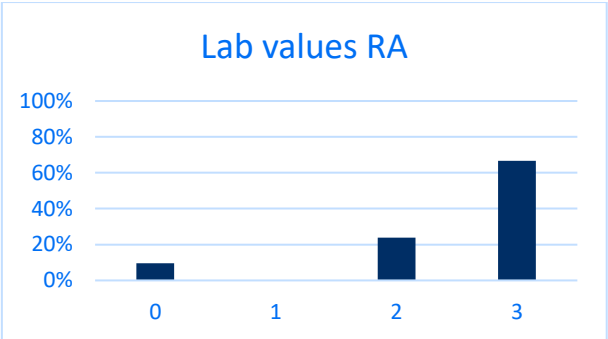
Appendix 6.1 Distribution of the scores for the quality criteria in the reports of RA and T2DM

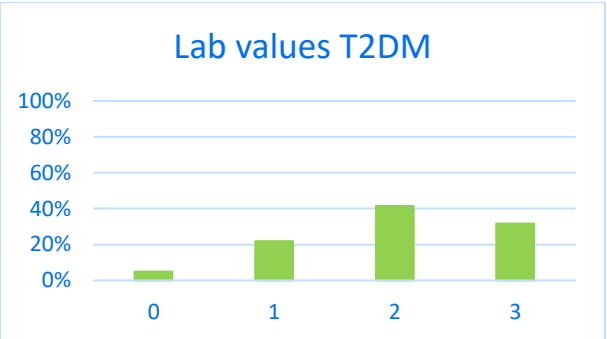


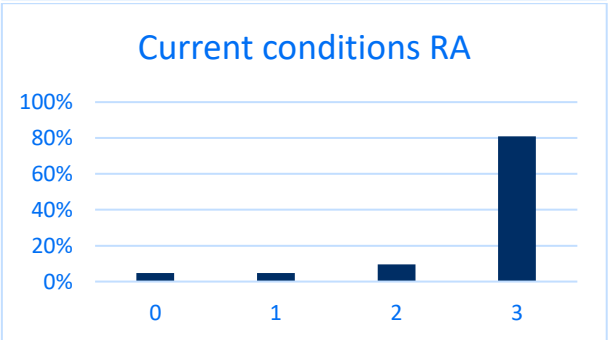


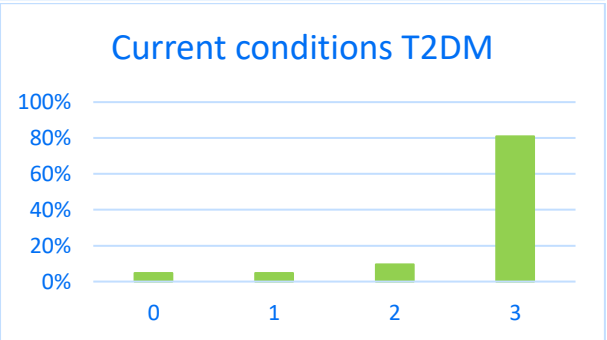


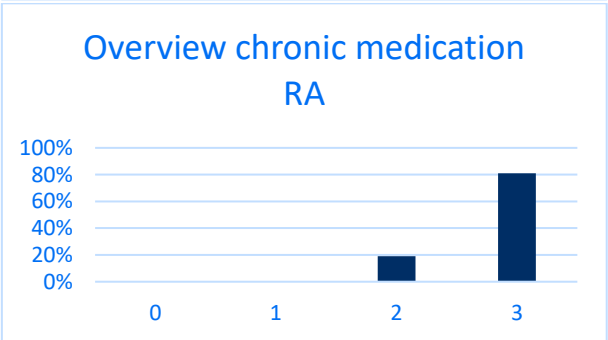


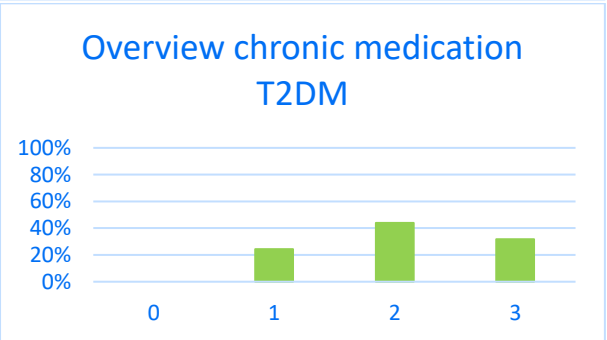


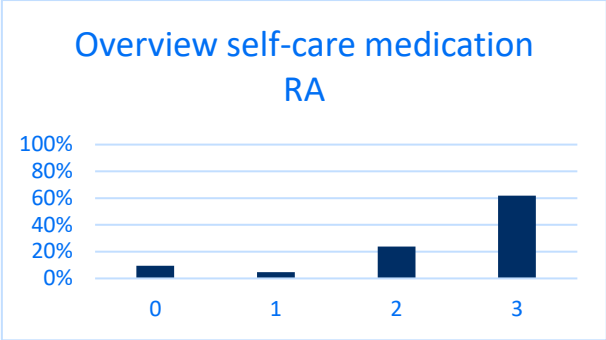








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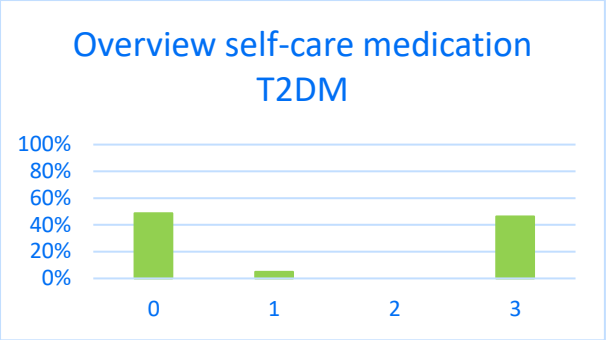
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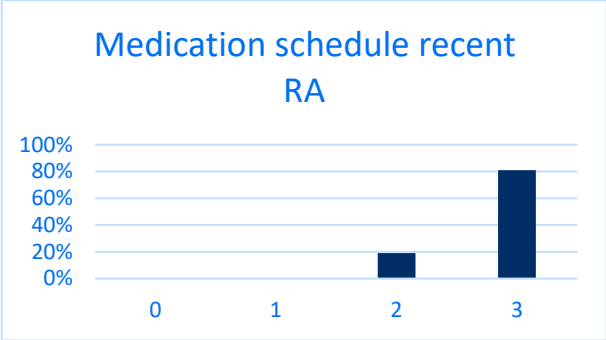
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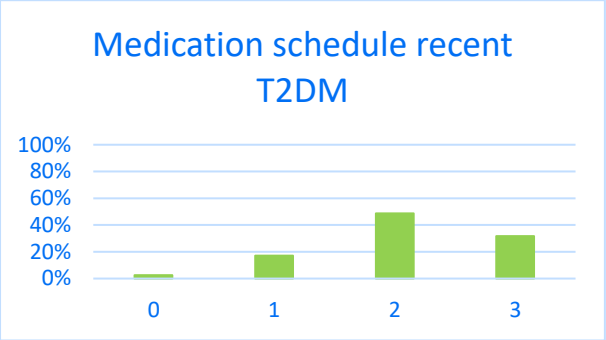
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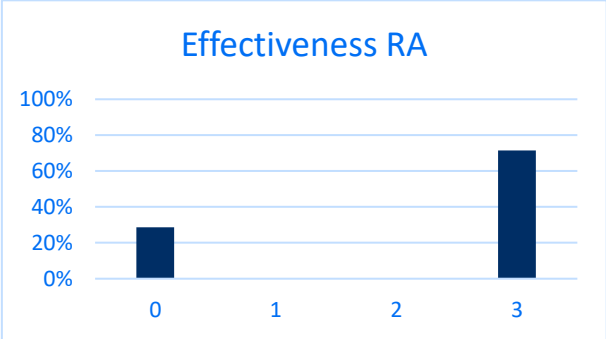
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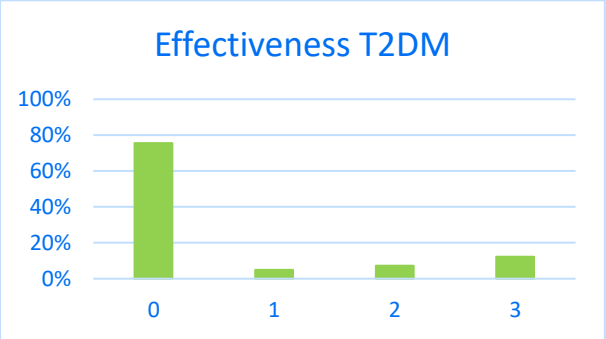
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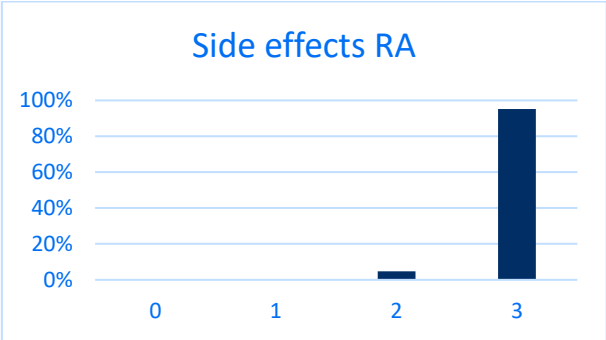
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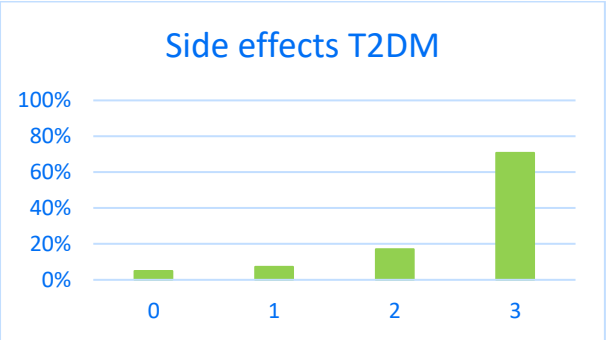
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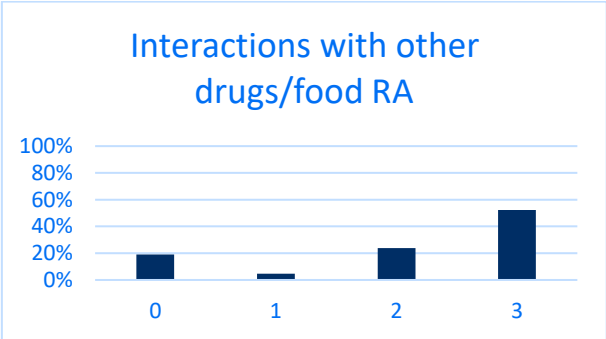
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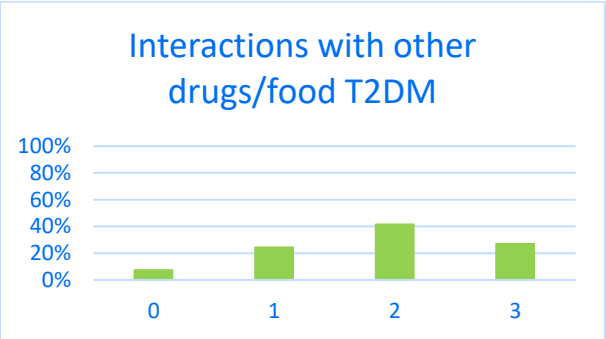
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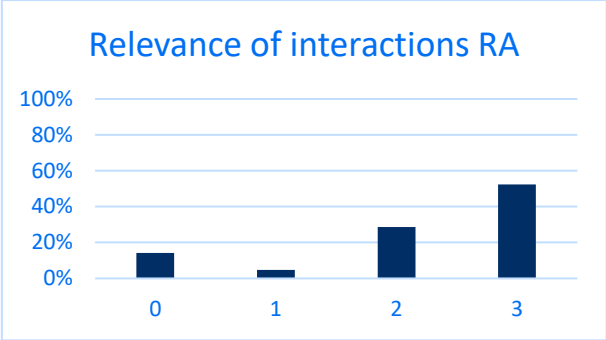
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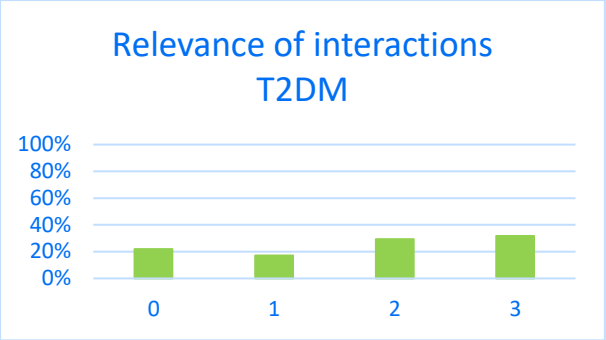
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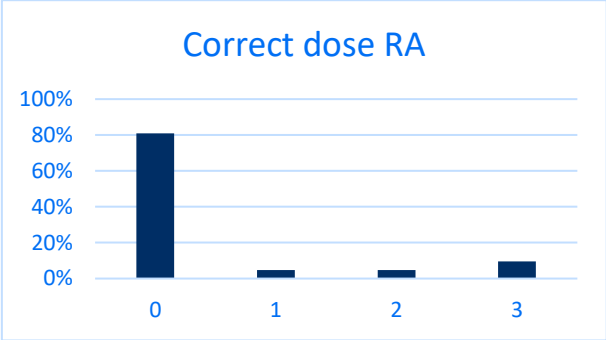
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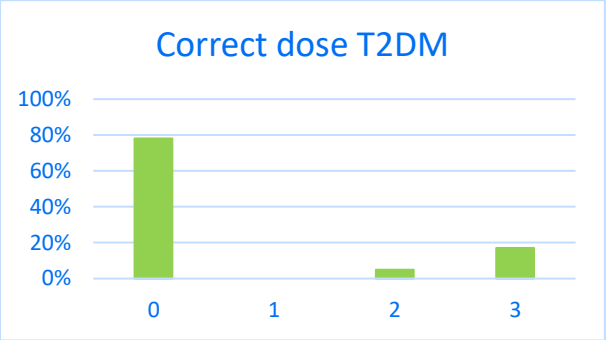
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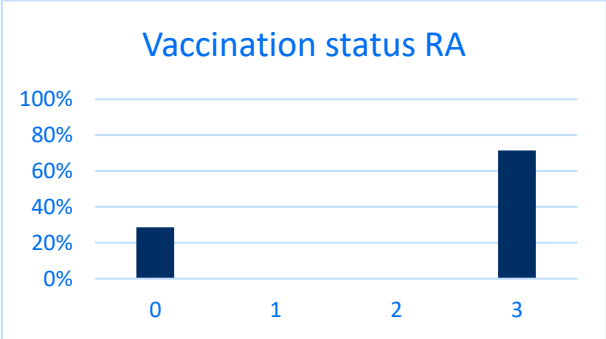
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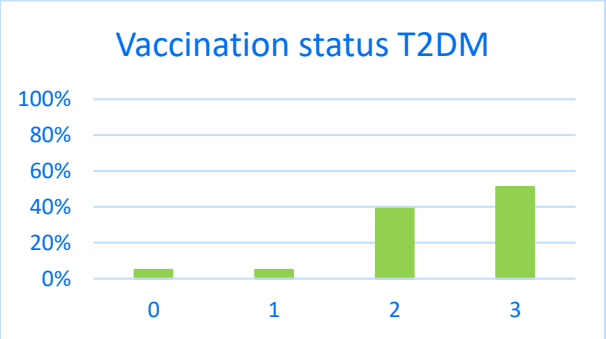
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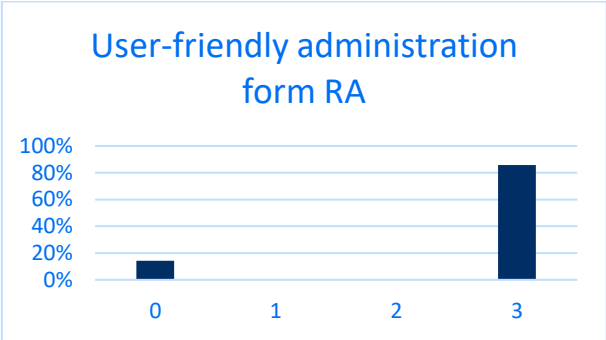
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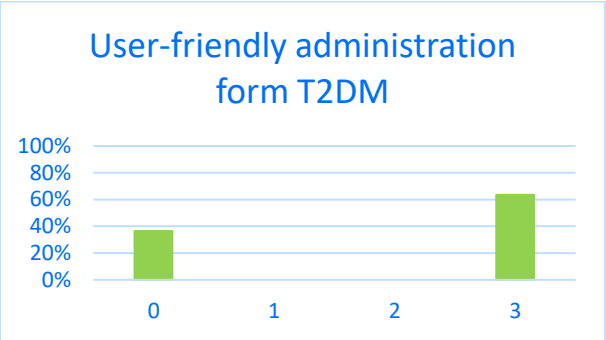
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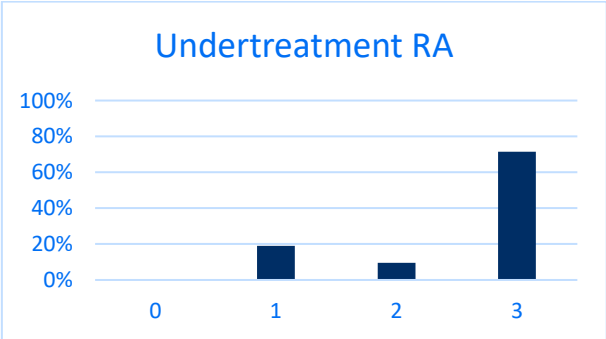
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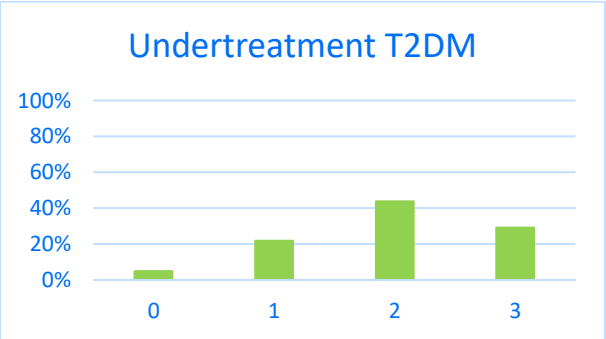
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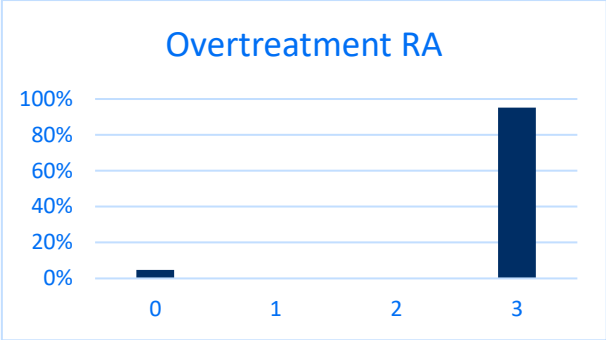
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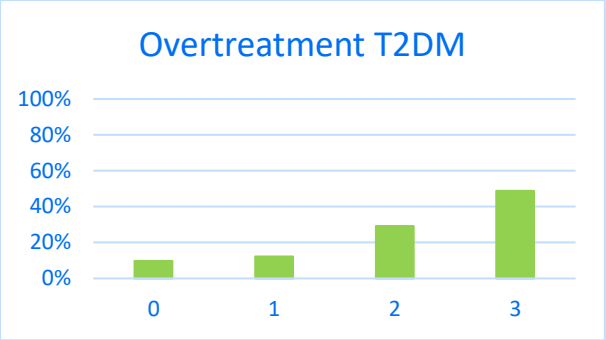
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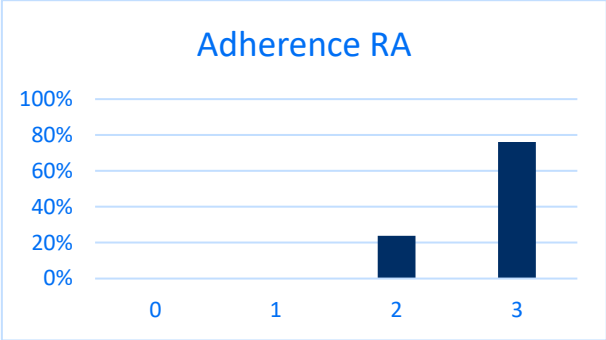
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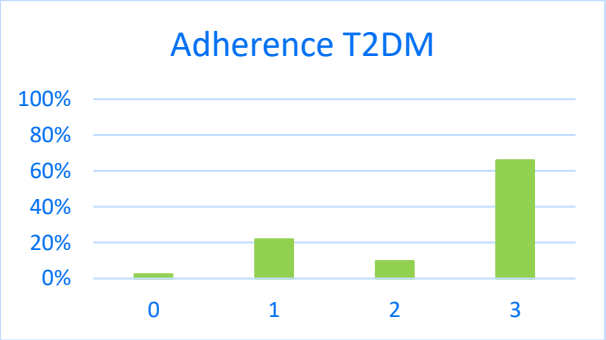
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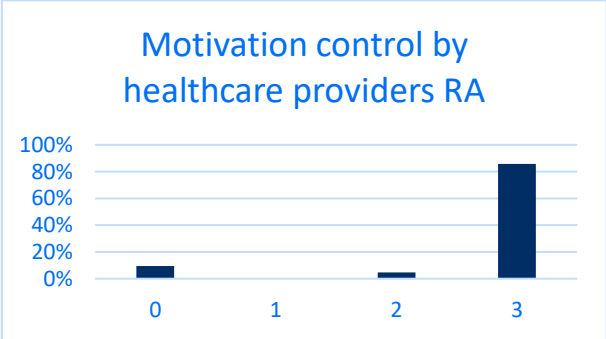
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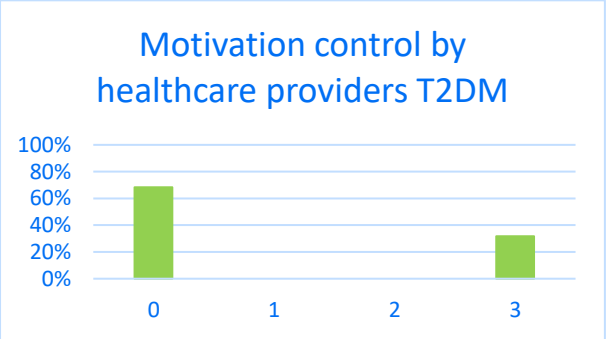
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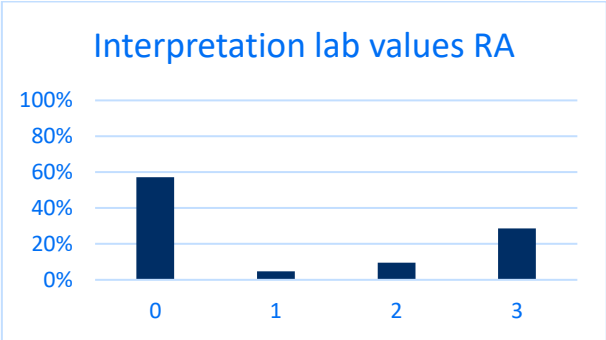
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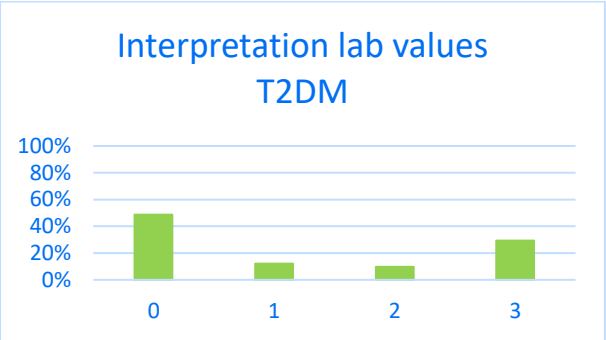
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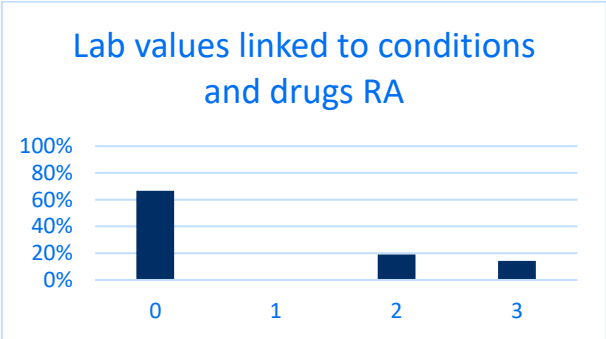
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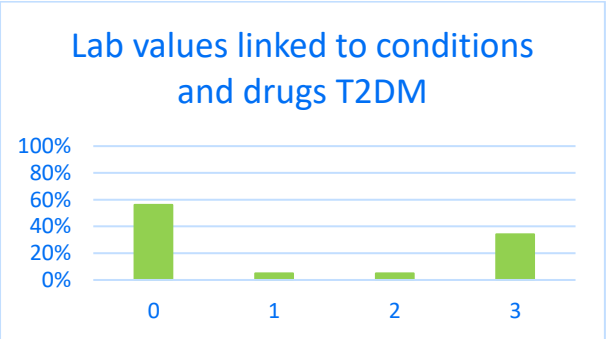
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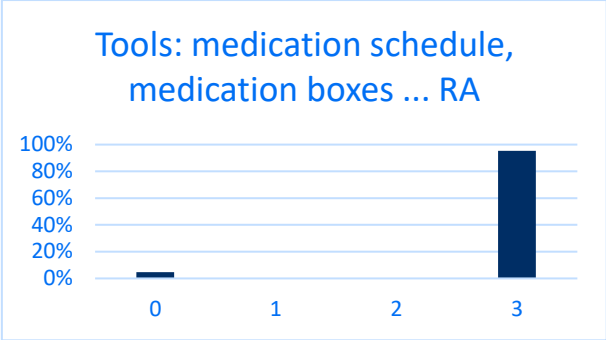
Tools: medication schedule, medication boxes ... RA
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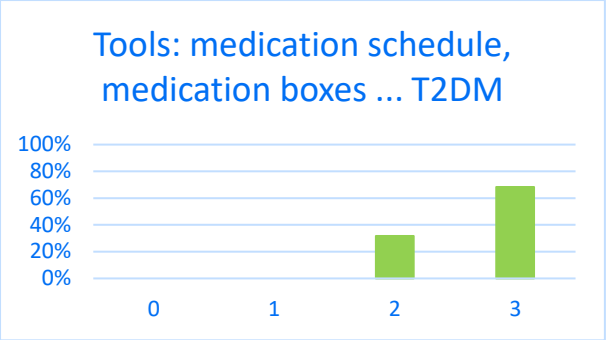
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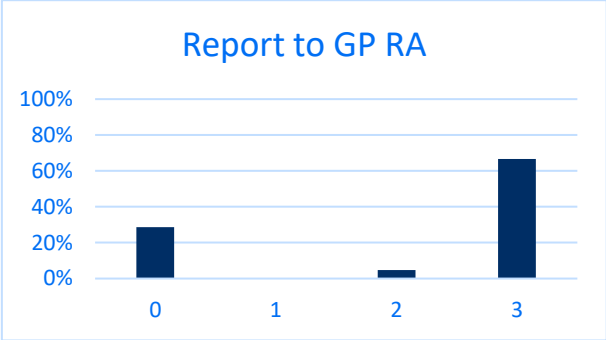
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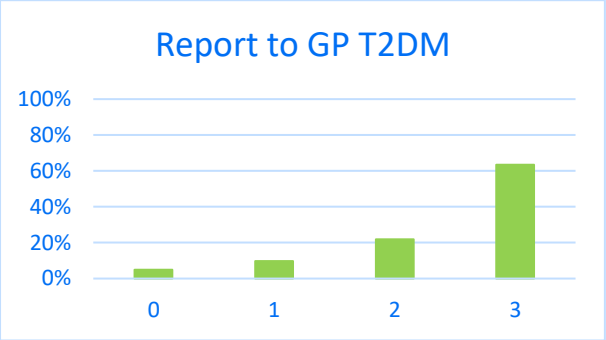
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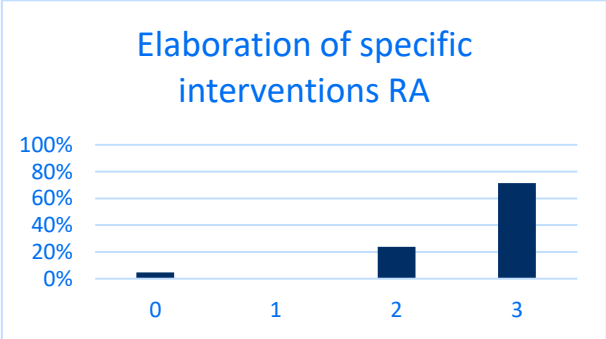
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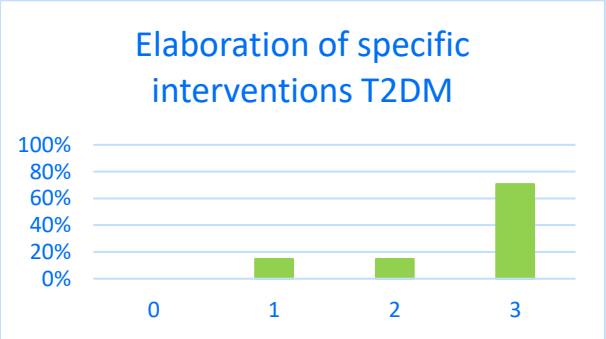
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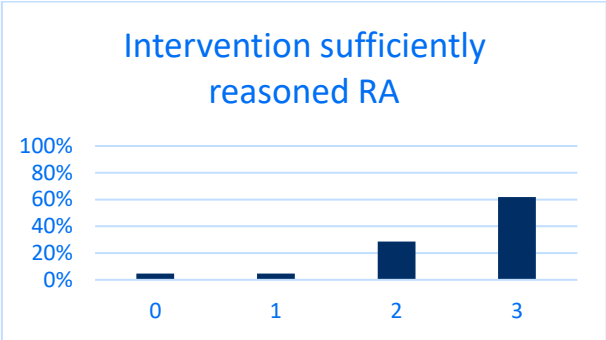
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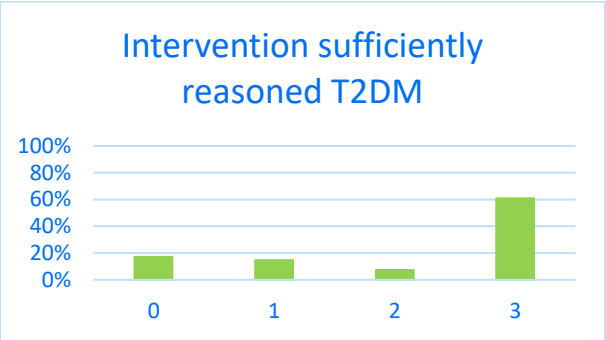
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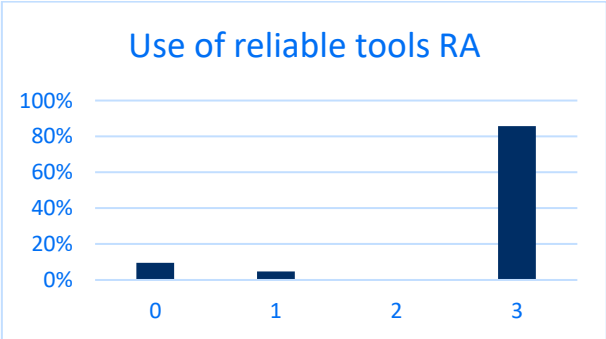
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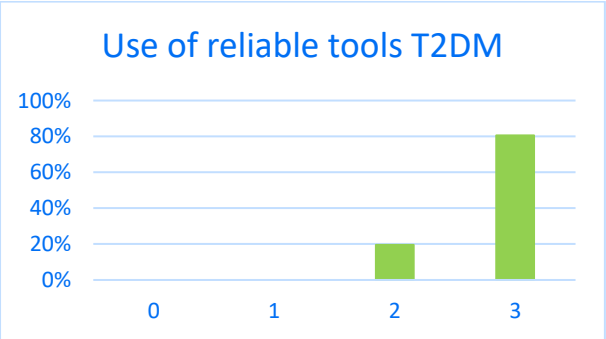
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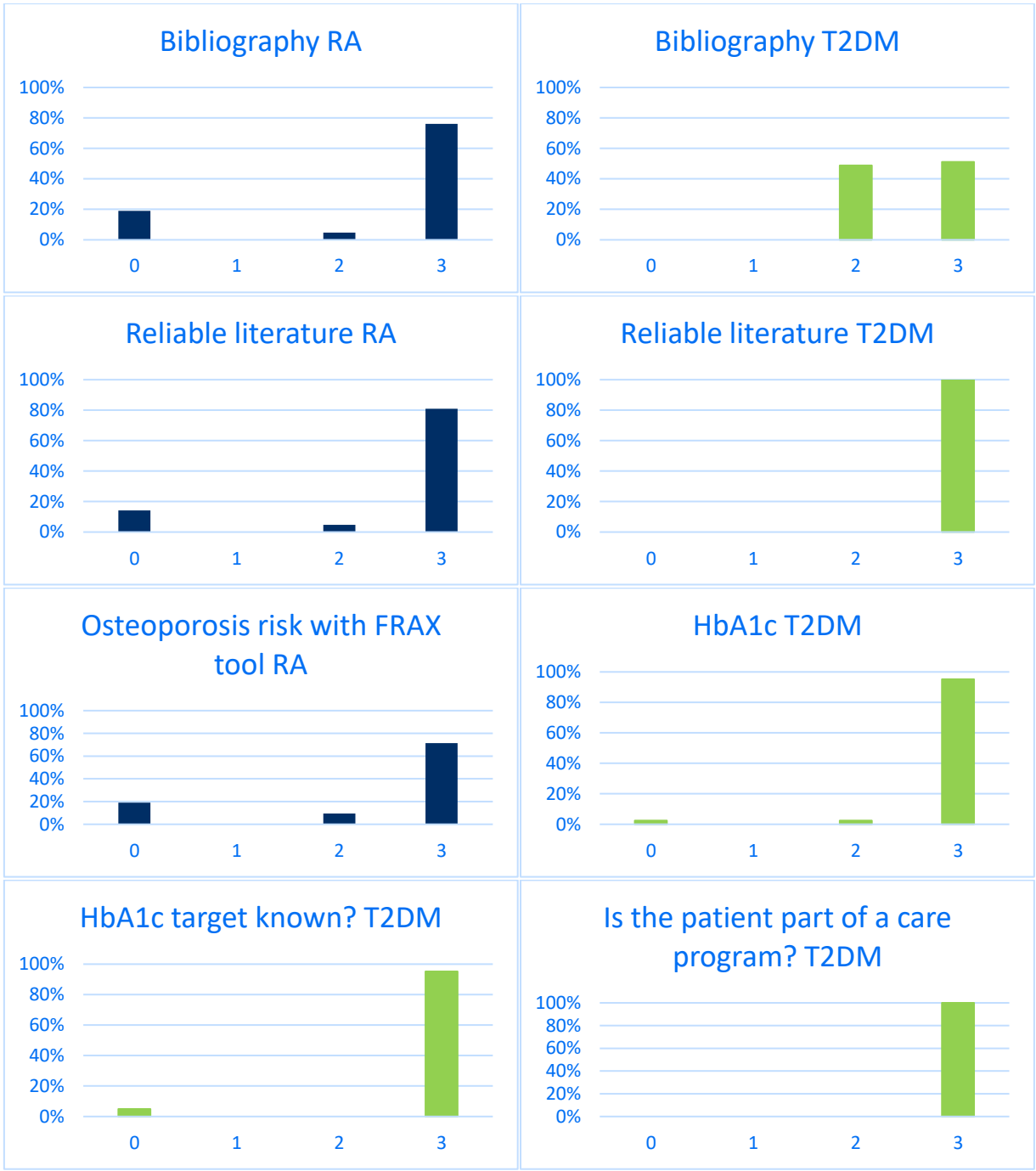


Appendix 6.2 Google Form template (translated version)

Questions 16-21 were specifically introduced for the T2DM subproject, while no particular questions were assigned to the RA subproject.

1. Gender of the patient
2. Date of birth of the patient
3. Living conditions of the patient
4. Medical history
5. Medication schedule BEFORE the medication review. Anonymise patient's and doctor's data
6. Medication history until 2 years before the medication review. Anonymise patient's and doctor's data
7. Clinically relevant data (including date of sampling)
8. Extra general info (vaccination, care program …)

9. Patient follow-up: by which healthcare providers is the patient followed up and with what regularity?
10. Why did you suggest a MR tot his patient? What selection criteria were met?
11. What are the patient's concerns that came up during the interview?
12. Are there side effects that the patient suffers from? If yes, which one(s)?
13. Are there relevant interactions? If yes, which one(s)?
14. Are there potential overtreatments? If yes, which one(s)?
15. Are there potential undertreatments? If yes, which one(s)?
16. In your opinion, is the patient eligible for a care program?
17. If the patient is eligible for one, is he/she actually in that program?
18. What is the patient's HbA1c value before the medication review? Please add the unit.
19. Does the patient know what his guide values of HbA1c are? If yes, what are they? Please include the unit.
20. Is the patient eligible for a combination preparation so that the complexity of his drugs would be reduced? If yes, what can be replaced by which preparation?
21. How is the patient's self-monitoring? Does he use enough test strips/lancets ...? Explain briefly.
22. Load your Excel file of the calculation of the adherence here. Anonymise the patient's and doctor's data.
23. For the chronic medications where good adherence is required, adherence is never good – sometimes good – mostly good – always good.
24. For which medications is adherence substandard?
25. The patient has problems taking the medication (think of blister opening, injections, tablet too big, bad taste, anxiety, side effects, does not know indication well enough)
26. The patient uses the following devices for taking his medicines:
    - Medication schedule
    - Individual medication preparation
    - Pill box
    - Other: ……

27. In the pharmacy, we have already had the following conversations with the patient:
    - GGG asthma
    - GGG diabetes
    - Other: ……
    - None of the above

28. What 'problem(s)' will be tackled? Make a priority list of the 'problem(s)' that will be tackled.
29. Also note for each 'problem' how it will be tackled and who will follow it up.
30. What 'problem(s)' will not be addressed until later? Who is responsible for the follow-up?
31. What digital resources did you use?
32. Which textbooks did you use?
33. What screening tools did you use?
34. Load the adapted medication schedule here. Anonymise the patient's and doctor's data.

Appendix 6.3 Google Form template (original version)

1. Geslacht patiënt
2. Geboortedatum patiënt
3. Woonsituatie patiënt
4. Medische voorgeschiedenis

5. Medicatieschema VOOR aanvang van de medication review. Anonimiseerde de patiënten- en artsengegevens.

6. Medicatiehistoriek tot 2 jaar VOOR aanvang van het gesprek binnen de medication review. Anonimiseerde de patiënten- en artsengegevens.

7. Klinisch relevante gegevens (incl. datum van de bloedafname), mag evt. ook door bestand te uploaden, zie volgende vraag.

8. Extra algemene informatie (bv. vaccins, zorgtrajecten ...)

9. Opvolging patiënt: door welke zorgverleners wordt de patiënt opgevolgd en wat is de regelmaat hiervan.

10. Waarom heb je aan deze patiënt voorgesteld om een MR uit te voeren? Welke selectiecriteria werden er voldaan?

11. Wat zijn de bezorgdheden van de patiënt die tijdens het gesprek naar voor kwamen?

12. Zijn er nevenwerkingen waar de patiënt last van heeft? Indien ja, welke?

13. Zijn er relevante interacties? Indien ja, welke?

14. Zijn er mogelijke overbehandelingen? Indien ja, welke?

15. Zijn er mogelijke onderbehandelingen? Indien ja, welke?

16. Komt de patiënt volgens jou in aanmerking voor "voortraject diabetes"; "zorgtraject diabetes" of "diabetesconventie"?

17. Indien de patiënt in aanmerking komt voor een van de trajecten, zit hij/zij daadwerkelijk in dat traject?

18. Wat is de HbA1c waarde van de patiënt voor de medication review? Geef de eenheid erbij.

19. Weet de patiënt wat zijn richtwaarden van HbA1c zijn? Indien ja, wat zijn ze? Geef de eenheid erbij.

20. Komt de patiënt in aanmerking voor een combinatiepreparaat zodat de complexiteit van zijn geneesmiddelen zou minderen? Indien ja, wat kan vervangen worden door welk preparaat?

21. Hoe is de zelfcontrole van de patiënt? Gebruikt hij voldoende teststrips/lancetten ...? Leg kort toe.

22. Laat hier je het Excelbestand 'bereken de therapietrouw' op. Anonimiseer de patiënten- en artsengegevens.

23. Voor de chronische medicatie waar goede therapietrouw vereist is, is de therapietrouw:

24. Voor welke geneesmiddelen is de therapietrouw ondermaats?

25. De patiënt heeft problemen met de inname van volgende medicatie (denk hierbij aan blister openen, inspuitingen, te grote tablet, slechte smaak, angst, bijwerkingen, kent indicatie niet goed genoeg)

26. De patiënt gebruikt volgende hulpmiddelen voor de inname van zijn geneesmiddelen:

- Medicatieschema
- IMV (individuele medicatievoorbereiding)
- Pillendoos
- Andere: ……

27. In de apotheek hebben we reeds volgende gesprekken gehad met de patiënt:

- GGG astma
- GGG diabetes
- Andere: ……
- Geen van bovenstaande

28. Welk(e) 'probleem/problemen' zal/zullen aangepakt worden?

29. Noteer hier een prioriteitenlijstje van de aan te pakken 'problemen'? Noteer ook per 'probleem' hoe het aangepakt zal worden en wie het opvolgt.

30. Welk(e) 'probleem/problemen' zal/zullen aangepakt worden?

31. Welke digitale bronnen heb je gebruikt?

32. Welke handboeken heb je gebruikt?

33. Welke screeningstools heb je gebruikt?

34. Laat hier je het aangepast medicatieschema op. Anonimiseer de patiënten- en artsengegevens.

Appendix 6.4 Word template (translated version)

Report medication review (initials + date)

Patient data: (unique number) Male/female:

Living conditions: Date of birth:

Confidential counselor:

Medication	**Indication**	**Relevant clinical data (+ date of values)**

The precise medication schedule is enclosed.

Allergies:

Care programs:

Initiation of conversation

Concerns of the patient

Adherence to therapy (excel file attached)

1. Patient adherence, based on the medication delivered is generally:

   Never good - sometimes good - usually good - always good

   Comments:

2. The patient has problems taking the following medication
   - Drug a
   - Drug b

- Reason: blister opening, injections, tablet too big, bad taste, anxiety, side effects, does not know indication well enough

3. In the pharmacy, we have already had the following conversations with the patient
   - ☐ GGG asthma
   - ☐ GGG diabetes
   - ☐ Other, namely:
   - ☐ None of the above

4. The patient uses the following tools from the pharmacy:
   - ☐ Medication schedule
   - ☐ Individual drug preparation
   - ☐ Pill box
   - ☐ Other, namely:

Relevant drug interactions

Drug interaction 1

- Drug:
  Explanation:

Drug interaction 2

- Drug:
  Explanation:

Adverse effects suffered by the patient

Possible overtreatment

Possible undertreatment

Further appointments with treating doctor(s)

Priority	Action point	Who does the follow-up?	By when?

Appendix 6.5 Word template (original version)

Verslag medicatiebeoordeling (initialen + datum)

Patiëntgegevens: (uniek nr.) Man/vrouw:

Woonsituatie: Geboortedatum:

Vertrouwenspersoon:

Medicatie	**Indicatie**	**Relevante klinische gegevens (datum van de waarden)**

In bijlage kan u het accurate medicatieschema vinden.

Allergieën:

Zorgtrajecten:

Aanleiding gesprek

Bezorgdheden van de patiënt

Therapietrouw (Excelbestand in bijlage)

5. De therapietrouw van de patiënt, op basis van de afgeleverde medicatie is in het algemeen:

   Nooit goed – soms goed – meestal goed – altijd goed

   Opmerkingen:

6. De patiënt heeft problemen met de inname van volgende medicatie
   - Geneesmiddel a
   - Geneesmiddel b

- *Reden: blister openen, inspuitingen, te grote tablet, slechte smaak, angst, bijwerkingen, kent indicatie niet goed genoeg*

7. In de apotheek hebben we reeds volgende gesprekken met de patiënt gehad
   - ☐ GGG astma
   - ☐ GGG diabetes
   - ☐ Andere, namelijk:
   - ☐ Geen van bovenstaande

8. De patiënt gebruikt volgende hulpmiddelen uit de apotheek:
   - ☐ Medicatieschema
   - ☐ IMV (Individuele medicatievoorbereiding)
   - ☐ Pillendoos
   - ☐ Andere, namelijk:

Relevante interactie

Interactie 1

- Geneesmiddelen:
  Uitleg:

Interactie 2

- Geneesmiddelen:
  Uitleg:

Ongewenste effecten waar de patiënt last van heeft

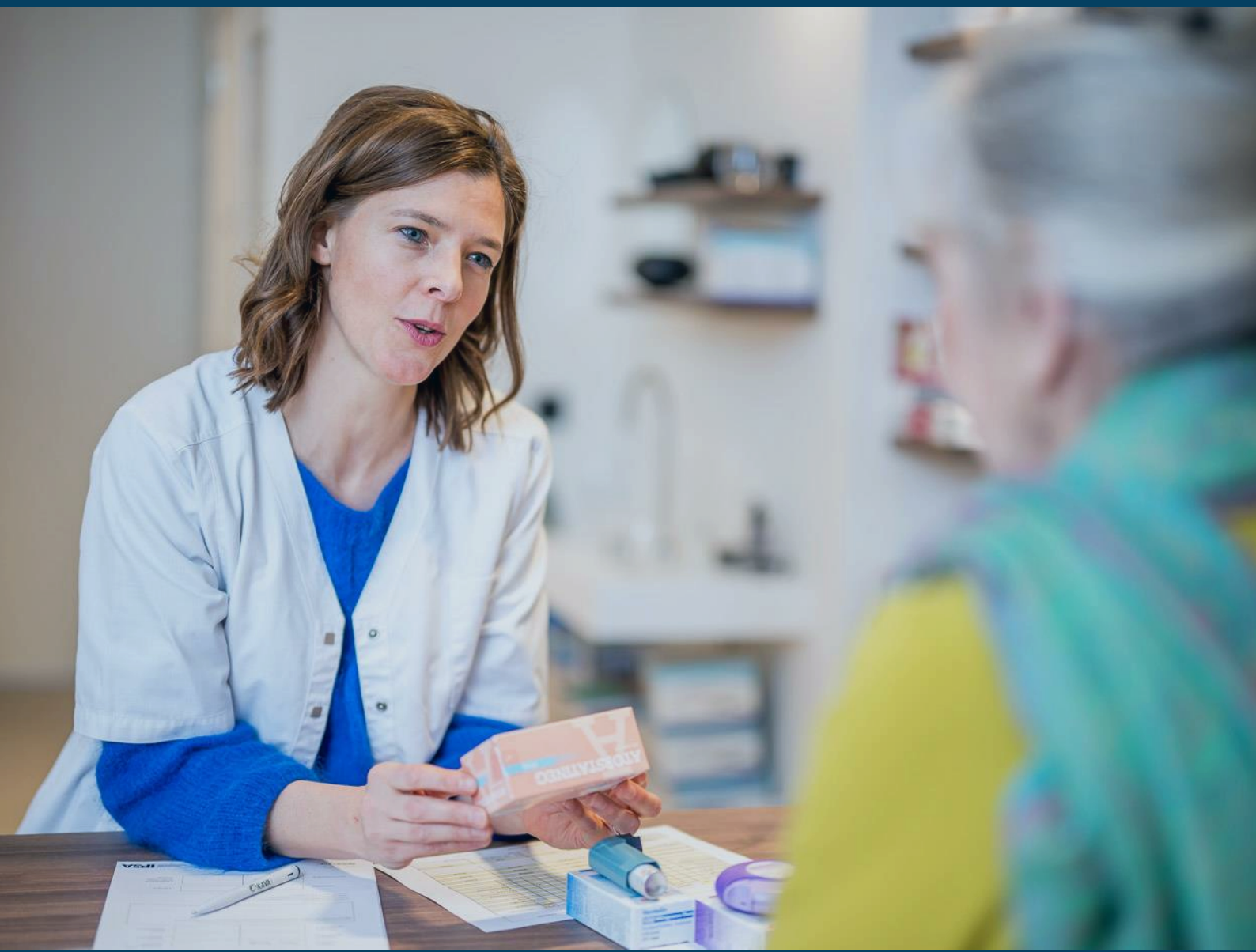
Mogelijke overbehandeling

Mogelijke onderbehandeling

Verdere afspraken met behandelende arts(en)

Prioriteit	Actiepunt	Wie volgt het op?	Tegen wanneer?

Chapter 7: General discussion and future perspectives



7.1 General discussion

This research was initiated based on KAVA's dedication to enhance endeavours in optimizing medication use, recognizing the significant future potential of the MR3, as do many others (1). In order to endow the project with a solid scientific foundation, a cooperative alliance was formed with the University of Antwerp and the Vrije Universiteit Brussel, thereby enabling the realization of this PhD thesis during the first implementation of MR3 in Belgian community pharmacies.

The research in this thesis document significant enthusiasm among both healthcare providers and patients involved in the pilot projects. Community pharmacists (further referred to as pharmacists) demonstrated a proactive engagement in MR3s. Additionally, there was a parallel demonstration of physicians' receptiveness to collaborative efforts with patients genuinely expressing their appreciation for the provision of this service.

7.1.1 Implementation strategies for our study

In the execution of this study, a systematic gathering and thorough analysis of data was carried out, stemming from detailed training sessions and projects conducted in collaboration with KAVA, with a specific focus on MR3, as illustrated in Figure 7.1. In the qualitative investigations (**Chapters 3 and 4**), the perspectives of healthcare providers and patients actively involved in the projects were considered, respectively. To ensure a comprehensive perspective, a diverse group of pharmacists with varying levels of practical, academic, and administrative experience was engaged in the questionnaire on quality criteria (**Chapter 5**). **Chapter 6** utilized reports from two subprojects organized by KAVA for pharmacists who completed the MR3 course and subsequently participated in projects focusing on MR3 for patients with specific conditions, namely rheumatoid arthritis and type 2 diabetes mellitus.

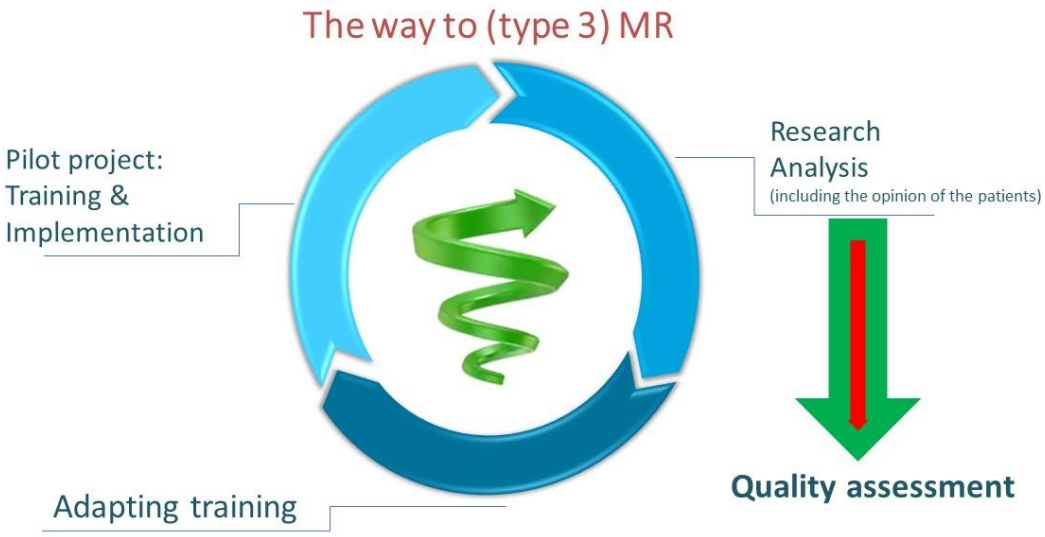


Figure 7.1: Operational implementation plan of our study.

This approach was selected to guarantee that the findings and conclusions of the study actively contribute to the ongoing enhancement of MR3 training and the support for its implementation, thereby laying a solid groundwork for continual exploration and development in future studies. It is worth mentioning that a formal implementation framework or theory was not employed, bringing about both advantages and disadvantages. The advantage of not using an implementation framework lies in the capacity to expedite

the process and react in a flexible way to unforeseen circumstances. However, on the flip side, there are undoubtedly valuable lessons to be drawn from implementation frameworks (2). Numerous implementation frameworks and models exist, such as the Consolidated Framework for Implementation Research (CFIR) (3, 4). Currently, there is no comprehensive framework available to guide researchers seamlessly from intervention development to achieving sustainable practice change (4).

Different concepts related to "implementability", which assess the probability of an intervention being adopted into routine practice and influencing health consumer behaviours across settings and over time, are gaining attention in the implementation science literature (3). These concepts primarily concentrate on the early stages of intervention development or the subsequent phases of evaluation and encompass acceptability, fidelity, feasibility, scalability, and sustainability (3). In our study, emphasis was placed on the initial three concepts: acceptability, fidelity and feasibility. The investigation began by assessing whether healthcare providers and patients perceived added value in the service provision and identified any barriers, followed by the initiation of preliminary steps to qualitatively integrate the service.

7.1.2 Collaboration in healthcare

A synergistic partnership between GPs and community pharmacists is a cornerstone of successful MR3s (5, 6). Recognizing this, our study sought to incorporate GPs' valuable insights and perspectives from the outset (**Chapter 3**). Our findings documented the enthusiasm among pharmacists and GPs regarding medication reviews and the potential to enhance that collaboration. Currently, there is no formalized routine collaboration between GPs and pharmacists in Belgium. Consequently, some pharmacists may be hesitant to engage with GPs. Medico-pharmaceutical consultations represent a potential avenue for collaborative endeavours (7). Fortunately, there is now a noticeable rise in the frequency of medico-pharmaceutical consultations (8). Awareness-raising, targeted communication and interprofessional education of the involved healthcare providers could provide a good solution for improved collaboration (9). An Australian study suggested the need to establish systems, including the development of local protocols for collaboration between GPs and pharmacists on the Home Medicine Review (HMR), a program involving pharmacists conducting a domiciliary to review patient’s medications (10). These might involve a team care approach or employing accredited pharmacists within GP practices (10, 11).

In our study, a conventional arrangement was employed, featuring pharmacists in pharmacies and physicians in practices. However, exploring alternative settings like the CombiConsultation (12), where pharmacists work alongside practice nurses and/or GPs, has potential benefits. In this model, patients consult with the pharmacist first and then immediately see the nurse and/or GP, aiming to enhance the implementation rate of recommendations. The pharmacist's physical presence in the general practice during the joint consultation promotes the effective exchange of clinical data (12) and can contribute to positive measurable outcomes, particularly concerning medication usage (12). However, the community pharmacist in the local pharmacy plays a unique role in Belgium. Unlike in many other countries, Belgian pharmacists forge strong personal bonds of trust with their patients, a vital component particularly during the provision of services like MR3.

Our research revealed that all healthcare providers involved in the study identified the lack of a shared, user-friendly digital platform as a significant impediment to effective collaboration. Strict privacy regulations, such as the General Data Protection Regulation (GDPR), have rendered insecure electronic mail channels unsuitable for transmitting patient data. As a result, the data had to be exchanged in person or sent by postal mail, considerably slowing down the process. Streamlining technological solutions could significantly reduce these delays. While advancements in patient data exchange have emerged in recent years, significant improvements in user-friendliness are still needed (13).

Pharmacists expressed a highly positive outlook on their interactions with patients, reporting no perceived barriers. The consultations with the patients served as an avenue to discern the patient's interests, and it was deemed crucial for identifying pertinent Drug-Related Problems (DRPs), which is further discussed in the patient-centred approach.

Incorporating other healthcare providers, including specialist physicians, was highlighted by both healthcare providers and patients (**Chapters 3 and 4**). Furthermore, other studies have demonstrated that home care nurses can also play a potential role in the MR3 process (6). This aspect is certainly worth considering for future research and implementation. In research not included in this thesis, nephrologists and geriatricians showed interest (14, 15), while cardiologists were less familiar with the concept and potential benefits of medication reviews (16). Moreover, it would be intriguing to explore the possibility of a structured data exchange between community pharmacists and hospital pharmacists. Given that medications are occasionally dispensed through the hospital system, establishing a reciprocal system during hospitalization could also enhance overall patient care (17).

Our study identified further challenges that emerged as significant hurdles, such as the considerable time investment and limited or no remuneration for pharmacists and GPs. The pharmacists who participated in the projects we studied were given a modest compensation. The topic remuneration will be discussed below in the future perspectives. Additionally, pharmacists voiced a need for extra training, a concern that we addressed by integrating additional training sessions in subsequent phases. The pharmacists that identified time management as a barrier to consulting with the patient, expressed difficulty in maintaining focus on the patient's pharmacotherapy without veering into less critical topics (**Chapter 3**). According to the literature, effective external support can reduce the required time investment by two-thirds (18). The assistance provided aimed to help pharmacists organize and plan their services, alleviating them of technical and administrative responsibilities. Furthermore, a mentoring pharmacist was available to offer support about pharmacotherapeutic topics (18). Participating pharmacists in our studies had access to a pharmacist for assistance with substantive and practical questions, mostly through phone calls or emails.

The time required for the MR3 process will diminish as caregivers grow accustomed to this new responsibility since increased experience leads to a more efficient execution (19). Adequate support, such as setting up telephone support for pharmacists, plays a crucial role in facilitating the service (**Chapter 6**). Furthermore, ongoing and effective training with real-life cases remains essential. Ultimately, a robust digital support is expected to further enhance successful implementation.

7.1.3 Patient-centred approach

The viewpoint of the patient regarding pharmaceutical care carries substantial importance, although its implications have not been fully examined (20, 21). This prompted our focus on incorporating patient opinions (**Chapter 4**). Patients almost universally expressed very positive feedback regarding the service, noting its informativeness and acknowledging the valuable time invested by pharmacists, findings that corroborate previous research. (20, 21). However, patients lacked information about the process of medication review often hindering their preparedness for the pharmacist consultation. This unexpected feedback exemplifies the strength of qualitative research by revealing perspectives that were not anticipated during the design of the interview template. The recruitment of participants for the MR3 medication review program was initiated by their respective pharmacists, leading to a diverse range of responses from the patient population. Some felt concerned about being singled out for the MR, while other patients did not inquire further. Their participation was driven by self-interest and curiosity, and at times, a willingness to accommodate or aid their pharmacist, indicative of not being adequately informed about the goals of a MR. Improved communication strategies are required, consistent with prior studies (21-24). The absence of common understanding about and/or a fully established and standardized

language for describing medication review and its outcomes was noted, emphasizing the importance of clear communication among stakeholders, something recent studies also showed (25).

Patients in our study concurred on the necessity and desirability of data exchanges between physicians and pharmacists. While many assumed this as common practice, some patients raised concerns, particularly in relation to confidentiality and privacy, as previously reported in Australia (20). Hence, it is essential to have transparent communication with the patient from the beginning regarding the nature of the data to be shared. Moreover, patients may have some apprehension about which additional healthcare providers have access to that specific data (26), and this should also be communicated to them.

The importance of the patient-pharmacist conversation during medication reviews cannot be overstated. A study revealed that over 25% of all Drugs related problems (DRPs) were detected during the patient consultation (27). Active patient involvement throughout the medication review process is essential to detect and address issues such as suboptimal therapy outcomes, inefficient medication utilization, and intentional or unintentional nonadherence (28). Studies have shown that the majority of DRPs identified during medication reviews do not always align with standard screening tools like START/STOPP criteria (29). To have a full clinical overview of the patient and maximize the efficacy of these interventions, implicit criteria should be integrated alongside patient interviews and interprofessional collaboration (30). Emphasizing this has been a core aspect since the early stages of training with KAVA, and it is inherently rooted in the Systematic Tool to Reduce Inappropriate Assistant (STRIP) (31).

7.1.4 Quality assessment of a MR3

Comparing studies on medication review proves challenging due to frequent ambiguity regarding the type of MR employed and the specific regional interpretation of MR. Therefore, the aim in the introduction was to clarify various definitions, types, and origins of medication review (**Chapter 1**). For example, the definition of medication review lacks clarity, especially concerning “post-review” processes like follow-up. In Spain, the term "medication review with follow-up" is used, potentially improving overall comprehension (32). There is an urgent requirement for standardization and more thorough information about the service's content and quality to enable comparisons between projects and streamline implementation (25). This should also facilitate reliable assessments of outcomes, aiming to bolster the adoption and acceptance of this new service with the ultimate goal of enhancing pharmaceutical care for patients requiring complex pharmacotherapy.

While medication reviews are acknowledged as important for optimal pharmacotherapy, disparities in their quality are only occasionally described (33, 34), and much more frequently, quality descriptions are conspicuously absent. This is the reason why research into identifying the key elements for medication review was initiated.

To establish quality criteria, a ranking questionnaire was developed and deployed, as detailed in **Chapter 5**. A panel of pharmacists from Belgium and the Netherlands were assigned to rank distinct quality criteria based on their perceived importance. The investigation unveiled a broad consensus on the key elements crucial for evaluating the quality of MR3. Eight key statements emerged as integral components for a comprehensive MR3, with minor differences noted, related to the participants' level of experience. Building upon the empirical evidence gathered from this study and incorporating a small number of additional criteria proposed by participants, the creation of a streamlined and effective quality instrument for medication reviews was initiated, as outlined in **Chapter 6**.

The process involved creating a scoring table called BRANT-MERQS, which comprehensively analysed all the quality criteria identified in the previous study. Data from two subsequent projects were scrutinized: one with patients having rheumatoid arthritis (RA) and another with patients having type 2 diabetes mellitus (T2DM). It was noted that most of the quality criteria were quantifiable through the use of the

scoring table. However, further improvement is needed for practical application, for instance, a clear guide is necessary in case total scores from different projects are to be compared. Furthermore, the scoring method couldn't measure all quality criteria, and improving the report could contribute to enhancements, such as achieving better alignment between the report and the scoring table. It is crucial to maintain a balance between the thoroughness of the report and its practical feasibility. Other quality criteria, e.g., the understandable language that should be used by the pharmacist during the conversation with the patient, are not quantifiable through this kind of reporting. This underscores the potential necessity of incorporating Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs) to comprehensively evaluate the quality of the MR3 process. The quality criteria that received lower scores included aspects such as the accurate interpretation of laboratory values. Extra training about this topic can be beneficial, particularly among pharmacists with more work experience as newly qualified pharmacists may have received more education on these subjects. The training concerning laboratory values at KAVA has therefore undergone substantial transformations over time to improve its relevance.

In conclusion, our research emphasized the pivotal role of providing appropriate support to pharmacists engaged in MR3. This was evidenced in the subproject of Chapter 6, where the project researcher engaged in telephonic discussions with the participating pharmacists. Furthermore, the quality criteria we have established can also help with self-assessment.

7.1.5 Strengths and weaknesses

The research presented in this thesis acknowledges both strengths and weaknesses.

One notable limitation is the absence of integration of a theoretical framework into the study, which may affect the overall contextual understanding. Additionally, the quantitative study focused on the opinions of a relatively small number of motivated GPs and pharmacists (**Chapter 3**), and patient selection (**Chapter 4**) was non-random, potentially introducing bias based on inclusion criteria and the choice of patients by pharmacists and/or GPs. In the qualitative study involving patients (**Chapter 4**), a potential limitation is the one-year gap between the MR and the research interview, which could introduce recall bias. For the questionnaire regarding the key elements for the quality assessment of MR3 (**Chapter 5**), there may have been a small possibility of bias among those without an interest in MRs because they would have been less inclined to participate in our survey. Furthermore, in the quality assessment of the MR3 reports (**Chapter 6**), one limitation was the availability of two reporting options in the first subproject, hindering a comprehensive comparison of the scoring. The anonymized reports in both subprojects did not allow for a complete assessment of all aspects of MR3s, such as evaluating plain and comprehensible language with the patient. Another limitation was the potential inconsistency in researcher evaluations. In subproject 1, a single researcher conducted the report analysis, consulting senior researchers when uncertainty arose, while in subproject 2, two researchers with the option to seek guidance from senior researchers were involved. Establishing a manual guiding a uniform scoring process could prove beneficial for future applications.

Analysing the strengths, this study marked the initial endeavours involving MR3 in community pharmacies in Belgium. Additionally, the methodology stands out for its integration of diverse study designs and its application of a mixed-method approach, incorporating both qualitative (interviews) and quantitative (questionnaires, report analyses) research. Another noteworthy strength is the dedicated effort in Chapter 1 to provide clarity on definitions, types, and the historical context of medication reviews MR. The research extensively explored the perspectives of patients in **Chapter 4**, a dimension often overlooked in studies. Additionally, it reflects the enthusiasm of participating physicians and pharmacists, shedding light on both their engagement and the obstacles to practical implementation (**Chapter 3**). Furthermore, the study represents the pioneering effort to identify key elements for quality assessment of MR3 (**Chapter 5**) and to evaluate MR3 quality using a scoring system (**Chapter 6**). This approach provides transparency regarding

pharmacists' actions during MR3. Establishing a manual to guide a uniform scoring process would be advantageous for future applications.

7.2 Future perspectives

7.2.1 Prospects for future implementation

The successful implementation of services relies heavily on their uptake. Initiatives, including ongoing studies, have been launched to drive and enhance the implementation process. To facilitate the broader implementation of MR3, one may consider employing the six steps in quality intervention development (35). These six steps encompass: [1] define and understand the problem and its causes, [2] identifying which causal or contextual factors are modifiable: which have the greatest scope for change and who would benefit most, [3] identify how to bring about change: the change mechanism, [4] identify how to deliver the change mechanism, [5] test and refine on small scale and [6] collect sufficient evidence of effectiveness to justify rigorous evaluation/implementation.

Our study revealed that the majority of community pharmacists considered MR3 to be the most effective form of medication reviews in a community pharmacy. Yet, some pharmacists acknowledged difficulties in initiating this type of medication review, specifically citing its time-consuming nature, a concern they believed would be less pronounced with a type 2a MR (MR2a). It's noteworthy that this study was conducted prior to the reimbursement for MR2a, which became applicable from April 2023 in Belgium. While this development is positive, our concerns linger about the necessity of specific laboratory values and the patient's medical history for optimizing the value of MRs. Participating pharmacists and physicians highlighted the crucial role of the medical record in preparing a high-quality MR. All GPs unanimously agreed that pharmacists need access to a patient's medical file. Furthermore, the majority of the interviewed GPs underscored the importance of laboratory values, specifically focusing on kidney function and liver values, as essential parameters for conducting a comprehensive MR. Crucial in this context is the introduction of a secure digital method for exchanging data, as it will contribute to a positive impact on the time investment. Initial steps have already been taken for this purpose (36).

On a broader note, studies indicate that the participation of pharmacists in practice research is influenced by the research design (35). Clear descriptions, flexible time management options, straightforward patient inclusion processes, and task delegation possibilities can all contribute to increased participation (37). Improved time management is expected to play a crucial role in the continued implementation of various pharmaceutical care tasks in pharmacy settings. Regardless of how well-designed a service may be, practical time allocation is essential for successful implementation. Moreover, skills associated with coordination, communication, and planning in the context of delivering cognitive pharmaceutical services are highlighted as crucial elements (38). Adequate remuneration will also be necessary, encompassing both pharmacists and physicians. In an Australian initiative, compensation was granted to GPs for their consultations, phone discussions with pharmacists, and participation in conferences involving the GP, pharmacist and other healthcare team members. Pharmacists received remuneration for home visits, medication reviews (including conference participation), and phone discussions with the GP (39).

In the current Belgian context, pharmacists are already remunerated for MR2a, but the overall reimbursement model is predominantly influenced by the volume of dispensed medicines. The disparity between the value provided by pharmacists and the reimbursement structure underscores the importance of a thorough assessment of the reimbursement system to promote effective care monitoring practices. This imperative for a shift is acknowledged in other countries as well (40-42). In this context, Belgium lags behind other (European) countries.

When evaluating the quality of MRs, the key elements for quality assessment can be applicable in different contexts, including self-assessment, peer evaluation, or external audit. Instead of employing the entire list of criteria for auditing, which can be time-consuming, this study proposes an alternative approach. It suggests using a random subset of criteria, with their frequency weighted based on the rankings obtained from the survey. This approach has the potential to enhance the efficiency of the auditing process while safeguarding against reactive subversion (43). Among the criteria that proved challenging to evaluate, many were considered (very) important according to previous research. Hence, it is vital not to disregard these aspects when comprehensively assessing the quality of MR3s. PROMs and PREMs could serve as valuable tools for this purpose. By integrating PROMs and PREMs, a more thorough evaluation of MR3 quality can be attained (37).

The careful selection of patients for MR3 is an aspect that requires further consideration. In our research, there was a significant divergence in opinions among the participating pharmacists and GPs regarding the appropriateness of the inclusion criteria. While many pharmacists and GPs found the age criteria in the pilot project too restrictive and advocated for the inclusion of younger patients with complex needs, some healthcare providers expressed the view that patients with excessively complex therapies, psychiatric issues, or limited awareness might be better excluded, particularly for pharmacists with limited experience with MR3. In the subprojects on rheumatoid arthritis and type 2 diabetes, the age restriction has been accordingly removed. In cases of multimorbidity, where patients consult multiple specialists in addition to their GP, all pharmacists believed it would be valuable to involve these specialists in the medication review. Most patients in our research, especially those who are polymedicated or have limited understanding of their medications, would recommend the MR service to other patients. Nevertheless, a medication review can be pertinent for all patients with chronic conditions necessitating prolonged drug use, aiming to optimize prescription effectiveness and mitigate the long-term risks associated with drug use (44). In European countries where MR3 is available, the most common overlapping selection criterion is patients taking more than five long-term medications. Additionally, selection criteria in some cases are influenced by financial aspects, as observed in a German project where the patient's insurance status determined the selection (6).

7.2.2 Future research directions

During this study, novel areas for further research came to light. For comparing studies, it is crucial to introduce standardization and clarity regarding the type and content of MRs (25). In light of our findings and motivated by current advancements (12, 39, 45-58), we propose that these issues be addressed in forthcoming research.

- How best to reimburse physicians and pharmacists for MR3? Healthcare providers emphasized the implementation challenge in the absence of reimbursement. If reimbursement is instituted, thoughtful organization in Belgium is essential. The fee might fluctuate based on the time invested and for example the complexity of the case.
- How do GPs react to pharmacists' suggestions? This knowledge will play a pivotal role in optimizing collaborative efforts and enhancing patient care. Issues or challenges on a global scale that arise during the MR3 process can be addressed, such as in a medico-pharmaceutical consultation.
- Which target group would benefit most from type 3 MR? Research into this topic is important, but simultaneously, it is essential to place trust in the expertise of physicians and pharmacists, as they often possess insight into which patients require a MR3.
- What are the perspectives and roles of other stakeholders and potential payers, such as insurance and private insurers and other healthcare providers?

- Wat is the clinical impact of MR3, given the diversity of the population and the intricacy of the intervention? The BRANT-MERQS scoring table can be used to help monitor quality. Furthermore, conducting a patient survey using PROMs and PREMs is crucial to obtain a patient perspective on the services.
- What is the relationship between the clinical outcomes and the quality of MR3?
- How to improve pharmacist-physician collaboration? Should this be structured or ad hoc? How can we foster the growth of trust on both sides?
- Should the pharmacist perform MR3s within the pharmacy, in the patient's home to observe their medication management, or could this also be conducted in a healthcare provider's office, such as a physician's office where various healthcare professionals may be present? How can we actively and structured involve other healthcare providers such as nurses, hospital pharmacists, informal carer and specialists in a MR3?
- How can the issue of time management be more effectively tackled within the pharmacy? Can theories like Multicriteria Decision Analysis (MCDA) and Lean Six Sigma (LSS) help?
- How can we engage the informal caregiver in the process of MR, and what functions do they perform in this context?
- Which technological or computerized assistance can enhance the MR process, encompassing tools like online questionnaires for patients at home, compiling patient data, and providing scientific support?
- Medication review initiatives are currently in progress within nursing homes in Belgium. What insights can we gain from this setting for community dwelling patients, and conversely, what lessons can be applied back to the former setting?

7.3 Practical recommendations

This PhD thesis imparted several valuable insights for pharmacy practice, including:

1. Initiate the MR3 process with a small, motivated group of pharmacists capable of providing effective guidance for the healthcare providers. Utilize this group of healthcare providers to inspire others, fostering organic expansion within the group.
2. Inform and involve the patient thoroughly in the MR3 process to make the service even more patient-centred.
3. Ensure appropriate compensation for both the participating physician and pharmacist, potentially adjusting it in proportion to the complexity of the patient's medication and their Social Determinants of Heath (SDOH). It is a strategic decision that will benefit the healthcare system.
4. Offer high-quality in-service training, not only for newly starting pharmacists but also to support those actively participating. Focus on peer-education and lessons on accurate interpretation of laboratory values, as these were identified as crucial topics.
5. Strengthen the collaboration between GPs and community pharmacists, ideally employing a structured approach, to establish authentic trust for efficient teamwork in the MR3 process and fairly compensating collective efforts. This may include medico-pharmaceutical consultations, as well as individual collaborations to discuss specific patients.
6. Facilitate digital accessibility for data sharing between GPs and community pharmacists, employing a platform easily accessible to both healthcare providers through their software programs.
7. Avoid allowing the administrative departments to make decisions regarding the required administration independently; instead, involve all stakeholders and collaborate closely with software suppliers in the decision-making process, so that the healthcare providers can allocate time for MR3.

8. Begin with non-complex cases and emphasize the process of MR3, for both healthcare providers and patients. After successfully completing these initial reviews, proceed to handle more complex ones.
9. Implement continuous quality monitoring from the outset, utilizing the BRANT-MERQS tool. This enables pharmacists to grasp essential aspects and facilitates ongoing improvement as they become more familiar with the process.
10. For broader implementation, maintain the organization of training sessions to increase the group of trained pharmacists, enabling the conduct of larger-scale studies that delve into sustainable, high-quality implementation practices.

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Summary

Medication reviews type 3 (MR3s) represent a collaborative initiative involving both healthcare providers and patients, with the overarching goal of attaining optimal medication therapy and enhancing overall health outcomes. On a global scale, there is a growing interest in medication review practices, evident in the initiation of pilot projects and subsequent widespread implementation efforts. This thesis mainly focused on the questions related to the sustainable deployment of MR3s in community pharmacies in Belgium. This involved an exploration of the factors influencing successful implementation like quality assessment, potential challenges encountered, and strategies to ensure the enduring and effective incorporation of MR3 practices in the Belgian healthcare system.

Chapter 1 provides a general introduction. In a first part we endeavoured to clear up the confusion surrounding the different definitions, classifications, and historical underpinnings of MR. Subsequently we directed our attention to the evolution, in Belgium, of pharmaceutical care with a focus on medication review. This part also described the origin and local context of this project as part of the training and professional development initiatives of KAVA and the subsequent academic involvement.

Chapter 2 provides an overview of the aims and structure of this doctoral thesis.

Chapter 3 discusses the perspectives and experiences of community pharmacists and general practitioners (GPs) active in a MR3 pilot project. This startup affirmed the preparedness of Belgian healthcare professionals to participate in MR3 and generated positive feedback from GPs and pharmacists. The input from these healthcare professionals indicated a positive outlook on the potential benefits of MR for patients and informed the subsequent training initiatives. This enthusiasm for MR during the pilot study points to its future potential, but further efforts will be needed to realize the widespread adoption of this service in Belgian community pharmacies.

Chapter 4 examines the views and experiences of patients who took part in a MR3 pilot project. They generally appreciated the attention and time invested by pharmacists during MR3s. However, some patients were not fully aware of the service's purpose and goals, making it crucial to offer them a thorough explanation of MR3. This strategy is expected to alleviate potential stress for patients when they are invited to engage in MR3 and during subsequent inquiries about their medications. Patients overwhelmingly expressed positive feedback regarding this new service, providing valuable insights for its further development and implementation. Improved communication by pharmacists and GPs to patients regarding the goals and components of this type of MR is, however, crucial.

Ensuring a high level of quality is essential for the effective implementation of MR3 in community pharmacies. Currently, there is, however, no tool or instrument available that can thoroughly evaluate the overall quality of MR3. This led to research into the creation of quality criteria (as detailed in **Chapter 5**) and the formulation of a scoring table (as described in **Chapter 6**), both specifically designed for MR3.

To establish the quality criteria, a ranking questionnaire was developed and deployed as described in **Chapter 5**. A panel of pharmacists from Belgium and the Netherlands, were tasked with ranking distinct quality criteria based on their perceived importance. Our investigation unveiled a broad consensus on the key elements crucial for evaluating the quality of MR3. Eight key statements emerged as integral components to be incorporated into a comprehensive MR3. Minor differences, related to the participants' level of experience, were noted.

Building upon the empirical evidence gathered from the study described in **Chapter 5** and incorporating a small number of additional criteria proposed by participants, we initiated the creation of a streamlined and effective quality instrument for medication reviews as outlined in **Chapter 6**. This process included the development of a scoring table, called BRANT-MERQS, with a thorough examination of all the quality criteria identified in the preceding study. Data from two subsequent projects were examined, one involving patients with rheumatoid arthritis (RA) and another involving patients with type 2 diabetes mellitus (T2DM). This evaluation method clearly demonstrated its viability for assessing MR3 reports submitted by the community pharmacists, through requiring some improvements in the handling of the scoring table.

The reports received favourable to very favourable scores, although it is premature to establish a definitive benchmark value for the MR3 quality. Certain criteria were not directly quantifiable from the reports, and BRANT-MERQS may be further enhanced through combination with Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs). In this regard, we observed the additional benefit of incorporating patient experiences in the initial pilot project, as demonstrated by a qualitative survey. The quality criteria established in the **Chapter 5** study are crucial, illustrating the diversity in conducted MRs and underscoring the necessity for rigorous control before initiating outcome studies. The BRANT-MERQs scoring table serves as both a self-assessment tool for pharmacists initiating the process and a peer assessment tool. It also provides insight for other stakeholders and third payers into the specific elements addressed during MR3. Nevertheless, this research underscores the significance of practical elements, such as the availability of a template or the provision of telephone feedback opportunities.

Chapter 7 presents a comprehensive discussion and exploration of future perspectives. Furthermore, the thesis's strengths and weaknesses are highlighted. Finally, the section includes recommendations for the implementation of MR3 in Belgian community pharmacies, accompanied by a delineation of areas that deserve further research.

In conclusion, we demonstrated the feasibility of implementing MR3 in pilot projects and identified key elements for the quality assessment of MR3. In addition, we demonstrated a remarkable level of enthusiasm for MR3 among both healthcare providers and patients. This research not only opens up new areas for further study, but also provide practical recommendations for enhancing clinical practice and patient care through the implementation of MR3.

Samenvatting

Het uitvoeren van een medication review of medicatienazicht type 3 (MR3) vereist een goede samenwerking tussen zorgverleners en patiënten, met als overkoepelend doel medicamenteuze therapie te optimaliseren en de algehele gezondheidsresultaten te verbeteren. Wereldwijd neemt de belangstelling voor medication reviews toe, wat zich vertaalt in verschillende pilootprojecten en implementatieprojecten op grotere schaal. Deze thesis richtte zich voornamelijk op vragen met betrekking tot de duurzame inzet van MR3's in Belgische openbare apotheken. Dit omvatte het onderzoeken van factoren die van invloed zijn op succesvolle implementatie, zoals kwaliteitsbeoordeling, mogelijke uitdagingen en strategieën om ervoor te zorgen dat MR3-praktijken duurzaam en effectief worden geïntegreerd in het Belgische gezondheidszorgsysteem.

Hoofdstuk 1 biedt een algemene inleiding. In een eerste deel trachtten we de verwarring rond de verschillende definities, classificaties en historische achtergronden van MR op te helderen. Vervolgens richtten we onze aandacht op de evolutie van farmaceutische zorg in België, met een focus op medication review. Dit hoofdstuk beschrijft ook de oorsprong en lokale context van dit project als onderdeel van de opleidings- en professionele ontwikkelingsinitiatieven van KAVA en de daaropvolgende academische betrokkenheid.

Hoofdstuk 2 geeft een overzicht van de doelstellingen en structuur van deze doctoraatscriptie.

Hoofdstuk 3 bespreekt de perspectieven en ervaringen van apothekers en huisartsen die betrokken waren bij een MR3-pilootproject. Het onderzoek polste de bereidheid van Belgische zorgprofessionals om deel te nemen aan MR3 en genereerde positieve feedback van huisartsen en apothekers. De input van deze zorgprofessionals duidde op een positieve kijk op de potentiële voordelen van MR voor patiënten en informeerde de daaropvolgende opleidingsinitiatieven. Hoewel het enthousiasme voor MR tijdens de pilootstudie wijst op toekomstig potentieel, zullen verdere inspanningen nodig zijn om de brede acceptatie van deze dienst in Belgische openbare apotheken te realiseren.

Hoofdstuk 4 onderzoekt de meningen en ervaringen van patiënten die deelnamen aan een MR3-pilootproject. De patiënten waardeerden over het algemeen de aandacht en tijd die apothekers investeerden tijdens MR3's. Sommige patiënten waren echter niet volledig op de hoogte van het doel van de dienstverlening, wat aantoont dat een grondige uitleg voor de start van MR3 cruciaal is, wat mogelijk de stress die patiënten kunnen ervaren wanneer ze worden uitgenodigd om deel te nemen aan MR3 kan verminderen. Patiënten uitten overwegend positieve feedback over deze nieuwe dienstverlening, wat waardevolle inzichten opleverde voor verdere ontwikkeling en implementatie. Verbeterde communicatie door apothekers en huisartsen naar patiënten over de doelen en onderdelen van dit type MR is echter cruciaal.

Daarnaast is het waarborgen van een hoog kwaliteitsniveau essentieel voor de effectieve implementatie van MR3 in openbare apotheken. Momenteel is er echter geen instrument beschikbaar dat de algehele kwaliteit van MR3 grondig kan evalueren. Daarom is onderzoek nodig naar de ontwikkeling van kwaliteitscriteria (zoals gedetailleerd in **Hoofdstuk 5**) en de formulering van een scoringsinstrument (zoals beschreven in **Hoofdstuk 6**), beide specifiek ontworpen voor MR3.

Om de kwaliteitscriteria vast te stellen, werd een rangschikkingsvragenlijst ontwikkeld en ingezet zoals beschreven in **Hoofdstuk 5**. Een panel van apothekers uit België en Nederland kreeg de taak om onderscheidende kwaliteitscriteria te rangschikken op basis van hun belangrijkheid. Ons onderzoek bracht een brede consensus aan het licht over de cruciale elementen voor het beoordelen van de kwaliteit van MR3. Acht essentiële verklaringen kwamen naar voren als integrale componenten die moeten worden opgenomen in een uitgebreide MR3. Kleine verschillen, gerelateerd aan het ervaringsniveau van de deelnemers, werden opgemerkt.

Op basis van de bevindingen die zijn verzameld uit de studie die is beschreven in **Hoofdstuk 5**, en rekening houdend met enkele extra criteria voorgesteld door de deelnemers, zijn we gestart met de ontwikkeling van een efficiënt en doeltreffend kwaliteitsinstrument voor medicatiebeoordelingen, zoals beschreven in **Hoofdstuk 6**. Dit proces omvatte de ontwikkeling van een scoringsinstrument, genaamd BRANT-MERQS, met een grondige evaluatie van alle kwaliteitscriteria geïdentificeerd in de voorafgaande studie. Gegevens van twee daaropvolgende projecten werden onderzocht, één met patiënten met reumatoïde artritis (RA) en een ander met patiënten met type 2 diabetes mellitus (T2DM). Deze evaluatiemethode toonde duidelijk aan dat het levensvatbaar is voor het beoordelen van MR3-rapporten ingediend door de openbare apothekers, zij het met enkele verbeteringen in de verwerking van het scoringsinstrument. De rapporten kregen gunstige tot zeer gunstige scores, hoewel het te vroeg is om een definitieve benchmarkwaarde voor de kwaliteit van MR3 vast te stellen. Bepaalde criteria waren niet direct kwantificeerbaar uit de rapporten, en BRANT-MERQS kan verder worden verbeterd door het te combineren met Patiëntgerapporteerde Uitkomstmaatregelen (PROM's) en Patiëntgerapporteerde Ervaringsmaatregelen (PREMs). In dit opzicht merkten we het aanvullende voordeel op van het opnemen van patiëntervaringen in het initiële pilotproject, zoals aangetoond door een kwalitatieve enquête. De in hoofdstuk 5 vastgestelde kwaliteitscriteria zijn cruciaal, illustreren de diversiteit in uitgevoerde MR's en benadrukken de noodzaak van rigoureuze controle voordat er gestart kan worden met uitkomststudies. De BRANT-MERQS-scoretabel dient zowel als een zelfevaluatietool voor apothekers die het proces initiëren als een peer-evaluatietool. Het biedt ook inzicht voor andere belanghebbenden en derdebetalers in de specifieke elementen die worden aangepakt tijdens MR3. Desalniettemin benadrukt dit onderzoek het belang van praktische elementen, zoals de beschikbaarheid van een template of de mogelijkheid van telefonische feedback.

Hoofdstuk 7 presenteert een uitgebreide discussie en verkenning van toekomstperspectieven. Bovendien worden de sterke en zwakke punten van de thesis belicht. Ten slotte bevat het gedeelte aanbevelingen voor de implementatie van MR3 in Belgische openbare apotheken, vergezeld van een afbakening van gebieden die verder onderzoek verdienen.

Samenvattend toont deze thesis de haalbaarheid aan van de implementatie van MR3 in pilootprojecten en identificeert het sleutelelementen voor de kwaliteitsbeoordeling van MR3. Daarnaast tonen we een opmerkelijk enthousiasme voor MR3 bij zowel zorgverleners als patiënten. Dit onderzoek opent niet alleen nieuwe gebieden voor verder onderzoek, maar levert ook praktische aanbevelingen op ter verbetering van klinische praktijk en patiëntenzorg door de implementatie van medication review type 3.

Curriculum Vitae

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EXPERIENCE

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Community pharmacist
Moderator for different medical pharmaceutical consultation (MFO) programs certified by NIHDI
Pharmaceutical Expert in Covid vaccination centre
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Proper use of medicines coach asthma for Association of Pharmacists Belgium (APB)
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Co-operator pharmaceutical care department Meduplace (KAVA)
January 2017 – January 2021
Project coordinator department vocational development KAVA
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Pharmacist
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Pharmacy Lloyds Pharma Brasschaat: August 2014 – September 2014
Internship pharmacist
Pharmacy Eelen 's-Gravenwezel: August 2013 - January 2014
Hospital ZNA Jan-Palfijn Merksem: July 2013
Student job
Pharmacy Broeckx Antwerp: July 2012
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Janssen Pharmaceutica department Toxicology/Pathology: August 2009

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PhD Student
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Laboratory of Physiopharmacology (UA) and Research Group Clinical Pharmacology and Clinical Pharmacy (VUB)
Implementation of medication review type 3 in Flanders, Belgium
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Internship: Department of Cardiology, CARIM School for Cardiovascular Diseases
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Master thesis: The role of non-coding RNAs in regulation of cardiac autophagy in heart failure
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Master of Science (MSc), Drug development: Pharmacist
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Bachelor of Science (MSc), Pharmaceutical Sciences
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ADDITIONAL COURSES

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The Global Health Network
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Basic principles of statistics
StatUA, University of Antwerp
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PIAF education Medication Review
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A1 PUBLICATIONS

- Robberechts A, Brumer M, Garcia-Cardenas V, et al. Medication Review: What's in a Name and What Is It about?. Pharmacy (Basel). 2024;12(1):39. Published 2024 Feb 19. doi:10.3390/pharmacy12010039
- Robberechts A, Michielsen M, Steurbaut S, De Meyer GRY, De Loof H. Key elements in the quality assessment of a type 3 medication review. Front Pharmacol. 2023;14:1258364. Published 2023 Oct 4. doi:10.3389/fphar.2023.1258364
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- Leysen B, Rydant S, Dom G, Robberechts A, Matheï C, De Loof H. Hoe opioïden veilig voorschrijven? Huisartsen en apothekers samen op Medisch-Farmaceutisch Overleg. Huisarts Nu 2020;49:12-16.

OTHER PUBLICATIONS

- Robberechts A. (2023). "Medication review type 3: hoe organiseer je dit lokaal?" AFT 2: 20-24.
- Robberechts A. (2023). "ESCP congres Praag 2022." AFT 1: 18-19.
- Robberechts A. (2022). "Kritisch omgaan met bronnen." AFT 5: 23-27.
- Robberechts A. (2022). "Voorschrift gestript: Ozempic®." AFT 3: 20-22.
- Robberechts A. (2022). "Medication Use Review (MUR) - iets voor jou?" AFT 3: 18-19.
- Robberechts A. (2022). "Opleidingen medication review: antwoord op al je vragen!" AFT 1: 20-21.
- Robberechts A. (2021). "Voorschrift gestript: Behandeling van reuk- en smaakstoornissen door COVID-19-infectie." AFT 4: 20-23.
- Robberechts A. (2021). "Opvolgtraject medication review 2021." AFT 3: 19-21.
- Robberechts A. (2020). "Voorschrift gestript: Switch tussen opioïden." AFT 7: 24-25.
- Robberechts A. (2020). "Medication review op KAVA: waar staan we na twee jaar?" AFT 6: 28-32.
- Robberechts A. (2020). "Adviezen voor jonge ouders: farmacokinetiek & farmacodynamiek bij kinderen " AFT 6: 18-21.
- Robberechts A. (2019). "Voorschrift gestript - Neus Keel Oor." AFT 3: 21-25.
- Robberechts A. (2019). "Interacties - complexvorming en serotonerg effect." AFT 2: 24-26.
- Robberechts A. (2019). "Medication review." AFT 1: 12-14.
- Robberechts A. (2018). "Medication review." AFT 6: 30-33.
- Robberechts A. (2018). "Van medicatieschema naar medication review." AFT 3: 20-21.
- Robberechts A. (2017). "Orale oncolytica." AFT 3: 28-29.
- Robberechts A. (2016). "Welke rol neemt de apotheker op bij chronische nierinsufficiëntie?" AFT 9: 16.
- Bodequin C, Robberechts A. (2016). "Een medicatieschema op maat van de patiënt." AFT 7: 22-23.
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- Robberechts A. (2015). "Multidisciplinair overleg ... kansen voor de apotheker!" 6: 18-19.
- Van Pottelbergh G, Robberechts A. (2015). "Farmaceutische zorg bij nierinsufficiëntie." AFT 6: 6-12.

CONFERENCE PATICIPANTIONS: oral presentations

Medication review type 3: experiences of general practitioners
FIP PPR Summer Meeting (Granada, Spain)
July 2023

Het ontwerpen van een vragenlijst als aanzet voor een medication review opportuniteiten en obstakels
PRISMA symposium (Amersfoort, The Netherlands)
May 2023

Medication review type 3: de ervaringen van huisartsen: Hiaten in de samenwerking tussen apotheker en huisarts
PRISMA symposium (Amersfoort, The Netherlands)
May 2023

Workshop management of diabetes in patients with multimobidity and medication review
ESCP Spring workshop congress (Antwerp, Belgium)
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Medication review in de Belgische openbare apotheek: Implementatie-struikelblokken vanuit het perspectief van apothekers en artsen
Pharmcare (APB) (Zemst, Belgium)
September 2019

CONFERENCE PATICIPANTIONS: poster presentations

Medication review in Belgian community pharmacy: challenges for further implementation
FIP PPR Summer Meeting (Granada, Spain)
July 2023

Quality assurance of a medication review type 3: what are the key elements to assess quality?
FIP PPR Summer Meeting (Granada, Spain)
July 2023

MASTER THESIS SUPPORT

- Eline Tobback, Optimizing medication review type 3 quality through the implementation of a streamlined and standardized assessment framework, UAntwerpen, 2024
- Laura Poppe en Margot Puttemans, Research on the quality of medication review type 3 in the context of diabetes mellitus type 2, UAntwerpen, 2023
- Pauline Bleys, Medication review type 3: de ervaringen van huisartsen: Hiaten in de samenwerking tussen apotheker en huisarts, UAntwerpen, 2023
- Sarah Kokx, Evaluatie van 'Medication Regimen Complexity' en aanpassingen aan de lokale context, UAntwerpen, 2022
- Andjela Durmis, Het ontwerpen van een vragenlijst als aanzet voor een medication review: opportuniteiten en obstakels, UAntwerpen, 2022
- Sana Boumazzoughe en Youssra Azrout, Mening van huisartsen rond type III medication review, UAntwerpen, 2021
- Kaat Stas, Medicatiereview type III bij reumatoïde artritis, UAntwerpen, 2021
- Malika Solombaeva, Bevraging bij cardiologen over hun verwachtingen van apothekers met betrekking tot medication review en gerelateerde randvoorwaarden, VUB, 2021
- Karen De Bondt, Hulpmiddelen bij het uitvoeren van een medication review. Wat werkt er? Wat is nuttig? Is een stappenplan voor medication review type 3 inhoudelijk haalbaar in de praktijk?, UAntwerpen, 2020
- Sofie Bontenakel, Wat denken geriaters over medication review door de Vlaamse apotheker?, UAntwerpen, 2020
- Melissa Michielsen, Kwaliteitsbewaking bij medication review: hoe doen we dit op een efficiënte, gebruiksvriendelijke manier?, UAntwerpen, 2020
- Laura Van Loon, Medication Review: wat is het standpunt van de patiënten, UAntwerpen, 2019
- Hanne Vanhoof, Medication Review door een apotheker. Wat zijn de hindernissen om reviews uit te voeren in de praktijk, UAntwerpen, 2019
- Wendy Nuyens, Wat verwachten nefrologen van een medication review, wat verwachten ze van apothekers?, UAntwerpen, 2019
- Celine De Petter en Lindsey Van Loon, Medication Review in de Belgische apotheek: struikelblokken gezien vanuit het standpunt van de artsen en apothekers, UAntwerpen, 2018

TEACHING ACTIVITIES

Training sessions and projects for community pharmacists

- Advanced medication review: IPSA and Meduplace. 2022, 2023 and 2024
- Apinto: type 2a medication review (MR2a): IPSA. 2023
- Info sessions GUM medication review (MR2a): IPSA, OPHACO, APB and Meduplace (KAVA). 2023
- Medication Use Review trainings: Meduplace (KAVA). 2022
- Follow-up project MR: type 2 diabetes: Meduplace (KAVA). 2022
- Follow-up project MR: Rheumatoid Arthritis: Meduplace (KAVA). 2021
- Workshop: chronic management of pain: KAVA. 2021
- Training of MR3: Meduplace (KAVA). 2017,2018, 2019, 2021 and 2022
- Update on pain and hypertension medication: KAVA. 2017, 2018
- Workshops chronic kidney failure: KAVA. 2016

Training sessions for community pharmacists and GPs:

- Info moment Medico-Pharmaceutical Consultation MR3. 2021, 2022 and 2023
- Moderator for different Medico-Pharmaceutical Consultation programs certified by NIHDI (MR3, MR2a, discontinue benzodiazepines, chronic kidney failure and GP & family pharmacist in duo.

Teaching course for nurses:

- Polypharmacy and its risks: Postgraduate cardiology nurses KDG University of Applied Sciences and Arts. 2019, 2022 and 2023
- Update course on pain medication; medication for sleep and anxiety disorders: 2021, 2022 and 2023

EXTRA INFORMATION

Student faculty member, member of the commission of education and faculty board of the Master of Science (MSc), Drug development: Pharmacist, University of Antwerp

2012 – 2014

Student faculty member, member of the commission of education and faculty board of the Bachelor of Science (MSc), Pharmaceutical Sciences, University of Antwerp

2009 – 2012