Medication Safety

in Municipal Health and Care Services

Rose Mari Olsen and Hege Sletvold (ed.)

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CHAPTER 1

Introduction: Medication Safety in Municipal Health and Care Services

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Background

Medicines constitute an essential part of healthcare delivery, and help to prevent or treat illness, influence quality of life, and generally increase life expectancy. However, medications can cause harm if prescribed irrationally, dispensed or used incorrectly, and monitored or followed up insufficiently (Ofori-Asenso & Agyeman, 2016). Furthermore, medication harm can be a result of errors, accidents, or communication problems (World Health Organization (WHO), 2017). Unsafe medication management and practices have consequences on both the patient and healthcare system level in the form of injuries, failure of therapy, worsening of illness, increased use of healthcare services, and large financial expenditures (Donaldson et al., 2017; Elliot et al., 2020; Panagioti et al., 2019).

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We understand medication safety as freedom from avoidable harm while using medicines, or those actions that avoid, prevent, or correct harm caused by medicines. Since 2017, WHO has focused on medication safety in the global patient safety challenge, "Medication Without Harm", where the goal is to reduce severe, avoidable medication-related harm (Donaldson et al., 2017). Furthermore, medication safety is central in WHOs Global Patient Safety Action Plan 2021–2030, where the goal is to achieve the maximum possible reduction in avoidable harm due to unsafe healthcare (WHO, 2021).

Rational use of medicines and safe medication management have been important focus areas in patient safety initiatives both in Norway (The Norwegian Directorate of Health, 2020) and internationally (Bates & Singh, 2018). Generally, the past 20 years have witnessed a positive development in solutions for patient safety measures, however there remains some inconsequence in clinical practice implementation (Bates & Singh, 2018). Most of the documentation relating to preventable patient harm and medication errors in healthcare originates from studies conducted in general hospitals or in advanced speciality care (Panagioti et al., 2019; WHO, 2016). However, the risks present in primary care may differ from the hospital setting, since there are differences in the type of clinical problems, medicine use, and the organization and systems of medication practices (Bates & Singh, 2018; WHO, 2016). Therefore, there is still a need to seek more knowledge, and focus on the prevention of medication harm in primary care settings, that is, municipal health and care services, which encompass a high patient volume.

The Scope of the Anthology

In this anthology, we want to showcase the challenges of medication management and the rational use of medicines in municipal health and care services, and present various strategies and measures related to medication safety. The anthology hopes to raise awareness, engage, and enable discussion of initiatives and strategies to improve patient safety related to medications in municipal health and care services. Furthermore, this is a scientific anthology, which can create a basis for

further research to promote safe medication management and rational use of medicines.

The anthology will be of interest primarily to healthcare professionals, academic staff, researchers, policymakers, and managers in healthcare services. Furthermore, anyone involved in, or concerned with, medication safety will hopefully benefit from reading the anthology.

Structure, Chapters, and the Contributors

The anthology is structured according to the four domains of WHOs strategic framework of the third global patient safety challenge, "Medication Without Harm", wherein medications are described as able to cause inadvertent harm: 1) patients and the public, 2) medicines, 3) healthcare professionals, and 4) systems and practices of medication (Donaldson et al., 2017).

This anthology includes 17 chapters compiled through contributions from 35 researchers who represent a wide range of disciplines, and who have experience from different levels of healthcare services, and from different parts of the research and education sectors. Thereby, the anthology provides valuable insights based on expertise in the field of medication safety. The material investigates different aspects of medication safety in municipal health and care services, and highlights a wide range of ongoing initiatives and practices.

Part One: Patients and the Public

Part one consists of three chapters, all relating to patients' opportunities to play their part in ensuring safe medication use. A recognized challenge to medication safety is that users of healthcare services are often forced to be passive recipients of medicines, without being empowered to participate in making their own medication use safer (Donaldson et al., 2017; WHO, 2021). In chapter two, Olsen and Sletvold present a systematic review of randomized controlled trials (RCT) testing the effectiveness of patient engagement interventions to enhance medication safety in long-term care. Five RCTs were identified, representing extensive

heterogeneity in intervention designs, populations, settings, and outcome measures. Although three RCTs report statistically significant effects of patient engagement interventions on medication safety, the limited body of evidence suggests that future research is needed to guide the practice field and stakeholders.

Medication treatment in cancer care has a potentially high risk of adverse events. In chapter three, Haukland and Bergerød provide new information on how to involve patients and next of kin to prevent unnecessary adverse events related to systemic anticancer treatment. They suggest essential components for preserving patient involvement, and argue that the use of electronic patient-reported outcomes can empower patients in everyday situations, and ensure safety for both patients and their next of kin.

Do patients know what medications they are prescribed? This question is raised by Andfossen and Bergh in chapter four, reporting a study among older patients receiving home healthcare in Norway. By comparing patients' answers as to what medications they were using to the list of prescribed medications for the person, the authors revealed that most of the participants were aware of their medication regimens, although a significant proportion of them were not fully aware. The study results emphasize the need for healthcare personnel to inform patients about their prescribed medications.

Part Two: Medicines

In part two, three chapters deal with potential safety issues related to medicines. The number of available medicines is increasing, and there are increasingly complex medication regimens. Consequently, medication errors are widespread (WHO, 2016).

It is expected that healthcare professionals know how to handle and administer medicines, and that they seek reliable information if they are unsure. However, to what extent is relevant information about the medicine available? In chapter five, Zeiss and Amundstuen describe results from their review of the pharmaceutical preparation monographs in Felleskatalogen®, which is a frequently used source of information for

healthcare professionals administering medicines in Norway. They found that information relating to the modification of oral solid dosage forms varied widely, and that recommendations may be interpreted differently.

Medication interaction is a well-known yet often avoidable cause of patient harm (WHO, 2016). In chapter six, Waaseth, Rønning and Skeie report a study investigating the prevalence of interactions between dietary supplements and medication use in a general population of middle-aged women. Although the prevalence of high-risk interactions was low, the substantial potential for clinically significant interactions indicates that healthcare personnel should take dietary supplements into account when assessing the safety of medication use among their patients.

Assessing the scope and nature of avoidable harm from medicines, and strengthening the monitoring systems to detect and track this harm, is one of the specific objectives described in the medicine without harm strategic framework (WHO, 2017). In chapter seven, Mulac and Granås present an overview of methodologies for detecting adverse drug events and medication errors, and discuss the advantages and limitations of these methods. They reveal a great variation between the methods with regard to detection rate, and demonstrate that none of the methods alone can serve as a gold standard in monitoring medication safety. Instead, a combination of methods should be used to detect adverse drug events and medication errors.

Part Three: Healthcare Professionals

Part three contains six chapters that elucidate how healthcare professionals affect medication safety among patients in community settings. Healthcare professionals are known to pose a risk for medication safety through, for example, their involvement in medicine prescribing, dispensing, administration, and communication (Ofori-Asenso & Agyeman, 2016; WHO, 2017).

Nurses play an important role in medication management in all healthcare settings, but we lack knowledge about their involvement in interventions on medication safety in municipal health and care services. In chapter eight, Sletvold, Jordan, and Olsen describe how nurses can aid

adults in community care in taking their medicines as prescribed, thus achieving medication adherence. The chapter reports a systematic review, in which out of a total of 17 RCTs, four (23.5%) report significant effects on medication adherence, and seven (41,2%) report significant effects on clinical outcomes, such as blood pressure. The nurse-led interventions are typically complex, and target adherence through behaviour and knowledge strategies, such as motivational interviewing, adherence aids, patient education and eHealth components.

As healthcare professionals, pharmacists also contribute to medication safety in municipal health and care services. Chapter nine focuses on pharmacists and their actions to improve quality medication use among patients in nursing homes. In this review, Halvorsen describes and discusses how pharmacists contribute to medication safety on both the healthcare level and the system level. Examples of pharmacist actions are: collaboration in multidisciplinary teams; education in medication management; development of procedures for medication management; management of medication statistics; investigating costs; and facilitating tender rounds. Also, Halvorsen debates whether Norwegian municipalities and the healthcare system lack a strategy for effective use of pharmacists to ensure medication safety.

Medicines sometimes cause serious harm due to communication problems, and good communication between healthcare professionals and patients is vital (WHO, 2017). Chapter ten discusses patient-centered communication and the importance of effective communication skills among healthcare providers to ensure patient safety, and the appropriate use of medicines. In this literature review, Krogstad, Larsen, Holm, Landmark, and Granås explain several communication challenges in medicine information and counselling. Furthermore, the authors discuss experiences with medicine information relating to patient care in transition and at community pharmacies, with regard to for example, prescribed and over the counter medicines.

Healthcare professionals need access to information about patients' health and treatment to provide safe care. Chapter eleven expands our understanding of how healthcare providers experience using medication lists in managing medications used as needed. Based on a secondary

analysis of qualitative data, Nilsen and Bell found that medication lists are important tools to ensure medication safety. Healthcare providers expect updated and unambiguous medication lists. However, medication lists are often ambiguous, and this can pose a challenge for quality of care. Close collaboration with general practitioners is important, and the authors suggest medication reviews as a measure to maintain patient safety.

In chapter twelve, nurses and medical doctors in Norwegian nursing homes and home care services are participants in a qualitative study. Manskow and Kristiansen present in-depth documentation on how the study participants experience access to and exchange of core patient information (CPI). Nurses and medical doctors have extensive experience with situations of inadequate access to CPI, described through challenges of excessive time-consumption, frustration, uncertainty, dependence, complexity, and risk. These challenges are perceived as a threat to patient safety and quality of care, especially in relation to medicine information in patient transitions between levels of care.

Distractions and interruptions during the management of medicines are among factors known to influence medication errors (WHO, 2016). But how the healthcare professionals experience working under such work situations is less known. In chapter thirteen, Alteren elucidate nurses' perspectives on and experiences of work interruptions in nursing homes. Using Gadamer's hermeneutical circle, she developed a sample narrative based on own nursing and research experience, along with narratives shared by nurses during medicine rounds. She discusses the significance of the nurses' perspectives for safe medication management, and concludes that a work interruption can be interruptive or a source of knowledge important for medication treatment and care in nursing homes.

Part Four: Systems and Practices of Medication

The last part of the anthology includes four chapters focusing on aspects of systems and practices of medication. The systems, processes and procedures that healthcare professionals work with are often flawed or

dysfunctional, but can be made more resilient to errors and medication harm if they are well understood and designed (Donaldson et al., 2017). In chapter fourteen, Odberg and Aase describe facilitators of and barriers to safe medication administration in nursing homes. By using data from interviews with staff, and applying a socio-technical systems approach, they reflect on the work system complexity of nursing homes, and how this influences the safety of medication administration. Based on their findings, they suggest that future medication safety interventions in nursing homes should be multifaceted and involve all healthcare personnel, including leaders.

Multidose drug dispensing has in recent years become a common adherence tool for patients receiving multiple medications. But what effect does the tool have on patient safety? Drawing on 60 peer-reviewed articles, Jøsendal, Bergmo and Granås summarize in chapter fifteen the current evidence on the multidose drug dispensing system's effect on patient safety in home-dwelling patients. The studies indicate that multidose drug dispensing can increase medication adherence and reduce discrepancies in medication records. However, it may also result in more medication errors during discharge from hospitals, more inappropriate prescribing, and increase the number of drugs prescribed. The review shows that multidose drug dispensing systems can affect all steps in the medicine-use process, and the authors thus emphasize the need for involving all actors in the process and clearly defining their responsibilities.

Medication-related problems are a common yet potentially avoidable reason for hospital readmissions. In chapter sixteen, Glette and Wiig describe the role of medication management in hospital readmissions in Norwegian primary healthcare services. Drawing on interviews with general practitioners, physicians in nursing homes and hospitals, nurses and leaders in nursing homes, as well as observations in nursing homes, they describe how healthcare personnel perceive medication management as a factor influencing hospital readmissions. In addition, they explore which elements may lead to medication-related hospital readmissions from the primary healthcare service. According to the authors, the study illuminates the need for proper communication tools and well-functioning coordination routines regarding medication management,

as well as a need for expanding the knowledge healthcare personnel have of each other's activities and treatment capacities.

Inadequate medicines knowledge and experience are known to influence medication errors (WHO, 2016). One of the seven strategic objectives of the WHO global patient safety action plan 2021–2030, is to educate, skill, inspire and protect healthcare professionals so that they can contribute to the design and delivery of safe healthcare systems (WHO, 2021). In chapter seventeen, Knutsen, Johnsrud, Slorafoss, Haugen and Joranger report experience, competence and competence needs related to medication management among nurses working in home nursing care and in nursing homes. The vast majority of the nurses answering a quantitative questionnaire, deemed their own competence of medication management to be good or very good, but fewer had confidence in drug interactions, effects and adverse drug reactions of medicines. Few nurses had attended formal medication management training, and few reported making medication errors resulting in patient harm. Based on these results, there is an apparent need for a system that facilitates increased medicines competence and medication management practices among nurses in this context.

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Part One:

Patients and The Public

CHAPTER 2

Patient Engagement Interventions to Enhance Medication Safety in Long-Term Care: A Systematic Review

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Abstract: The aim of this systematic review was to investigate the effectiveness of patient engagement interventions tested in randomized controlled trials (RCT) to enhance medication safety in long-term care. Searches for relevant studies were conducted in the databases Medline, CINAHL, and CENTRAL, and RCTs published between January 2011 and December 2021 that tested patient engagement interventions in long-term care, and measured medication safety. Eligibility and quality were determined independently by two researchers, and effects on medication safety were analysed descriptively. Out of 850 screened records, five studies reporting patient engagement interventions were included and classified as involvement (n = 3) and partnership/shared leadership (n = 2). The studies were heterogeneous regarding sample size, patient characteristics and outcome measures, and all had methodological quality limitations. The interventions were complex with multiple components. Three RCTs reported statistically significant effects of patient engagement interventions on medication safety, when compared to control arms. In conclusion, the limited body of evidence suggests that engaging patients in their own medication care may improve medication safety. Future research is needed to guide the practice field and stakeholders, and should include effect studies with a

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high degree of patient engagement. The research community should find consensus in medication safety outcome measurements.

Keywords: long-term care, medication safety, patient engagement, randomized controlled trials, systematic review

Increasing patient engagement has been recommended to improve medication safety (Donaldson et al., 2017; WHO, 2016). Improving medication safety is particularly challenging in long-term care. By long-term care, we mean settings that provide care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care (e.g., nursing homes, assisted living facilities, home healthcare). Patients in these settings are often old, have multiple chronic diseases, polypharmacy, and complex medication regimens, which make them especially vulnerable to drug-related problems (Assiri et al., 2018; Insani et al., 2021; Morin et al., 2016; Plácido et al., 2020). A major weakness of many of the improvement initiatives is that the service users are too often passive recipients of medicines, and are not informed and empowered to participate in making the medication management process safer (Donaldson et al., 2017; Lee et al., 2018; WHO, 2016). The perspective of the patient is particularly relevant, because there is a positive connection between recognizing the importance of taking a medicine, using it safely, and engaging in administration (Lee et al., 2018). Adopting a person-centred approach, that includes the patient`s beliefs, preferences, goals, and barriers to taking medication, also provides better clinical outcomes (Kangovi et al., 2014).

Patient engagement can be described as patients and healthcare professionals working in active partnership to improve health and healthcare (Carman et al., 2013). To elucidate the concept in relation to medication safety, the framework developed by Carman and co-workers is useful (Carman et al., 2013; NHS England, 2016). The framework is multidimensional, including the engagement of patients, families, their representatives, and healthcare professionals as active partners on multiple safety levels (i.e., own care, service provider, or system). Furthermore, the framework describes the continuum of engagement with increased levels

of power and engagement from information (power lies with the health-care professional, service provider or system), to involvement (patients have an active role, but no power), to partnership/shared leadership (patients share power) (Carman et al., 2013; NHS England, 2016).

Reviewing interventions can aid in designing more efficient patient engagement interventions, and guide decision makers in choosing approaches to improve medication safety. Two previous systematic reviews have been published describing the impact of patient engagement on patient and medication safety (Kim et al., 2018; Newman et al., 2021). The systematic review by Newman et al. (2021), including 26 studies with various designs and mainly from inpatient settings, reports four common factors that positively affect the success of patient engagement interventions in enhancing patient safety during direct care: 1) patient-professional collaboration; 2) pragmatic and user-friendly interventions; 3) proactive promotion of confidence and safety; and 4) organizational sponsorship or a culture of patient engagement. This narrative systematic review does not specify outcomes for medication safety issues (Newman, 2021). A systematic review of 19 studies with mixed designs (Kim et al., 2018), found that key themes for patient engagement strategies affecting medication safety involve patient education and medication reconciliation. Among the studies using intervention and control groups (n = 11), 55% (n = 6) improved at least one medication safety outcome with significant effect estimates. This systematic review includes studies of both inpatient and outpatient settings, and across populations, that is without age limits. (Kim et al., 2018)

A high prevalence of drug-related problems among patients in long-term care highlights the need for a review of interventions that improve medication safety in this context, where patient engagement interventions can play an important role. However, evidence of the effectiveness of patient engagement interventions is mixed, and, notably, existing reviews of such interventions are not based on randomized controlled trials (RCT) in long-term care settings.

The aim of this chapter is to report a systematic review investigating the effectiveness of patient engagement interventions tested in RCT to enhance medication safety in long-term care.

Methods

Study Design

The review was carried out according to the Cochrane collaboration methodology (Higgins et al., 2021), and the findings were reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Moher et al., 2009).

Data Sources and Search Strategy

Initial electronic and manual searches were performed to identify key terms, and the search strategy was determined after discussion in the research group, and after consultations with a librarian. Searches were performed by one researcher (RMO) on Medline, CINAHL and Cochrane central register of controlled trials (CENTRAL). In addition, manual searches in the reference lists of included studies were conducted to expand the search coverage. The PICO elements (population, intervention, comparator, outcome) were used to formulate the review question and set the inclusion criteria (see Table 1). In addition, only original studies with an RCT design (including cluster and stepped RCTs) were to be included. Search dates were limited to studies published from January 2011 to December 2021, and the studies must be published in English, Norwegian, Swedish or Danish. The Boolean operators "or" and "and" were used to combine search terms (Table 1).

Screening and Study Selection

The reference management software, EndNote™ 20.3, was used for bibliographic management of the search results. The study selection process was conducted in three stages. Firstly, after removal of duplicates, one researcher (RMO) undertook an initial screening of titles and abstracts and excluded articles that were not relevant according to PICO and inclusion criteria. Secondly, two researchers (RMO and HS) independently read and screened the full text of all potentially eligible articles. Thirdly, the same two researchers conducted a manual search of the reference lists of all the included studies to retrieve additional relevant articles. In case of disagreements between

Table 1. The PICO Elements of the Study, Including Search Terms

Element acronyms	Descriptor	Determinants	Search terms
P	Population	Adult (≥18 years old) medication users in long-term care settings, i.e., home healthcare, sheltered housing, residential facilities	community health services (MeSH) or residential facilities (MeSH) or long-term care (MeSH) or home healthcare (MeSH)
I	Intervention	Patient engagement interventions, i.e., interventions that encourage active participation or promote partnerships or shared leadership between patients and their health professionals. To be included, studies had to report patient engagement interventions at the "safety of own care" level (Carman et al., 2013; NHS England, 2016).	patient-centered care (MeSH) or shared decision making (MeSH) or patient decision making (MeSH) or empowerment (MeSH) or self-management or "patient participation" or "patient involvement" or "patient engagement" or "patient activation" or "patient empowerment" or "patient partnership"
C	Comparison	No specific criteria for the comparison	No search terms included
O	Outcome	Medication safety, i.e., medication errors, adverse drug events, medication list accuracy, inappropriate medication use, medication adherence or compliance, perceptions of medication safety, and knowledge of medications related to safety and side effects. To be included, studies had to report at least one outcome specifically related to medication safety	medication errors (MeSH) or adverse drug events (MeSH) or medication compliance (MeSH) or "adverse drug reaction*" or "inappropriate medication" or "adverse drug effect*" or "medication safety" or "drug safety" or "non-compliance" or "non-adherence"

researchers on eligibility, a third researcher (LA) read the article in full text, and consensus on inclusion was reached by discussion.

Data Extraction and Knowledge Synthesis

Data from all eligible articles were extracted into a pre-set form, that included: publication details; study design; study setting; and characteristics of study population (P); interventions (I); comparisons/controls (C); outcome measurements; and results of patient engagement interventions

on medication safety (O). The initial data extraction was performed by one researcher (RMO). Then, another researcher (HS) independently reviewed the extracted data for accuracy. Finally, both researchers discussed the evidence and summarized the findings according to study characteristics. Due to considerable heterogeneity of the included studies with respect to the study population, patient engagement interventions, medication safety measures and outcomes, a meta-analysis could not be carried out. Data from included studies were synthesized and analysed by using the framework of Carman et al. (2013; NHS England, 2016), focusing on a knowledge synthesis of the nature and content of the patient engagement interventions, and their impact on medication safety. Furthermore, the interventions were classified according to the framework. Results are presented narratively.

Quality Appraisal of Studies

To assess the quality of the included studies, we adapted the Cochrane collaboration tool for assessing risk of bias in randomized trials (RoB). The RoB tool includes seven domains: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; and other sources of bias (Higgins et al., 2011). Based on the answers provided within the tool, RCTs were rated as "low", "high" or "unclear" risk of bias. We defined an RCT as having a high risk of bias if there was a high risk of bias in four or more dimensions.

Excluded Studies

A total of 60 studies were excluded after a full-text assessment of eligibility. These studies were excluded because of: study design (n = 27, e.g., non-randomized trial, pre-post design); study setting (n = 23, e.g., hospital context, general practice, pharmacies); not a patient engagement intervention (n = 3); not presenting medication safety outcomes (n = 4); or poor study quality (n = 3, with a high risk of bias in ≥4 dimensions).

Results

An adapted PRISMA flow diagram in Figure 1 shows the information through the different phases of the review. The search strategy identified 850 studies, of which 170 were duplicates. After screening titles and abstracts for relevance, 65 studies were identified requiring full-text review for eligibility. Following review, a total of five studies were included for analysis and form the basis of the findings.

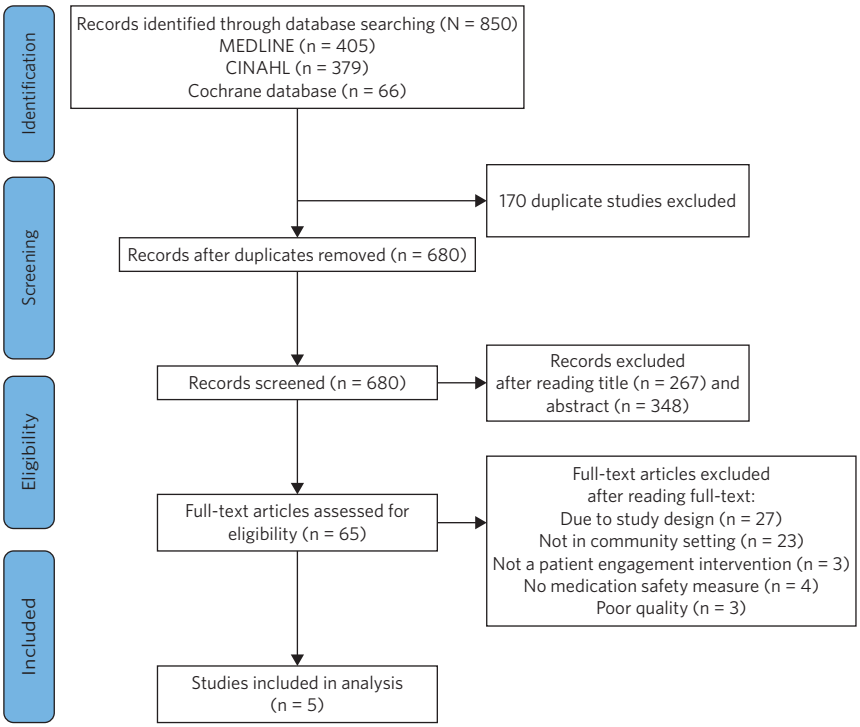

Figure 1. Study Flow Diagram

Characteristics of Studies

An overview of the characteristics of the included studies and the participants is shown in Table 2. All had a two-armed RCT study design. The follow-up of the intervention ranged from 3 to 12 months. Two of the studies were undertaken in China, two in the USA, and one in Australia.

Table 2. Characteristics of the Included Studies and Participants

Study reference	Country	Setting	N	Overall attrition (%)	Mean age (years)[a]	Condition[b]
Goeman et al., 2013	Australia	Community	124	10 (8.1)	67.7	Asthma
Graumlich et al., 2016	USA	Outpatient primary care clinics	674	118 (17.5)	63.7	Type II diabetes mellitus
Heisler et al., 2014	USA	Community health center	188	12 (6.4)	51.5	Type II diabetes mellitus
Sit et al., 2016	China	Ambulatory rehabilitation and home	210	35 (16.7)	69.3	Stroke
Wang et al., 2021	China	Community health service center	120	16 (13.3)	73.3	Cardiovascular disease

[a]Mean age of study participants at baseline in intervention and comparison groups combined.
[b]Health condition of study participants that was an inclusion criterion.

The sample sizes ranged from 120 to 674 (in total: 1,316; mean sample size: 263), randomized to intervention or control groups. Loss to follow-up was 191 participants (14.5%), and varied from 10 to 118 participants. The average age of the study participants at baseline was 65.1, and ranged from 51.5 (Heisler et al., 2014) to 73.3 years (Wang et al., 2021). Health conditions among study participants included diabetes (in two studies), asthma, stroke and cardiovascular disease.

Characteristics of Patient Engagement Interventions

The characteristics of the patient engagement interventions is shown in Table 3. The interventions were complex and included several components, which can be classified differently according to the engagement continuum (cf. Carman et al., 2013; NHS England, 2016).

Involvement. Patient engagement at the involvement level (Corman et al., 2013; NHS England, 2016) means that the patients were asked about their perspectives on medication safety in the context of their own care, and that communication between them and the healthcare professionals

Table 3. Characteristics of Patient Engagement Interventions and Synthesis of Intervention Effects on Medication Safety

	Aim of study	Intervention (I)	Control (C)	Outcome measurements[b]	Medication safety results
Goeman et al., 2013	To improve the asthma control and adherence to asthma preventer medication of older people using the patient asthma concerns tool (PACT) to identify and address unmet needs and patient concerns.	INVOLVEMENT[a] Person-centred face-to-face education sessions (60 min.) provided by asthma educators. The sessions addressed issues raised by the participants' responses to the PACT and according to a self-management checklist. In addition, inhaler device technique was taught according to a checklist. Follow-up: 3 and 12 months.	Passive education provided by an "Asthma in the Over 50s" brochure & device technique brochure & device collection (15 minutes).	1° Asthma Control Questionnaire, including lung function (ACQ7); adherence monitored by tracking device. 2° Asthma exacerbations measured by beta2 agonist and oral corticosteroid use; written asthma action plan ownership.	Adherence rate was significantly higher in I vs C group at 3 months (11.2% vs. 6.1%, respectively). Group difference was not significant at 12 months ($p = 0.17$). Only the intervention group achieved the goal of 80% adherence at 3 months, which continued to improve and was maintained at 12 months.
Graumlich et al., 2016	To test, among adult patients with type II diabetes mellitus, the effectiveness of a medication-planning tool (Medtable™) implemented via an electronic medical record to improve patients' medication knowledge, adherence, and glycemic control compared to usual care.	INVOLVEMENT[a] The Medtable: A structured tool implemented within the EMR that aimed to organize collaborative, patient/provider interactions for medication review, reconciliation, and education. Medtable includes searchable libraries of medication administration instructions in direct, actionable language, timelines that support text, and familiar icons that represent key daily events. Follow-up: 3, 6 and 12 months (only measure of HbA1c at 12 months)	Usual care	1° Knowledge of medicines questionnaire (6 items); patient-demonstrated medication knowledge of the medication regimen, measured by patients demonstrating filling a pillbox. 2° Medication adherence, measured by patient medication adherence questionnaire (PMAQ); satisfaction with information about medicines (5 items from the satisfaction with information about medicine scales (SIMS)).	Significant effect on patients' knowledge about the indications for medicines (aOR = 2.45, $p<.0001$ at 3 months; aOR = 2.53, $p<.0001$ at 6 months), and significant effect on patients' satisfaction with the information about their medication regimens (all adjusted *p* values for group were less than 0.0161 at 3 and 6 month). No significant effects on other outcomes between I and C group.

(*Continued*)

Table 3. (*Continued*)

	Aim of study	Intervention (I)	Control (C)	Outcome measurements[b]	Medication safety results
Heisler et al., 2014	To compare outcomes between community health worker use of a tailored, interactive, Web-based, tablet computer–delivered tool (iDecide) and use of print educational materials.	INVOLVEMENT[a] I1) An initial one-on-one, face-to-face session (2 hours) with a CHW and a copy of the printed materials to take home. The CHW used iDecide (a tailored, interactive, Web-based, tablet computer-delivered tool), which includes diabetes information; description of antihyperglycemic medications and their relevant harms, costs, and inconvenience; interactive demonstration of HbA1c control on risk for complications by using tailored risk estimation. CHW used a motivational interview–based approach in the session. I2) like I1, but the session lasted 1.5 hours and they received printed material instead of iDecide. The printed material included information on diabetes, medication effect on HbA1c, administration methods, costs, medication adverse effects, risks for diabetes complications. Follow-up: 3 months	I1 compared with I2	1º Knowledge about antihyperglycemic medications; medication decisional conflict, measured by medication decisional conflict ccale; satisfaction with clarity of medication information; satisfaction with helpfulness of medication information. 2º Diabetes care self-efficacy; Medication adherence, measured by Morisky medication adherence scale (MMAS).	For I1 there were significantly greater improvements in satisfaction with medication information between I and C groups (clarity, p = 0.028; helpfulness, p = 0.007). No other significant differences between the groups were found.

Sit et al., 2016	To examine the effects of the empowerment intervention on stroke patients' self-efficacy, self-management behaviour, and functional recovery.	PARTNERSHIP[a] The HEISS: *Part 1*, 6-weekly group sessions with nurse facilitator (in parallel with usual care), including personal goal setting and action planning, and self-efficacy activities provided through mastery, verbal persuasion, vicarious experience, and physiological feedback. Participants were given a personal stroke self-management workbook to guide their implementation at home. *Part 2*, home-based implementation (during 5 weeks) with biweekly telephone follow-up calls to encourage and commend participants on their actions for positive changes and to provide problem-solving skills to overcome any perceived barriers that participants encountered. Follow-up: 1 week, 3 and 6 months	Usual care	Chinese self-management behaviour questionnaire, including medication adherence (4 items); Barthel index (BI); Chinese Lawton instrumental activities of daily living (IADL).	No significant difference between I group and C group.

(*Continued*)

Table 3. (*Continued*)

	Aim of study	Intervention (I)	Control (C)	Outcome measurements[b]	Medication safety results
Wang et al., 2021	To assess the feasibility of a patient engagement and medication safety management (PE-MSM) program on medication errors, self-efficacy for appropriate medication and activation among older patients suffering cardiovascular disease in Chinese communities.	PARTNERSHIP[a] The PE-MSM program: 12 weekly one-on-one interventions (30–60 min.) by researchers, pharmacists, doctors, and nurses. Auxiliary tools: the "Instruction Manual of Patient Participating in Safety Medication", the check inventory for medication, the list of medication, the intelligent reminder box, the medication monitoring record form, and the flow chart of patients engaged in medication safety management Follow-up: Immediately postintervention, and at 3 and 6 months	Patients received medication safety education (by the community healthcare staff and researchers), i.e., medication information consultation and telephone follow-up services one-on-one.	Medication error questionnaire (MEQ); self-efficacy for appropriate medication use scale (SEAMS); patient activation measure (PAM).	The I group achieved significant lower incidence of medication errors ($p<.001$), higher self-efficacy for appropriate medication use ($p<.001$) and higher patient activation levels ($P<.001$) – both at 1 month and 3 months.

Abbreviations: ACQ7, asthma control questionnaire; aOR, adjusted odds ratio; CHW, community health worker; EMR, electronic medical record; IADL, Chinese Lawton instrumental activities of daily living; MEQ, medication error questionnaire; MMAS, Morisky medication adherence scale; PACT, patient asthma concerns tool; PAM, patient activation measure; PE-MSM, patient engagement and medication safety management; PMAQ, patient medication adherence questionnaire; SEAMS, self-efficacy for appropriate medication use scale; SIMS, satisfaction with information about medicines scales

[a]Level of patient engagement intervention (cf. Carman et al., 2013; NHS England, 2016)

[b]Primary (1°) and secondary (2°) outcomes are specified, if defined by the study authors

was two-way. Although patients have an active role at this level, the strategies are led by healthcare professionals. Three studies were classified on the involvement level (Goeman et al., 2013; Graumlich et al., 2016; Heisler et al., 2014), and all of them included one-to-one, face-to-face interactions between patients and healthcare professionals. In two of them, these sessions were supported by digital tools tailored to promote patient knowledge and facilitate medication planning for patients with type II diabetes mellitus, and varying health literacy skills in the USA. The tool Medtable used in Graumlich et al. (2016) was implemented within the EMR. The patient medication list was loaded into Medtable, and the technical language was customized so as to be appropriate for patients with low health literacy. During the clinic visit, the patient and nurse jointly reconciled the medication list, and the nurse added or deleted information in the EMR to obtain an accurate and current medication list. The nurses used teach-back techniques while discussing with the patient how to take the medicine. Finally, the patient and nurse worked together to create a medication plan, of which the patient received a paper copy. The tool iDecide evaluated by Heisler et al. (2014), was used on an iPad delivered to the participants in their homes. During the session, the healthcare professional used motivational interviewing, reviewed the content, and showed the patient how to use the program. The healthcare professional and the patient discussed the patient's diabetes, reviewed the medication regimen, discussed the need for medication changes or set goals for medication adherence, and identified any questions and concerns to raise at their next clinic visit. Finally, the patient set goals and received a printed summary.

The third RCT on the involvement level (Goeman et al., 2016) used the questionnaire, patient asthma concerns tool (PACT), as a tailored educational intervention to improve asthma-related health literacy, and address concerns and unmet needs among older patients in Australia. Instructions were given by asthma educators and addressed issues raised by the participants' responses to the PACT, and according to a self-management checklist. In addition, an inhaler device technique was taught according to a checklist.

Partnership or Shared Leadership. On the partnership/shared leadership level, communication is two-way, and patients and healthcare professionals share power and work together to improve medication safety (Corman et al., 2013; NHS England, 2016). Two of the RCTs included patient engagement intervention at this level (Sit et al., 2016; Wang et al., 2021). Both were conducted in China and used person-centred approaches to improve patient knowledge, facilitate patient communication, and empower patients to develop self-management skills. While the study of Wang et al. (2021) kept medication safety as the primary focus, both in relation to strategies and outcome measurements, the study of Sit et al. (2016) held medication safety to be implicit in an intervention targeted at stroke patients' self-efficacy, self-management behaviour, and functional recovery. Both RCTs included face-to-face interactions between patients and healthcare professionals. However, in Wang et al. (2021) these were one-to-one and 12 weekly, while in Sit et al. (2016) the interactions were group-based and 6 weekly. The PE-MSM program evaluated by Wang et al. (2021) was performed gradually with a focus on stimulating and maintaining the behaviour of the participants. A range of auxiliary tools were included, such as a check inventory for medication, the list of medications, the intelligent reminder box, and a medication monitoring record form. The HEISS intervention reported by Sit et al. (2016) included personal goal setting and action planning, and self-efficacy activities during the group sessions. In the last part of the intervention period, biweekly telephone follow-up calls were conducted in order to encourage actions for positive changes, and to provide problem-solving skills.

Effect on Medication Safety

An overview of the medication safety measurements used and the interventions' effects on medication safety are shown in Table 3. The most used measure for medication safety was medication adherence, found in four of the RCTs (80%). Three used self-reported measurements (questionnaires), and one study used an objective measurement. Other medication safety measurements were self-reported or demonstrated

medication knowledge (Sit et al., 2016; Heisler et al., 2014), self-reported medication errors (Wang et al., 2021), and self-reported satisfaction with information on medication information (Sit et al., 2016; Heisler et al., 2014). Heisler et al. (2014) also disclosed self-reported medication decisional conflicts, and Wang et al. (2021) reported self-efficacy for appropriate medication use.

Three of the included RCTs reported a statistically significant effect of patient engagement interventions on medication safety (Goeman et al., 2013; Graumlich et al., 2016; Wang et al., 2021). For details on outcome measurement results, see Table 3. The target of the interventions were behaviour and knowledge, and the components in these studies were education, motivational interviews, questionnaires to identify patient concerns and unmet needs, and a digital medication-planning tool.

Risk of Bias and Quality of Studies

The overall quality of evidence in this systematic review is illustrated in Figure 2. In total, a low RoB was observed in 54% of the dimensions, and across all studies in reporting bias and selection bias by random sequence generation. A high or unclear RoB was observed in 23% of the dimensions.

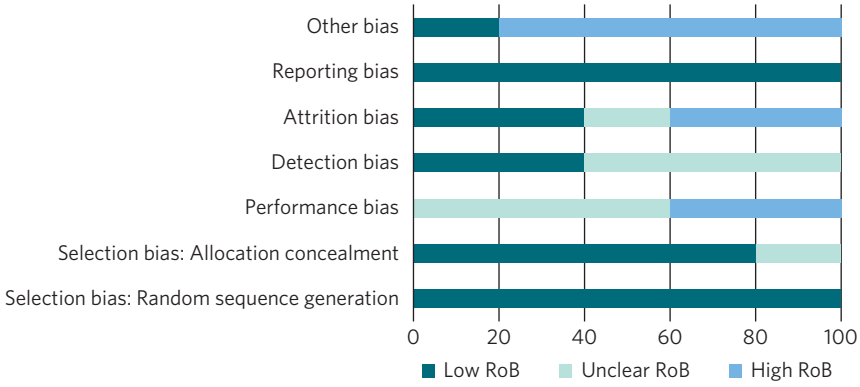

Figure 2. Cumulative Risk of Bias (RoB) in the Five Included Studies, Given in Percentage

The RoB analysis shows a high risk of other bias in four of the included studies (Figure 3). This was mainly due to small sample size or unbalanced groups of study subjects in the interventions groups versus control groups, in relation to characteristics at baseline, which would likely affect the study outcome. Performance bias was considered a high risk in two studies, since neither participants nor study personnel were blinded, and unclear RoB was considered when only personnel were blinded (n = 2). Differential attrition >9% combined with overall attrition above 10% were observed in two studies and considered a high RoB, while differential attrition of 8.7% was observed in one study and considered unclear. No information on blinding of outcome assessments in the studies was considered as unclear detection bias (n = 3).

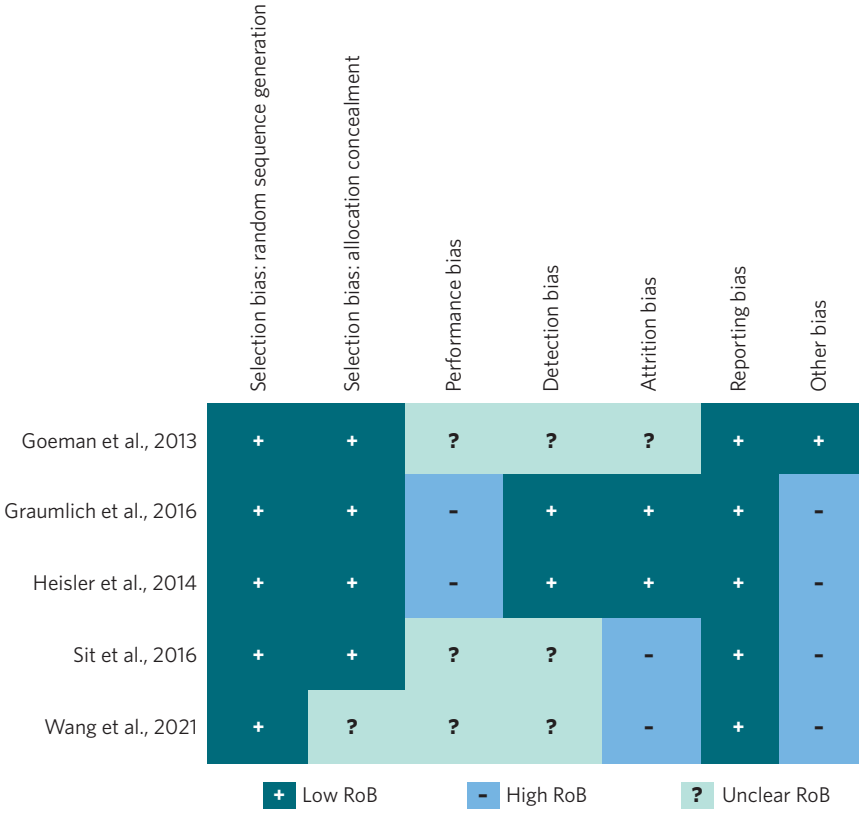

Figure 3. Risk of Bias (RoB) Analysis Results of the Included Studies

Discussion

This systematic review identified five RCTs describing patient engagement interventions that affect medication safety in long-term care. Involvement and partnership/shared leadership interventions were used in three and two studies, respectively, according to the framework for patient engagement in patient safety of own care (Corman et al., 2013; NHS England, 2016). Involvement characterization means that interventions entailed patients having an active role in medication safety measures, but power remains with the healthcare professional. Partnership or shared leadership interventions entailed patients sharing power with healthcare professionals. Patient engagement interventions reported statistically significant effects on medication safety in three of the studies (Goeman et al., 2013; Graumlich et al., 2016; Wang et al., 2021), within several outcome measures: medication adherence (Goeman et al., 2013); self-reported knowledge of medicines (Graumlich et al., 2016); medication errors (Wang et al., 2021); and self-efficacy for appropriate medication use (Wang et al., 2021). However, due to the limited evidence base in five studies, and their extensive heterogeneity in relation to intervention designs, population, settings, and outcome measures, we are not able to draw further conclusions on patient engagement effects on medication safety among patients in long-term care settings. Nor can we attribute changes in medication safety outcomes to a particular level of patient engagement (cf. the framework of Carman et al., 2013). We know from previous research that interventions to improve medication safety remain on a low level of patient engagement, typically involving informing patients about engagement, encouraging patients to engage, to ask questions, and communicate with their healthcare professionals (Kim et al., 2018). Other systematic reviews of patient engagement interventions affecting patient or medication safety are scarce and have not limited the setting to long-term care or to RCT study designs (Kim et al., 2018; Newman et al., 2021). Hence, they are not readily comparable. However, this study aligns with previous studies in describing heterogeneity between studies in for example, design, population, setting, outcome measurements, and quality (Kim et al., 2018; Newman et al., 2021).

A systematic review of interventions can guide decision makers and the practice field in choosing approaches to improve medication safety. Due to the evidence base of the five studies in this chapter, the implications for practice are limited. However, the result of this systematic review aligns with previous research describing the importance of including patients in their own care and management of medicines, and empowering patients may enhance medication safety (Lee et al., 2018, Kangovi et al., 2014, Kim et al., 2018). This study expands our knowledge of interventions to engage patients, and typically involve several behavioural or knowledge components. Examples were medicine reconciliation, medication review, medication information in written or digital formats, individual follow-up and/or counselling by healthcare professionals, and various eHealth components (e.g., digital tools to provide information or communicate with health providers). This result is partly in line with previous research. Kim et al. (2018) found in their review that key strategies for engaging patients in medication safety included education and medication reconciliation, often involving information technology or patient portal use.

In recent years, the global health community has focused on measures to increase patient engagement to ensure safe medicine practices, anchored by WHOs global patient safety challenge on medication safety (Donaldson et al., 2017; WHO, 2017). However, the results of this review show that effect studies testing patient engagement interventions in long-term care are limited, but achievable. Further research on patient engagement interventions in community settings are needed, and should include a greater amount of patient engagement, and patient-centred approaches to assess medication safety (Lee, 2018). Furthermore, there is a need for international consensus and guidelines for medication safety outcome measurements, which is necessary to perform meta-analyses and provide the practice field and stakeholders with reliable evidence and trustworthy effect estimates.

Strengths and Limitations

The strength of this chapter is the rigorous, systematic approach in reviewing studies, following the PRISMA 2020 statement for reporting (Moher et al., 2009). The method used to identify all relevant information was

comprehensive and feasible for the scope of the review. In addition, the eligibility screening, quality assessment, data extraction and knowledge synthesis were performed by researchers with professional healthcare education, as a registered nurse (first author) and a pharmacist (second author). This interdisciplinary approach with relevant areas of expertise, strengthens the study.

The main limitation of this systematic review is the small number of studies included, limiting the evidence base available to create new knowledge and draw conclusions. This could be due to the scope of the review and the selection criteria, and limitations used in the search process. For example, we selected patients in community settings, and the safety of their own level of care according to the patient engagement framework, including only RCTs. Furthermore, a more comprehensive search strategy including grey literature could have provided a larger evidence base. However, we strongly believe that the five included studies reveal a knowledge gap in the literature, and highlight the need to perform medication safety effect studies using patient engagement interventions with a high amount of engagement in community settings.

Conclusion

This chapter provides a systematic review of patient engagement interventions and how they affect medication safety among patients in long-term care. A limited body of evidence suggests that key strategies for patient engagement to ensure medication safety in long-term care should include several components to increase medication knowledge and change behaviour. A knowledge gap in the literature has been detected, and additional effect studies are needed. Preferably, future RCTs should include comparable medication safety outcomes, to guide the practice field and stakeholders utilizing reliable evidence.

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CHAPTER 3

Involving Patients and Next of Kin to Mitigate Adverse Events Related to Systemic Anticancer Treatment

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Abstract: Medication safety in cancer care is an inherently complex field, with a potentially high risk for adverse events. Medication harm is the most common type of adverse event in cancer patients, and is often related to both systemic anticancer treatment and other medications. New systemic anticancer treatments have improved outcomes for many cancer patients, but have also introduced a whole range of new medication-related adverse events. The aim of this chapter is to provide new knowledge on how to involve patients and next of kin to prevent unnecessary adverse events related to systemic anticancer treatment. To achieve safer cancer care we need to meet the individual needs of patients and next of kin. Essential components for preserving involvement include: creating good processes for transitions of care with medication reconciliation, structured facilitation and discharge communication; patient and next of kin education; and timely follow-up after discharge. The use of electronic patient-reported outcomes can provide personalized follow-up and feedback for patients, and give healthcare professionals the opportunity to mitigate harm before it results in a severe adverse event. This empowers patients in everyday situations, and can ensure safety for patients and their next of kin. Moreover, there is a growing realization that such feedback should co-create more sound involvement of next of kin. Creating collaborative learning arenas with multiple stakeholders, including next of kin as natural and equal partners, can contribute to more targeted real-time solutions for mitigating adverse events within cancer care.

Keywords: cancer, medication safety, next of kin, patient involvement, patient safety

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Medication safety in cancer care is an inherently complex field, with a potentially high risk for adverse events related to systemic anticancer treatments. The complexity is often caused by several compelling factors connected to the biology of the disease, high-risk systemic treatments and care processes involving many different stakeholders across service levels in the healthcare system (Bergerød, 2021; Haukland, 2020). This chapter will provide insight and discussions on patient safety in cancer care focusing on how to mitigate adverse events related to medication safety through the sound involvement of the patient and next of kin.

The aim of this chapter is to provide relevant new knowledge for patient safety researchers and healthcare professionals on how to involve patients and next of kin to prevent unnecessary adverse events related to systemic anticancer treatment. The following research question will guide this chapter: What is the role of patient and next of kin in mitigating adverse events in systemic anticancer treatment, and how can appropriate involvement improve medication safety? This chapter will add to the body of knowledge on how reliable stakeholder involvement can potentially contribute to understanding more about medication safety, and how to create and sustain safe work practices across service levels in the healthcare system (Ugalde et al., 2019).

Methodology and Research Ethics

This chapter is a synthesis of knowledge based on the findings of two PhD studies and an updated literature search (Whittemore et al., 2014). We have interpreted and summarized the results from these studies in the context of medication safety to provide new knowledge on how to operationalize the perspectives of patient and next of kin involvement, in order to inform best practice in mitigating adverse events related to systemic anticancer treatment (Bergerød, 2021; Haukland, 2020).

The chapter is based on previously published healthcare research and quality assurance work done by the authors. According to the Regional Committee for Medical and Health Research Ethics in Norway, healthcare research and quality assurance work does not require approval by the committee, compare The Health Research Act §9 and The Research Ethics Act § 4.

The Norwegian Cancer System

Norway has a nationalized healthcare system that is semi-decentralized, meaning that the central government is responsible for secondary healthcare services. The service is delivered through four regional health authorities, which own and operate 20 hospital trusts (Saunes et al., 2020). The municipalities are responsible for primary care, including nursing homes, homecare, general practitioners, casualty clinics and rehabilitation services. The Norwegian Board of Health Supervision is the independent supervisory authority in Norway. All service providers are by law responsible for providing sound professional practice and for establishing safety management systems. Documentation and follow-up of adverse events should be done internally in the healthcare organizations. It is mandatory to report the most severe adverse events to the Norwegian Board of Health Supervision and the Norwegian Healthcare Investigation Board. In 2020, more than 1,000 severe events were reported (Saunes et al., 2020).

Cancer Care in Norway

In Norway nearly 300,000 people have a cancer diagnosis, and the numbers are increasing. There are approximately 35,000 new cases per year, and patients are also living longer (Cancer Registry of Norway, 2020). A typical course for a cancer patient in Norway is to first consult their general practitioner (GP). If the patient has suspicious cancer symptoms, the GP refers the patient to the hospital in line with national guidelines and care pathways. The patient is then integrated into care pathways, and goes through a rapid schedule of essential tests and requirements for the suspected diagnosis. A multidisciplinary team along with the patient reach a decision on diagnosis and treatment options. Cancer treatment and care are in general paid for by the public sector, and the patient is followed up by the hospital and the GP. The municipalities appoint a cancer coordinator for the individual patient after diagnosis. At first glance this seems like a seamless system with an appropriate distribution of responsibility and division of work. However, the cancer patient will alternate back and forth between service levels, as well as several actors in and between hospitals and services in the municipalities during the care trajectory, causing challenges related

to care transitions and involvement (Aase et al., 2017; Aase & Waring, 2020; Bergerød & Braut et al., 2020; Saunes et al., 2020).

Patient Safety and Adverse Events

There are many definitions of patient safety. This chapter uses the well-known definition provided by Vincent: "The avoidance, prevention and amelioration of adverse outcomes or injuries stemming from the process of healthcare" (Vincent, 2010, p. 14).

This definition links patient safety to adverse outcomes or injuries, caused, for example, by medication harm. An adverse event is defined by the World Health Organization as "an injury related to medical management, in contrast to complications of disease. Medical management includes all aspects of care, including diagnosis and treatment, failure to diagnose or treat, and the systems and equipment used to deliver care. Adverse events may be preventable or non-preventable" (World Health Organization, 2005).

This means that an adverse event is not caused by the disease itself, but is rather harm inflicted in or by the process of treatment or care. This is highly relevant for the cancer care field because systemic anticancer treatment not only cures or postpones the development of the disease, but could potentially cause harmful acute or subsequent effects, such as fatigue, pain and psychological harm. The harmful side effects of anticancer treatment can perhaps be regarded as poorly managed safety, however for the cancer field this is often considered to be unavoidable, justified by the argument that the patient will be able to live longer with their cancer or be cured. These potentially harmful effects may cause challenges for how the patient copes with treatment and care, but consequences and interventions seldom integrate the next of kin perspective, in terms of involvement, to mitigate these adverse events (Barlow et al., 2021; Moghli et al., 2021).

Adverse Events in Cancer Treatment in Norway

In Norway, the Patient Safety Campaign, In Safe Hands 24-7, was launched in 2011 aiming to reduce the number of patient injuries by 25%.

This campaign has continued within a patient safety program, and is now integrated into an action plan for quality and patient safety at the national level (Norwegian Directorate of Health, 2020a). None of the program initiatives focus specifically on improving patient safety in cancer care. In general, serious adverse events in the Norwegian healthcare system continue to be a big problem, and the numbers remain stable. In 2020 adverse events occurred in 13.1% of all hospital stays in Norway (Norwegian Directorate of Health, 2021b). In comparison, hospitalized cancer patients experienced an adverse event in 24.2% of admissions.

During the last decade there have been multiple studies indicating that cancer patients experience higher rates of adverse events than the general population, with an average of nearly 40% of admissions having at least one event (Cihangir et al., 2013; Hébert et al., 2015; Lipczak et al., 2015; Lipitz-Snyderman et al., 2017; Mattsson et al., 2013). Hospitalized cancer patients have a 39% higher risk of adverse events compared to other hospitalized patients. This is not due to the cancer diagnosis itself, but is associated with older age, longer hospital stays, and surgical complications (Haukland et al., 2017). By examining deceased hospitalized patients, one finds that for cancer patients dying in hospitals, the rate of severe adverse events is as much as seven times higher than for the general population (Haukland et al., 2020). The potential risks for hospitalized cancer patients are most often related to medication harm and infection (Haukland, 2020).

Several risk analyses conducted by the Norwegian Board of Health Supervision have also found that the risk for adverse events in cancer care is high in Norway (Hannisdal et al., 2013; Haukland et al., 2017) There is also a lack of national overview relating to how large the problem is within the cancer care field (Hannisdal et al., 2013).

However, the national compensatory systems and many good quality registries provide measures for surveillance. In Norway we have a national system for patient compensation after patient injuries caused by the healthcare services. Numbers from this system show that cancer is the second largest medical area with reported cases in Norway. Common reasons for compensation reported in the cancer field are failures in treatment or diagnosis (The Norwegian System of Patient Injury

Compensation, 2020). Nevertheless, even if Norway has a mandatory reporting system for the most severe adverse events, underreporting in documentation and disclosure of adverse events in hospitals remains a problem. Studies show that only one in four adverse events causing injury or death are reported through incident reporting systems in hospitals (Smeby et al., 2015).

Measuring Adverse Events

It is no surprise that cancer patients experience treatment-related toxicities, but accurate and reliable measurements of adverse events remain a major challenge for the patient safety field (Jha & Pronovost, 2016; Shojania & Thomas, 2013). Measuring adverse events is more difficult than measuring many other healthcare processes or outcomes, because adverse events need to be understood in the context of the complex systems within which they occur.

Many methods have been developed to detect adverse events, and reporting them in oncology has evolved in response to new treatments and modalities. Patient-reported outcomes (PROs) are considered the gold standard for data collection in research. Based on this, the National Cancer Institute has also developed a patient-reported outcome assessment system (PRO-CTCAE) used to evaluate symptomatic toxicity reported by the patients themselves (Basch et al., 2014; Dueck et al., 2015). The patient-reported assessment consists of 78 symptom-related questions relevant to oncology, grading common adverse events in relation to anticancer treatment. By involving cancer patients in reporting symptoms electronically themselves at an early stage, there is a potential to mitigate harm before it develops into a severe adverse event. Implementing a follow-up with PRO-CTCAE as standard clinical practice could be part of a safety surveillance system to prevent adverse events related to systemic anticancer treatment.

Next of kin are often excluded from evaluation measures (patient surveys) in healthcare services, despite the fact that healthcare professionals describe the next of kin within the cancer field as collaborative partners in quality and safety efforts (Bergerød & Dalen, et al., 2020; Stenberg

et al., 2014; Stolz-Baskett et al., 2021).We suggest a change in the evaluation of cancer care services to include measurement from the next of kin perspective. Surveys of next of kin satisfaction with care and other experiences can be useful at the department level, and could provide meaningful information as a compass and a guide in co-creating and collaborative learning, with the next of kin as an equal and natural collaborative partner in hospital cancer care (Bergerød & Dalen, et al., 2020).

Medication Harm in Cancer Care

Medication harm is reported as the most common type of adverse event in cancer patients, and is related to both systemic anticancer treatment and other medications (Haukland et al., 2017; Lipczak et al., 2011; Schwappach & Wernli, 2010; Weingart et al., 2018). Adverse drug events related to systemic anticancer treatment are of serious concern for patient safety, and in many cases cause extra unnecessary burdens to already vulnerable cancer patients (World Health Organization, 2019a).

Figure 1 compares the number of adverse events per patient for general patients, deceased patients and deceased cancer patients at a Norwegian hospital. Deceased patients experienced significantly more adverse events than general patients, and for deceased cancer patients medication harm,

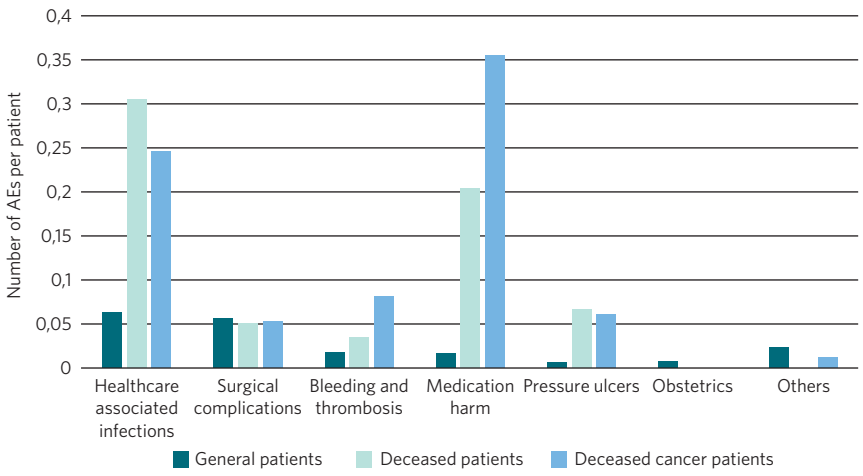

Figure 1. Comparing Types of Adverse Events Between General Patients, Deceased Patients and Deceased Cancer Patients in a Norwegian Hospital

often related to systemic anticancer treatment, such as chemotherapy and immune-checkpoint inhibitors, is by far the most common cause of adverse events (Haukland, 2020).

Chemotherapy-Related Adverse Events

Chemotherapy is classified as high-risk medication, since it has a low therapeutic index, which increases the risk of harm. Having a low therapeutic index means that the ratio of the maximally tolerable dose of the medicine to the minimal effective dose is low (Habet, 2021). In clinical practice this means that even a minimal increase in the chemotherapy dose, due to for example: drug interactions, weight changes, concomitant clinical conditions or individual variation to eliminate the medication, may cause a significant increase in effect, and potentially result in harm to the patient. For chemotherapy even doses within the recommended range often cause adverse drug reactions. Short-term toxicities such as nausea, vomiting and diarrhea are well-known adverse events related to chemotherapy treatment. For most patients, current procedures to control these are reasonably effective, preventing such side effects from developing into severe adverse events (Nurgali et al., 2018). On the other hand, neutropenia infection is a feared dose-related complication connected with chemotherapy. In the worst cases such a reaction can led to sepsis and septic shock, which is a leading cause of intensive care unit admission and mortality in cancer patients undergoing intensive cytotoxic chemotherapy (Kochanek et al., 2019). Neutropenia is itself an independent risk factor for infection. Cancer patients more often experience adverse events related to healthcare-associated infections than general patients. Chemotherapy, contributing to a reduced immune system, makes cancer patients more vulnerable to severe infections, and contributed to death in 58% of deceased cancer patients in a retrospective study from 2011–2012 (Haukland et al., 2020). The adverse events were mainly lower respiratory infections, and occurred nearly three times more frequently in cancer patients, and were the most common cause of death for cancer patients not receiving anticancer treatment during the last 30 days of life. This high incidence of hospital-acquired infections in cancer patients can be

explained by the severity of the illness, age, underlying conditions, and use of immunosuppressive medications such as chemotherapy and steroids. In addition, cancer patients often spend more time being hospitalized, contributing to a susceptibility to infections.

More than 70% of medication-related adverse events contributing to death occur in cancer patients, and most of these adverse events were related to lethal complications after chemotherapy. Patients receiving anticancer treatment during the last 30 days of life had the highest rate of medication-related adverse events, more than twice the rate of cancer patients not receiving such treatments. Anticancer treatment related adverse events contributing to death occurred only in patients who received such treatment during the last 30 days of life (Haukland, 2020). This accentuates the increased risk of severe adverse events when systemic anticancer treatment is given during the last 30 days of life, and should encourage caution when consideration providing systemic cancer treatment to patients near the end of life.

Immunotherapy-Related Adverse Events

New systemic anticancer treatments, such as targeted therapies and immunotherapy are now well-established treatments for many cancer types, and their indication for use is continuously expanding across malignancies and disease situations. The introduction of these new treatments has improved outcomes for many patients with advanced cancer. However, their introduction is also associated with a whole range of new medication-related adverse events. Unlike conventional chemotherapy, immune-checkpoint inhibitors boost the immune system and can lead to a unique constellation of inflammatory toxicities known as immune-related adverse events that are distinctly different from classic chemotherapy-related toxicities. Symptoms occur as inflammation, and can affect every organ system in the body, thus being sometimes challenging to identify. Many of the adverse events caused by targeted therapies are short-lived or reversible when therapy stops, and are often not associated with long-term adverse events (Shahrokni et al., 2016). However, if symptoms are not recognized and treated at an early stage,

immune-related adverse events can be life threatening. The rate of severe immune-related adverse events requiring immunosuppression and withdrawal of immunotherapy varies between the different immune-checkpoint inhibitors. For ipililumab (anti-CTLA-4 inhibitor), immune-related adverse events of any grade occur in up to 60% of patients, of which 10–30% are considered serious (defined as grade 3–4) (Martins et al., 2019). In comparison, anti-PD-1 inhibitors, such as nivolumab and pembrolizumab, cause severe immune-related adverse events in approximately 16% of patients (Magee et al., 2020). The combination of these two immune-checkpoint inhibitors (anti-CTLA-4 and anti-PD1) increases the incidence of severe adverse events in more than 50% of patients (Martins et al., 2019; Xing et al., 2019). Another challenge is that unlike chemotherapy-related toxicities, immune-related adverse events are not related to cumulative doses or organ reserve function, and occur more unpredictably during the course of treatment. Most often, adverse events occur during an early stage of treatment, but late-onset immune-related adverse events may also be severe. The fact that the incidence of immune-related adverse events is so high, and the outcome may be so serious and even fatal for some patients, intensifies the need for using personalized surveillance strategies that involve the patients to a greater extent.

Other Medication-Related Adverse Events

Most cancer patients are over 65 years old, and many of them often have other chronic conditions in addition to their cancer diagnosis. This adds complexity to the treatment, and is associated with polypharmacy, use of potentially inappropriate medications, and risk of adverse drug reactions. Systemic anticancer treatment potentially increases the risk of interaction with other medications and can pose a threat of increased or decreased efficacy of the cancer treatment or medication, thus causing an unintended adverse event. Thirty percent of overall cancer patients are at risk of drug-drug interactions related both to systemic anticancer treatment and supportive care treatment (Riechelmann & Girardi, 2016). Medications such as warfarin, antihypertensive medications, corticosteroids, and anticonvulsants especially have the potential for interactions

resulting in adverse events (Riechelmann & Girardi, 2016). This emphasizes the importance of medication reconciliation and close collaboration among all stakeholders involved during a course of treatment, especially the patients and their next of kin, who are often the "keepers of the story".

Narcotic agents such as opioids, sedatives and steroids are other high-risk medications often used as supportive care for many cancer patients. Patients in need of palliative care and near the end of life are also more likely to be vulnerable to medication-related adverse events. A study done in a specialist palliative care service found that 62% of the patients suffered from symptomatic adverse events (Currow et al., 2011). In palliative care the meaning of a medication-related adverse event may be considered in a broader perspective. The main fundamental goal of palliative care is the best possible symptom control with a focus on quality of life, instead of maximum prolongation of life. Not achieving these goals by, for example, omission of the administration of needed palliative medications, such as opioids, to relieve pain may also be considered an adverse event.

Mitigating Adverse Events by Involving Patients and Next of Kin

Communication and Medication Reconciliation

There is an increased availability of orally active anticancer medications that the patients administer either continuously or in periods by themselves at home. To ensure that the patient takes their anticancer medications as prescribed we need proper communication between health care personnel and patients before they leave the hospital and go home. Medication reconciliation is the formal process in which health care professionals' partner with patients and their next of kin to ensure accurate and complete medication information transfer at interfaces of care (Stolz-Baskett et al., 2021). In one randomized controlled trial, medication reconciliation decreased clinically significant medication errors by 26%. A systematic review by Herledan et al. found that medication reconciliation implemented at admission or discharge of cancer patients identified discrepancies and other medication-related problems in up to 88% and 94.7% respectively (Herledan et al., 2020).

On discharge the medication plan should always be discussed with the patient and next of kin. At the same time the patients should be made aware of the purpose of the anticancer medication they are using, the likely benefits, and potential risks. In this process patients should also be informed about possible adverse events they may expect from certain combinations, and other over-the-counter medications, food or herb interactions (e.g., grapefruit juice) that they need to avoid. These simple interventions could be the key to avoiding dangerous drug combinations.

This information should be communicated to the patient and the next of kin both orally, so that they can ask questions, and in writing so that they can consult the written information later when they get home. Communication is a two-way, relational process influenced by context, culture, words, and gestures, and it is one of the most important ways that clinicians can influence the quality of medical care that patients and their families receive (Bergerød, 2021). The format of the information provided should meet the needs of patients and next of kin while being easily understandable, with the emphasis on joint decision making. Before leaving the hospital, the patient and the next of kin need a plan for who to contact if their condition should deteriorate or if they experience side effects from the treatment generating a need for help (Nayak & George, 2021; Stolz-Baskett et al., 2021).

Personalized Follow-Up

To achieve a personalized follow-up of cancer patients and their next of kin we need to meet their individual needs, and the first step in doing so is to involve them more actively. Empirical evidence demonstrates that clinicians underreport the incidence and severity of symptoms compared to when patients themselves report how they feel (Basch et al., 2006; Lammers et al., 2019; Pakhomov et al., 2008). More importantly, most cancer patients are willing and able to self-report their own symptoms without substantial attrition. This is the case even among cancer patients with end-stage disease and poor performance status (Basch, 2010; Quinten et al., 2011).

> "It feels safe to know that my care team monitors how I am doing while at home." (Quote from a patient)

Patient-Reported Outcomes (PRO) and Outcome Measures (PROM) have shown to better describe patients' symptoms compared to reporting by health care professionals (Pakhomov et al., 2008). A recent systematic review of 22 studies including PROMs in daily cancer care found that follow-ups by PROMs had a positive effect on survival, symptoms, health-related quality of life and patient satisfaction (Graupner et al., 2021). Studies have demonstrated that electronic PROs (e-PROs) as follow-ups for cancer patients given chemotherapy treatment can reduce acute admissions to hospitals, improve quality of life and prolong overall survival by up to five months compared to standard care follow-ups (Basch et al., 2016; Jordan et al., 2018). Consequently, PROMs are seen as the preferred method and gold standard to gather information from patients in studies and in real life, as they more often give a more convincing picture of patients' wellbeing and side effects from interventions and treatments (Graupner et al., 2021).

> "It is good to sit in peace and quiet and fill in the questions when it suits me. Then it is easier to answer what I really feel." (Quote from a patient)

If cancer patients report symptoms electronically to a healthcare professional at an early stage, there is a potential to mitigate harm before it becomes severe and results in an adverse event for the patient. As the first hospital in Norway to do so, the cancer department in Nordland Hospital Trust implemented electronic patient-reported outcomes (e-PRO) follow-ups through digital monitoring as the standard of care for all patients receiving immunotherapy from June 2021, by using Kaiku Health (Kaiku Health LTD, 2020). The immunotherapy module in the Kaiku Health program is based upon the National Cancer Institute's reporting of adverse events in clinical trials of immunotherapy (Iivanainen et al., 2019). This is a web-based program for smartphones, I-pads, and home computers, and by using machine learning algorithms the software screens, grades, and alerts potential harm. Based on received treatment, each patient gets their own personalized follow-up symptom and quality

of life questionnaire sent out regularly in the software. If the patients have a high symptom burden at the start of the treatment or if the risk for adverse events is high, for example when combinations of immune-checkpoint inhibitors are given, the symptom questionnaire can be sent out every week to follow the patients closely. If the patient, on the other hand, has no symptoms the questionnaire can be sent out every second, third or even forth week, individualized to meet the specific needs of the patient. If symptoms should appear between the requested reports the patient can always fill in an extra questionnaire, measurement value or quality of life report to alert the care team of changes in his or her condition.

> "I simply feel freer, because I can fill out the form and use the app whenever and wherever I want." (Quote from a patient)

Filled-out questionnaires are submitted to the patient's care team in the cancer department, and they can see the patient's status in real time, and directly identify grades of the possible symptoms. This makes it easier to respond immediately to potentially serious immune-related adverse events and prevent further impairment of the patient, as many of the immune-related toxicities can be reversed with early intervention and use of steroids (Martins et al., 2019).

> "I was afraid it would be impersonal, but that did not happen. Now I get answers to my worries right away, if not immediately." (Quote from a patient)

At the same time as the health care professionals are alerted, the patient gets feedback on how their symptoms have evolved over time, how they should react and what they themselves can do at home to relieve the complaints. The feedback given to patients is based on international guidelines and is meant to support them in their everyday lives. Particularly mild symptoms, such as lack of appetite, feeling tired or sleeplessness, can affect quality of life for patients, but these rarely result in severe adverse events. In a busy clinical practice with limited time to talk to the patient, mild symptoms and advice on how to cope with them are often not prioritized. Providing standardized feedback to everyday symptoms encourages empowerment and safety for the patient and their family,

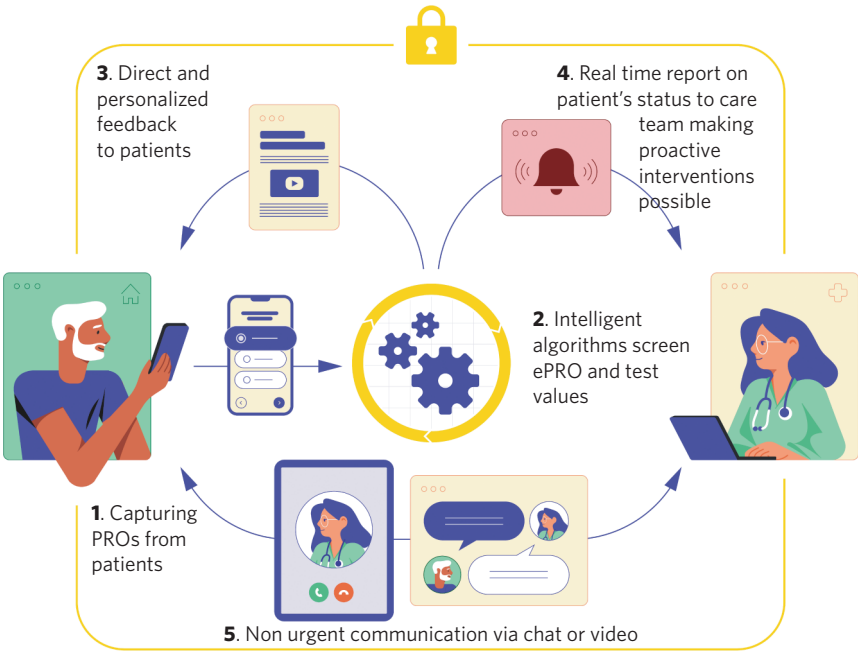

Figure 2. Illustration of How an e-PRO Follow-Up with Kaiku Health Works in Clinical Practice (Reprinted with permission from Kaiku Health)

and has proved to reduce symptoms such as pain, depression and fatigue and increase the patient's quality of life (Aapro et al., 2020). Importantly, patients are more active in their own patient journey, with more knowledge about their own symptoms and how to react to them. Figure 2 illustrates how an e-PRO follow-up with Kaiku Health works in clinical practice.

> "Like when I got a rash, I got feedback to treat it with a specific ointment. But then I got quite severe itching, and my doctor called me right away after I reported this on the app." (Quote from a patient)

The use of e-PROs can provide personalized follow-ups of patients and give healthcare professionals the opportunity to mitigate and prevent harm before it results in a severe adverse event. It could also decrease the need for emergency admissions or unplanned visits/phone calls to the outpatient clinic, which can be a burden for the patient, their family and the healthcare system (Aapro et al., 2020; Basch et al., 2016).

Knowledge about real-time follow-ups and adverse events can be clinically relevant in order to better inform patients before starting new treatments. Consequently, it may also provide information about when to end potentially harmful and high-cost anticancer treatment, as it gives healthcare personnel the opportunity to monitor and compare symptoms over time. This makes it easier to discover changes in the patient's clinical condition that might signal changing or ending a systemic anticancer treatment because of toxicities or progressive disease. For some anticancer treatments the clinical effects may occur before the response can be verified radiologically on CT or MRI scans. On radiological images we may, in such cases, see a pseudo-progression before a later response to the treatment with regression of the disease. In such cases the clinician must rely on clinical judgment, and therefore an overview of symptom development or changes in quality of life over a period are invaluable in making the right decision. If the symptom burden and quality of life of the patient have improved, this supports continuing the anticancer treatment, closely monitoring if there is a delayed radiological response.

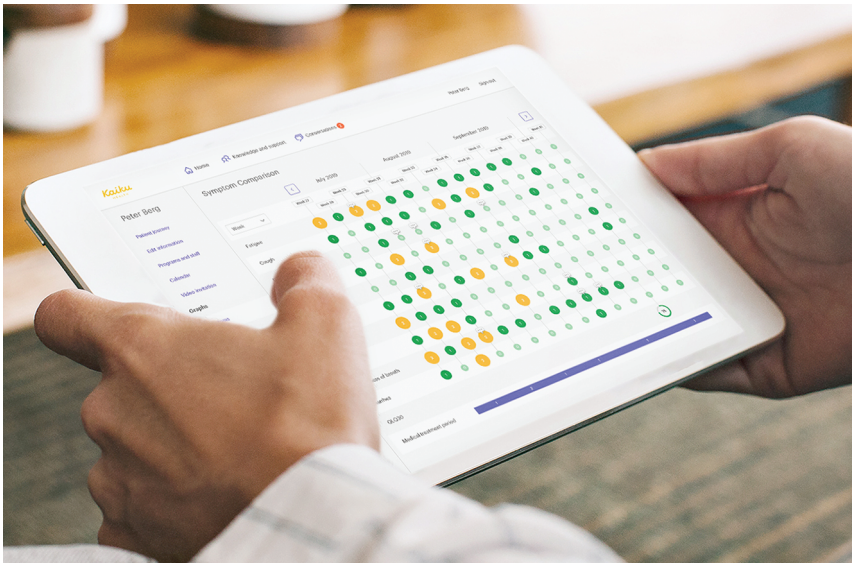

Figure 3. The Photo Illustrates How Changes in Symptoms and Values Can Be Easily Monitored Over Time Using ePRO Follow-Up (Reprinted with permission from Kaiku Health)

The Challenging Transitions

Transitions of care occur when a patient moves between facilities, sectors and staff members, for example: a transfer from the emergency room to the cancer unit; from a nursing home to a hospital; from a primary care doctor to a specialist; or from one nurse to another during a shift change. As part of their treatment cancer patients receiving systemic anticancer treatment often have numerous transitions between the outpatient clinic or cancer unit back and forth to their own home. Shifting between so many care providers and being left to yourself at home can create insecurity for patients and their next of kin. Such transitions of care increase the chances of communication errors, which can lead to serious medication harm (Aase et al., 2017; Aase & Waring, 2020).

Essential components in making the transition process safer include: medication reconciliation, structured facilitation and discharge communication, patient and next of kin education, and timely follow-up after discharge. All of these processes are unique to each cancer patient and their family and may change over time, so they need to be actively and consistently involved on all occasions. It is important to recognize that healthcare personnel always have the responsibility to facilitate the transition of care and provide safe care regardless of the service level in the healthcare system.

For post-discharge communication through new technologies, such as smartphones and applications, provide new opportunities to follow the patients closer when at home. A systematic review of studies using various technologies concluded that these technology-based interventions did not compromise safety or patient satisfaction when they measured symptoms, quality of life or psychological distress (Dickinson et al., 2014). The consequences for cancer patients in anticancer treatment can have potentially fatal outcomes in cases of missing responses to changes in the patient's condition (e.g., sepsis, bleeding). The next of kin's ability to observe the patient and to respond quickly to changes in their condition is therefore crucial, especially when the patient is between care levels. Next of kins living with the cancer patient are described as quality and safety resources, just as important as professional actors, and thus have a key role in safe transitions across care levels. Nevertheless, proper next of kin involvement is often lacking:

> "As a next of kin, you really get little information that is aimed at you on how to help and ease the treatment even if a lot happens at home." (Quote from a next of kin)

Healthcare service is a public responsibility in the Norwegian welfare state, and the formal expectations for next of kin participation are low. There are, nevertheless, strong indications that healthcare services do depend on support from next of kin to ensure high quality care for the patients (Bergerød & Braut, et al., 2020; Norwegian Ministry of Health and Care Services, 2020a; O'Hara et al., 2019). Healthcare professionals within cancer care in hospitals report that they depend on support from the next of kin to provide care quality and safety in the cancer field in hospitals. The next of kin role is often referred to as a "key piece of the puzzle", as a resource to cope with tasks they are unable to cope with because of internal (e.g., inadequate staffing, deteriorating patients) or external factors (e.g., culture, demands, economy) (Bergerød & Braut, et al., 2020).

> They often help to transport the patient, follow the patient to take blood samples, check the medicine list, and also ensure that the patient takes the medication at the right time, especially if the patient doesn't want homecare. They inject medication, measure temperature, and contact the hospital if the patient is experiencing fever. They have a huge sense of responsibility to the patient and are resource persons for the patient, us (hospital) and the municipalities. (Quote from a nurse)

Currently no recommendations exist on how to make safe transitions from hospitals to home for cancer patients or their next of kin. However, the Norwegian Directorate of Health is working on a care package process ensuring predictability for patients and their families, both in the specialist health service and in the municipal health and care services (Norwegian Directorate of Health, 2021c). Involvement is therefore crucial to strengthen the goal of creating an alliance between the family of the patient, healthcare services and voluntary organizations (Norwegian Ministry of Health and Care Services, 2020a). Next of kin involvement is more prominent than ever, and in 2021 the Norwegian government launched the first national strategy on next of kin involvement. The strategy is a clear acknowledgement of the next of kin role as a valuable societal and care contributor. The strategy has three overarching goals: 1) to acknowledge the next of kin role

as a resource; 2) attention and support so that next of kin can live good lives and combine the role of next of kin with education and work; 3) no child should have to take care of their family or others (Norwegian Ministry of Health and Care Services, 2020b). This strategy strives to have sound next of kin involvement, however there is also a long way to go before we reach these goals. Even if strategies, plans and sound involvement measures are slowly appearing, there is a great potential for translating these into clinical practice with a multi-stakeholder approach (Petkovic et al., 2020).

The development of the next of kin involvement guide for hospitals constitutes a good and promising tool (Figure 4) in terms of multiple

Figure 4. The Next of Kin Involvement Guide for Hospitals Adapted from Bergerød & Braut et al. 2021

stakeholders' engagement and sound involvement measures (Bergerød & Braut et al. 2021). The guide is built through a collective sharing of the experiences of 20 stakeholders including hospitals, healthcare professionals (nurses/doctors), patients and next of kin representatives, and researchers. The nominal group consensus method utilized in the development of the guide promoted a collaborative learning arena that resulted in mutual consensus. The guide is co-created and provides a requested tool that has the potential to support managers' and healthcare professionals' systematic work on next of kin involvement in hospitals. The next of kin involvement guide can be used either as a reflective tool to create a dialogue on how it can be refined to meet the context where involvement takes place, or as a guide with practical examples of relevant next of kin involvement measures (Bergerød & Braut et al. 2021). We argue that even if the guide is developed with the specialist healthcare system in mind, it could be pilot tested for other contexts (Bergerød et al. 2022).

Summary

This chapter has demonstrated that medication safety in cancer care is complex, with a high risk of adverse events related to systemic cancer treatment. It is no surprise that cancer patients experience treatment-related toxicities, since traditional systemic treatment, such as chemotherapy, have a low therapeutic index. This means that even a minimal increase in the chemotherapy dose due to, for example: drug interactions, weight changes, or concomitant clinical conditions, may cause a significant increase in effect and potentially result in an adverse event for the patient. Due to this, adverse events related to systemic anticancer treatment will always occur to some extent, but we argue that, by sound involvement of patients and next of kin throughout the whole cancer care continuum, severe adverse events can be reduced. Essential components in making the systemic anticancer treatment process safer include: medication reconciliation; structured facilitation and discharge communication; and sound patient and next of kin involvement focusing on individual education and timely follow-ups in the challenging transitions. The goal of measuring adverse events is to provide real-time

feedback to healthcare professionals, and thereby offer hospitals state-of-the-art quality improvement and learning opportunities to prevent such events from happening. New technology and innovations create new opportunities to engage the patient more actively in their own treatment and follow them more closely when they are at home. Personalized patient follow-ups using e-PROs give healthcare personnel a better opportunity to observe patients during treatment even when they are at home, and facilitates proactive interventions so severe adverse events can be mitigated. It also improves symptoms and quality of life, empowers patients in everyday living, and provides safety for patients and their next of kin. Next of kin play an essential role within the cancer field as collaborative partners in quality and safety efforts, and should be acknowledged as equal and natural partners in the same way as patients. The development of the next of kin involvement guide for hospitals provides a promising tool in terms of multiple stakeholders' engagement and sound involvement measures relevant for healthcare professionals and mangers throughout the healthcare system.

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CHAPTER 4

Do They Know What Medication They Are Prescribed? A Study Among Persons Older Than 60 Years in Norway Receiving Home Care Services

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Abstract: Older persons are prescribed multiple medications, which increases the risk of mistreatment and drug interactions. To ensure correct drug use, patients should be well informed about the medications they are prescribed. The aim of the study underlying this chapter was to describe the relationship between which medications are prescribed, and the information patients have about these medications. Two hundred eight persons 60 years or older receiving home care from one Norwegian municipality were asked questions about what medications they were using, and the answers were compared to the list of prescribed medications for the person. A high proportion of the participants were prescribed psychotropic drugs. Most of the participants who were prescribed sedatives or analgesics were informed about their prescription and for what condition the medications were prescribed, but 17.4% of participants prescribed anxiolytics were not informed about the reason for the prescription, and 27.6% of the participants not prescribed sedatives said they used sleeping pills. As many as 63.4% who were not prescribed analgesics said they used painkillers. In total, most of the participants were aware of what medications they were prescribed, but a significant proportion of the participants were not fully

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aware. Our results present a concern regarding patient safety. Health care personnel should inform patients more completely, and moreover, repeat information about the medication prescribed. Better knowledge about prescribed medication will help the patient understand his/her own diseases better, and thus make informed decisions about their own health.

Keywords: Home care, medication, older people, patient safety, prescription

The World Health Organisation (WHO) defines patient safety as: "A framework of organized activities that creates cultures, processes, procedures, behaviours, technologies and environments in health care that consistently and sustainably lower risks, reduce the occurrence of avoidable harm, make errors less likely and reduce the impact of harm when it does occur" (WHO, 2021, p. v). Moreover, the WHO patient safety framework for action is comprehensive and offers multiple action approaches by describing seven strategic objectives and 35 specific strategies. Each nation should prioritize areas of action, which range from the safety of clinical processes to patient and family engagement (WHO, 2021, p. 13).

An aim for patient safety work in Norwegian healthcare services is "a safe and secure healthcare service, without harm, for every patient and user, always and everywhere" (National Directorate of Health, 2022). During the last decade, patient safety work in health care services in Norway has received increased attention, and has been developed and enhanced especially through the campaign, In Safe Hands 24-7, which has targeted multiple topics and actions (National Directorate of Health, 2022). To improve patient safety in the healthcare services, all severe health-related incidents in Norway have been registered since 2019 (Ministry of Health and Care Services, 2017).

Relevant here are initiatives to reduce medication-related adverse events, including procedures targeting medication reconciliation, review, and control (National Directorate of Health, 2022). Due to the high number of medication-administration events reported, particularly in municipal healthcare services, the Norwegian National Commission of Inquiry has initiated a project to improve patient safety regarding the use of medication in municipal healthcare services (Norwegain Commision of Inquiry in Health and Care Services, 2021).

Statistics from 2019 show that adverse events occurred in 12.4% of hospital admissions, and that in all in-patient admissions to hospitals, injuries related to drugs occurred in 2.1% (National Directorate of Health, 2022). Healthcare services in municipalities lack similar statistics and registers (National Directorate of Health, 2022), and consequently fail to document changes related to this issue (Odberg, 2020). However, research shows that adverse events connected to medication do occur in municipal healthcare services, and they should get more attention. Particularly, studies that describe how patients living at home understand and comply with their medication treatment are needed (Olsen & Andreassen, 2016). Thus, continued efforts in patient safety work are essential.

In this chapter we will present results from a study in which elderly persons receiving home care services in Norway answered questions about what medications they were told they were prescribed.

Background

In Norway, national health reforms in the last two decades focus on quality improvements, coordination, continuity in care, and decentralization of services (Ministry of Health and Care Services, 2006, 2009, 2013, 2018). These national health reforms within healthcare services highlight health-promotion efforts, expecting the elderly to live longer in their own homes and, if needed, to receive home care services. Norwegian municipalities are obliged to provide health and care services for older adults, where institutional care, home care, and general practitioners are defined as core services (Skinner, Veenstra et al., 2020). Home care services typically consist of help for activities of daily living (ADL), for example, personal hygiene and meals, or medication administration (Ministry of Health and Care Services, 2011). In total, almost 200,000 persons receive home care services in Norway (Statistics Norway, 2021). Out of these, 110,000 persons are 67 years or older. Further, 28.9% of the population 80 years and older receive home care services (Statistics Norway, 2021).

In general, elderly persons are multimorbid, consequently causing a complex polypharmacy situation. Moreover, medication-related events

occur most frequently among the elderly (Olsen & Andreassen, 2016; Romskaug & Bakken, 2020). These events will typically appear as an increased risk of adverse effects from treatment, always considering the balance between benefit and harm. Given the situation and frailty of the elderly person, this demands a thorough clinical assessment in which the patient's preferences must be emphasized. This is crucial to ensure elderly patients safe and reasonable medication prescriptions (Romskaug & Bakken, 2020). Moreover, *event* is the preferred term according to the International Classification for Patient Safety (ICPS) conceptual framework, meaning "something that happens to or involves a patient" (WHO, 2009), and we have chosen to use this term in our study.

However, the particular characteristics of elderly patients is not the only factor associated with medication-related problems. How the healthcare services are organized is also of importance, since collaboration between different healthcare services and professionals has an impact and can affect the quality of outcomes (Skinner, Veenstra et al., 2020). Recent research has revealed a situation, as a result of the national healthcare reforms, where the decentralization of tasks from specialist health services[1] to the municipality and primary care service has led to a greater need for information exchange and collaboration between different healthcare providers within municipal health service organizations (Gautun & Syse, 2017; Skinner, Veenstra et al., 2020). To preserve the older person's need for continuity of care, better collaboration between nurses and general practitioners (GP) is needed (Skinner, Veenstra et al., 2020). Moreover, features of the municipality, such as number of inhabitants, socioeconomic factors, and limited resources in the healthcare sector, may also affect the situation (Gautun & Syse, 2017; Skinner, Veenstra et al., 2020).

Of special interest is the use of psychotropic medication among elderly people receiving home care services, and especially whether the patients are informed about what medications they are prescribed. Lack of information about what drugs they are prescribed and why,

1 In Norway, specialist health services have other obligations and provide other health services than the municipalities, including hospital admissions.

may influence their compliance. Psychotropic drugs are antipsychotics, antidepressants, anxiolytics, sedatives, and anti-dementia drugs (Lornstad et al., 2019). Side and adverse effects like sedation, weakened muscle tone, hypotension, and orthostatism from these types of medications are of particular concern to the elderly, because they can lead to falls and trigger delirium (Romskaug & Bakken, 2020). Beyond individual consequences, adverse drug reactions are also a source of economic burdens for the healthcare systems through increased hospitalization, prolongation of hospital stay, and additional clinical investigations in more serious cases (Sultana et al., 2013). A review study reveals that approximately 10–20% of geriatric hospital admissions are drug-related, moreover 32–65% of adverse drug reactions occur in nursing homes (Sultana et al., 2013). Unfortunately, there is a lack of similar statistics and registers for Norwegian municipal healthcare services (Odberg, 2020).

We know that the prescription of psychotropic medication among elderly people is high. In a group of 1,001 people aged 70 years or more, 40.3% used psychotropic drugs, and the prescription of psychotropic drugs was higher in those admitted to a nursing home than in those living at home (Lornstad et al., 2019). Additionally, the combined use of alcohol and medication among the elderly has been given attention, showing both a potentially serious alcohol-medication interaction when using central nervous system agents (Holton et al., 2020), and inadequate knowledge about these interactions. The first causes potentially harmful orthostatism and sedation, and the latter indicates a need for information to older adults about prescription drug safety via a variety of formats (Zanjani et al., 2013).

In summary, the high prevalence of multimorbidity and polypharmacy in the elderly population, psychotropic medications' risk of adverse effects, and the possible lack of information about what medication patients are taking, are all of concern. The aims of the study underlying this chapter were to describe the use of psychotropic drugs in a group of older persons receiving home care service, and to study the relationship between which psychotropic drugs the patients were prescribed, and which medications they were told they were prescribed.

Method

Participants

We invited 462 persons from one medium-sized municipality in south-eastern Norway to participate in the study. The inclusion criteria were: being 60 years or older, and receiving home care service in the municipality. The participants were invited to the study through a personal letter. Subsequently, staff from the home care service called the invited persons to find out if they had received and understood the invitation, if they agreed to participate, and to book time for the assessment. In total, 210 home-dwelling persons with home care service consented to participate, 22 persons were admitted to a nursing home before study start, and 230 persons were not included. The main reason for not participating was that the person or next of kin did not consent (n = 172). Of the 210 participants receiving home care service, two participants did not answer the questions about how well informed they were about psychotropic drug use, and thus we included 208 persons in our study. The participants were included between January 2017 and February 2018. Two research nurses trained in the assessment tools used in the study performed all the data collection.

Data Collection

In addition to information about the prescribed medication, we collected several other variables to explore connections including demographic information. Symptoms of anxiety were assessed with the rating anxiety in dementia scale (Shankar et al., 1999) (score 1–18 points, a score of 12 points or higher is regarded as clinically significant anxiety). Symptoms of depression were assessed using the 5-point version of the geriatric depression scale (Yesavage, 1988) (score 0–5 points, a score of 1 or more points is regarded as clinically significant depression). Cognitive function was assessed using the Montreal cognitive assessment test (Nasreddine et al., 2005) (score 0–30 points, higher scores mean better cognitive function). Physical health was assessed with the general medical health rating scale (GMHR), a four-category scale dichotomized in fair/poor versus

excellent/good (Lyketsos et al., 1999). More information about the other assessment scales, the data collection, and the study is found in a previously published paper by Bergh et al. (2021).

Information about prescribed medications was collected from the patients' medical journals. Prescribed psychotropic medication was categorized according to the anatomical therapeutic chemical (ATC) classification systems into anxiolytics (N05B), hypnotics/sedatives (N05C), and analgesics (N02 + M01A).

To study if the participants were informed about the medications they were prescribed, we asked them three short questions: "Do you use drugs for agitation or anxiety? (yes/no)"; "Do you use sleeping pills? (yes/no)"; and "Do you use painkillers? (yes/no)".

Analysis

Demographic and clinical data are presented as percentages (%) and mean (standard deviation, SD). Prescription of categories of psychotropic drugs are presented as percentages (%). The numbers of participants answering "yes" to the questions about how informed they were about their own medication, are presented as percentages (%). The relationship between the participants' prescribed medication and the participants being informed about taking medication were analyzed using a chi-square test.

The difference between patients being informed about their prescribed medications and patients not being informed was analyzed with a chi-square test and a student t-test, respectively. A logistic regression model with "informed about own medication" as a dependent variable was built, where age, sex, years of education, marital status, physical health, cognition, anxiety, and depression were independent variables.

Ethics

The study was approved by the Regional Committees for Medical and Health Research Ethics (REC), Norway, 2016/1134. Data collection started before the GDPR was launched, and no approval for the institutions'

data protection officer was necessary. Participation was based on informed written consent, from the participants or from their next of kin if the participant lacked the competence to consent. Forty percent of persons receiving home care service in Norway have dementia, while an additional 30% have mild cognitive impairment. A substantial part of these have reduced competence to consent and leaving them out of the research is unethical. Therefore, they were included in the study based on written consent from their next of kin. This procedure was approved by the REC.

Results

Demographic and clinical data are presented in table 1. For the whole cohort, the mean age was 80.7 (SD 8.8) years, 67.3% were women, and 74.0% had fair or poor physical health according to the General Medical Health Rating scale (GMHR).

Table 1. Demographic and Clinical Variables for the Whole Cohort, and for the Groups of Participants "Informed About Their Medication" and "Not Informed About Their Medication"

	All participants (n = 208)	Participants informed about their medication (n = 78)	Participants not informed about their medication (n = 130)	p-value
Woman, number (%)	140 (67.3)	43 (55.1)	97 (74.6)	**0.004**
Age, years, mean (SD)	80.7 (8.8)	80.9 (8.8)	80.6 (8.9)	0.78
Years of education, mean (SD)	10.2 (3.1)	10.0 (3.0)	10.6 (3.2)	0.21
Marital status	167 (80.3)	59 (75.6)	108 (83.1)	0.19
Unmarried, widow/widower, divorced, number (%)				
Fair/poor physical health (GMHR), number (%)	154 (74.0)	56 (71.8)	98 (75.4)	0.57
Montreal Cognitive Assessment test, mean (SD)	21.5 (6.6), n = 204	20.5 (7.8) n = 76	22.1 (5.7) n = 128	0.12
Geriatric Depression Scale – 5 questions version, mean (SD)	1.4 (1.4)	1.4 (1.3)	1.5 (1.5)	0.72
Rating Anxiety in Dementia, mean (SD)	5.9 (5.4)	5.3 (5.6)	6.2 (5.3)	0.26

SD = standard deviation, GMHR = General Medical Heath Rating scale.

Table 2 describes the proportion of participants informed about what medication they were prescribed, and the proportion of participants prescribed different classes of medication. Twenty-three participants (11.1%) were prescribed anxiolytics, 63 participants (30.3%) were prescribed hypnotics/sedatives, and 63 participants (30.3%) were prescribed analgesics.

Table 2. Reported and Prescribed Medication Use in the Sample

	All participants (N = 208)
Proportion of participants answering "yes" to the question about medication use, number (%)	
Do you use medication for agitation or anxiety?	53 (25.7), n = 206
Do you use sleeping pills?	103 (49.5)
Do you use painkillers?	152 (73.1)
Proportion of participants prescribed medication, number (%)	
Anxiolytic (N05B)	23 (11.1)
Hypnotics/sedatives (N05C)	63 (30.3)
Analgetic (M01A + N02)	63 (30.3)

Tables 3, 4, and 5 present the relationship between the proportions of participants prescribed anxiolytics, sedatives, and analgesics, respectively, and the proportion of participants confirming use of the same classes of drugs (answering "yes" to the questions about use of drugs).

Table 3. Cross-Table for Prescribed and Reported Use of Anxiolytics

	Prescribed anxiolytics		**p-value**
n = 206	**Yes (n = 23)**	**No (n = 183)**	
Do you use drugs for agitation or anxiety?			
– Yes	19 (82.6%)	34 (18.6%)	<0.001
– No	4 (17.4%)	149 (81.4%)	

Chi-square test for categorial data.

Of the 23 participants prescribed anxiolytics (Table 3), four participants (17.4%) answered "no" to the question, "Do you use drugs for agitation or anxiety?", while of the 183 participants not prescribed anxiolytics, 34 participants (18.6%) answer "yes" to the question, "Do you use drugs for agitation or anxiety?" ($p<0.001$).

Of the 63 participants prescribed sedatives (Table 4), zero participants answered "no" to the question, "Do you use sleeping pills?", while of the 145 participants not prescribed sedatives, 40 participants (27.6%) answered "yes" to the question, "Do you use sleeping pills?" (p<0.001).

Table 4. Cross-Table for Prescribed and Reported Use of Sedatives

	Prescribed sedatives		p-value
n = 208	**Yes (n = 63)**	**No (n = 145)**	
Do you use sleeping pills?			
- Yes	63 (100%)	40 (27.6%)	<0.001
- No	0	105 (72.4%)	

Chi-square test for categorial data.

Of the 63 participants prescribed analgesics (Table 5), three participants (4.8%) answered "no" to the question, "Do you use painkillers?", while of the 145 participants not prescribed analgesics, 92 participants (63.4%) answered "yes" to the question, "Do you use painkillers?" (p<0.001).

Table 5. Cross-Table for Prescribed and Reported Use of Analgesics

	Prescribed analgesics		p-value
n = 208	**Yes (n = 63)**	**No (n = 145)**	
Do you use pain killers?			
- Yes	60 (95.2%)	92 (63.4%)	<0.001
- No	3 (4.8%)	53 (36.6%)	

Chi-square test for categorial data.

In a logistic regression (Table 6) where "informed about the medication prescribed" was the dependent variable, females had higher odds (OR = 2.35) for being in the group of participants not informed about their medication, and participants with higher scores on the MoCA (better cognitive function) had higher odds (OR = 1.05) for being in the group of participants not informed about their medication.

Table 6. Logistic Regression with Informed About Medication as Dependent Variable, and Sex, Age, Years of Education, Marital Status, Physical Health, Cognition, Anxiety Symptoms, and Depressive Symptoms as Independent Variables

	B (SE)	Odds ratio	p-value
Constant	1.17 (1.95)		0.55
Sex (Ref. = male)	0.86 (0.35)	2.35	**0.02**
Age in years	–0.02 (0.02)	0.98	0.35
Years of education	–0.10 (0.05)	0.90	0.06
Marital status (Ref. = "Unmarried, widow/widower, divorced")	–0.09 (0.40)	0.92	0.83
Physical health, GMHR dichotomized (Ref. = Fair/poor)	0.19 (0.37)	1.22	0.60
Cognition, MoCA	0.05 (0.03)	1.05	**0.04**
Anxiety symptoms, RAID	0.01 (0.04)	1.01	0.85
Depressive symptoms, GDS	–0.03 (0.14)	0.97	0.55

B = unstandardized regression weight, SE = standard error, GMHR = General Medical Health Rating scale, MoCA = Montreal Cognitive Assessment scale, RAID = Rating Anxiety in Depression, GDS = Geriatric Depression scale.

The main findings in our study show that most of the participants prescribed sedatives or analgesics were informed about their prescription, and for which condition the medications were prescribed, while 17.4% of participants prescribed anxiolytics were not informed about the reason for the prescription.

Discussion

The fact that almost one out of five patients prescribed anxiolytics are not aware that they were prescribed medication usually used for agitation and anxiety is of concern, particularly since there are few other indications for the use of it. If you use anxiolytics, and are not aware of it, this may be because of lack of information from the GP and the health care staff, misunderstanding between the GP and the patients due to wording and use of phrases not familiar to the patients, and/or the stigma of psychiatric diseases. Some participants in our study had cognitive decline (mean MoCA score 21.5, SD 6.6), and it is reasonable to believe that some of them may have had home care service to help them remember to take their prescribed medications. Therefore, asking them questions about

what medication they are prescribed may give unreliable answers. This may explain some of the discrepancy between the information about one's own medication through asking the participants, and the information from medical records about their prescriptions. Our results indicate that information to the patients about what medications they are prescribed and why, must be repeated. The GPs and healthcare staff must also use common everyday language that the patients understand, and make sure that the information is understood, as pinpointed by authors referred to in this chapter (Olsen & Andreassen, 2016; Romskaug & Bakken, 2020).

As highlighted by the WHO in their safety action plan for 2021–2030, good quality care should include patient and family engagement, for example, information to and education of patients and families. Moreover, this insures patient safety in clinical processes in primary care and transition of care (WHO, 2021, pp. 13–14). The use of informal care is high in Norwegian municipalities (Skinner, Lorentzen et al., 2020), and education and information relating to prescribed medication must be shared with relatives of patients. This is even more important when the patient has a cognitive impairment. A high proportion (80%) of the participants were either unmarried, widow/widower, or divorced, indicating that they lived alone. However, we do not know this for sure since we did not ask them if they lived alone. In any case, it is highly relevant and important to involve and empower patients and families in relation to prescribed medications since the consequences for all parties are multiple and severe (Romskaug & Bakken, 2020). In addition, where and how information about the patient's medications and prescriptions are stored (i.e., a list of medicines) is important. Is this information only available on a digital medium (e.g., Helse Norge[2]), and/or is it available as a written version in the patient's home? However, since the participants in this study received home care services, the information is stored primarily where the medication is administered. Depending on the locale, the possibility for the health personnel to show and/or remind the patient/the relatives/

2 Helse Norge is a webpage for national online health services in Norway https://www.helsenorge.no/en/

informal caregivers, or for the parties themselves to obtain this information, is more or less good. This is also an important issue when there are changes to be made in the medication, and a need for medication reconciliation, which is a featured goal for patient safety work in Norway (National Directorate of Health, 2022).

Among the participants not prescribed anxiolytics, sedatives, or analgesics, a high proportion answered "yes" to the questions on whether they used these kinds of medication or not. This can be explained by the fact that we included only medication in the ATC group N05B (anxiolytics), N05C (hypnotics/sedatives), and N02 + M01A (analgesics) in our study, and participants may have been prescribed other medication groups for their anxiety, insomnia, or pain, such as antiepileptics, antihistamines, or antidepressants. Moreover, analgesics are available in stores without a prescription. The latter fact may also contribute to the understanding of why females had higher odds (OR = 2.35) for being in the group of participants not informed about their medications, since 72 out of 93 answers of "not informed about analgesics" came from females.

But it could also be the other way around. Some psychotropic drugs that are usually prescribed for anxiety, insomnia, and/or pain may have other indications. Participants answering "no" to questions about the conditions for which they were prescribed medication, may have been correct. In our opinion, our results, showing that participants that were prescribed medication but answered "no" to questions about taking medication for these conditions, are more reliable than the results showing that participants not prescribed medications but answered "yes" about taking medication for these conditions.

Also mentioned earlier, stigma may be a reason for answering "no" to the question, "Do you use drugs for agitation or anxiety?". Persons with mental illness experience stigma from both inside and outside the health services (Hoel, 2020). Stigma is a barrier to recovery, and stigma is described to be a larger problem for the person with mental illness than the disorder itself (Hoel, 2020). The answer "no" to the questions in our study, may indicate a denial of one's own problems or a fear of being stigmatized. The solution to stigma like this would be more openness. Consequently, contributing to more openness surrounding mental health

issues is an important patient safety task and a follow-up for health personnel. If they recognize or suspect this to be a problem for their patients, they must manage it in a responsible and professional way. What the right solution is must rely on individual considerations based on the patient's needs and condition. Whether the next of kin and/or informal caregiver should be included, is also an individual consideration.

We find it counterintuitive that participants with better cognitive function had higher odds for being in the group of participants not informed about their medications. We expected that participants with cognitive decline would have more trouble remembering what medications they were prescribed. But one possible explanation may be that participants with cognitive decline, because of their cognitive decline had been better informed about the medication they were prescribed.

A key point in this study is not mainly the fear of adverse effects from medication, but that events in administering the medication might lead to adverse effects. Considering persons who might live alone, suffering from cognitive decline in addition to limited knowledge about their own medication, this is not an optimal situation. Hence, more research is needed to map out this complex situation.

An interesting issue is that we can recognize WHO's definition of patient safety as less strict than the one used in Norway. Where WHO refers to "lower risk, reduce the occurrence of avoidable harm, etc." (WHO, 2021), the Norwegian definition specifies "without harm, for every patient and user, always and everywhere" (National Directorate of Health, 2022). This might be a theoretical issue, but worth noting. What are we aiming for in this important work?

Our study has some limitations and some strengths. One limitation is that all participants were recruited from the same municipality, and more than 50% of the invited eligible participants were excluded from the study. This may challenge the generalization of the results. One other limitation is the complexity of indications for medication prescriptions and diseases for which one medication may be prescribed. This has been elaborated earlier in the discussion. We are also aware that persons suffering from psychiatric problems and diseases still experience stigma related to their situation (Gulslett et al., 2014). This might have prevented

our participants from sharing information about their own situation, including what medications they were prescribed, affecting our results.

One strength of the study is that all persons receiving home care service in the included municipality were invited to the study. On the other hand, they were invited to a study with the aim of describing psychiatric symptoms, prescribed medication, and the use of alcohol and illegal drugs. Therefore, persons in the municipality may have declined to take part in the study due to stigma. Another strength of the study was that information about the prescribed medications was collected from the participants' medical records, which is a reliable source of information. We also used internationally recognized assessment tools to collect information about clinical variables, and the two study nurses had received a two-day training period before the data collection, which should result in reliable data for the study.

Closing Reflections

A high proportion of persons receiving home care service are prescribed psychotropic drugs. Although most of them are aware of what medications they are prescribed, our study shows that a significant proportion of persons receiving home care service are not fully aware of the medications they are prescribed. This is a concern regarding patient safety, and it shows that health care personnel should inform their patients more thoroughly, and moreover, repeat information about the medications prescribed. Better knowledge about prescribed medications, will help patients better understand their own diseases and make informed decisions about their own health.

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Part Two:

Medicines

CHAPTER 5

Information Regarding Modification of Oral Solid Medicines in Written Drug Information: Potential Consequences for Patient Safety

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Abstract: Oral solid medicines (oral solid dosage forms, OSDFs) are among the most used medications, and have various pharmaceutical designs ranging from relatively simple uncoated tablets with immediate-release properties, to advanced modified-release preparations slowly releasing the active ingredient. Taking medicines correctly is essential to preserve intended effects and avoid adverse effects. Still, modification of OSDFs is a common practice among patients and health care personnel, due to for example, swallowing difficulties. Modifications such as crushing tablets and opening capsules should only be done with a careful assessment of potential risks and benefits. In this study, we systematically reviewed the information relating to modification of OSDFs in the monographs of a commonly used source of medicine information in Norway, Felleskatalogen®. A total of 31 different OSDFs were identified. Results show that information on whether the medicines should be swallowed whole, could be divided, crushed, chewed, or opened, varied widely. Medicines with modified-release characteristic generally had more and stricter recommendations concerning modification than medicines with immediate-release characteristic. Recommendations varied largely between monographs, and different recommendations such as "shall", "should" or "must" may be interpreted differently among readers. Furthermore, a relatively small proportion of the monographs contained descriptions of the potential consequences of modification.

Based on our observations, a necessary risk-benefit assessment on dosage form manipulation for health care personnel and patients is possibly being impeded. Explicit and unambiguous information, or the development and implementation of

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a "traffic light model" for dosage form manipulation might reduce the risk of medication errors, and thereby increase patient safety.

Keywords: Oral solid dosage forms, modified-release, immediate-release, medicine safety, drug modification, medicine information

According to the World Health Organisation (WHO, 2017), medication errors are one of the leading causes of avoidable harm from medicines, and often occur during their administration. Solid medicines taken by mouth, so-called oral solid dosage forms (OSDFs), are most common, and vary widely in pharmaceutical form and design (Logrippo et al., 2017). Modifying the pharmaceutical form of a tablet or a capsule, for example, may alter the effect of the medicine due to changes in the rate and extent of absorption of the active ingredient (Anonymous, 2014; Logrippo et al., 2017). Thus, the correct handling and administration of each specific OSDF is essential to avoid medication errors and the risk of harm to the patient. However, a correct administration of OSDFs includes not only the intake of the unaltered dosage form, but also other factors, like an adequate amount of fluid during intake (Fuchs, 2009; Schiele et al., 2013) and correct head posture (Lau et al., 2018; Schiele et al., 2013).

Several sources of information, such as the package, the package label printed at the pharmacy, and the package leaflet, contain information on how to handle and administer medicines. In Norway, a frequently used source of information for nurses administering drugs is Felleskatalogen® (Johansen, 2019; Kirkevold & Engedal, 2010). Felleskatalogen® is a catalogue with monographs containing pharmaceutical preparations available in Norway. It is available online (www.felleskatalogen.no), as a version available for downloading, and as an application for smart phones and reading boards. The monographs are developed by pharmaceutical companies and the editorial staff at Felleskatalogen®, and based on the summary of product characteristics (SPC) (Felleskatalogen, 2021c). Information on administration and recommendations concerning manipulation of medicines are given under the dosing chapter for each medicine in Felleskatalogen®.

OSDFs, such as tablets, capsules and granules, have several advantageous features for both patients and manufacturers, including: a high degree of

self-administration, increased adherence, good stability attributes, and cost-effective production. OSDFs offer a large variety of products with different technological designs to fulfill various objectives, like a certain mode of drug release (immediate-release vs. modified-release) or managing a drug's stability issues (Logrippo et al., 2017). Conventional, immediate-release, solid dosage forms contain a single dose of a drug, and are designed to release its total amount within minutes into the gastrointestinal tract (GIT). Depending on the absorption rate following release, and the mechanism of action, a rapid pharmacological response is expected.

Modified-release solid dosage forms, on the other hand, are designed to release their contents in an either extended (i.e., continuously steady release over an extended period of time) or delayed manner (i.e., release with a time gap following intake) (Alderborn & Frenning, 2018). Extended-release dosage forms are intended to reduce the dosing frequency, that is, the number of drug doses per day, ideally to a once-daily or twice-daily dosage regimen (McConell & Basit, 2018). Less frequent dosing, compared to immediate-release dosage forms, needs to be compensated through a higher amount of the drug in an extended-release dosage form, in order to attain comparable drug levels in plasma within the extended dosing interval. Among delayed-release dosage forms, are OSDFs with a gastro-resistant release mechanism. The purpose of such dosage forms is to prevent the release of the drug into the stomach, thereby preventing either chemical degradation, with a subsequent loss of the drug, in the acidic environment, or gastrointestinal side effects from local irritation by the drug (Logrippo et al., 2017). Although many OSDFs should be swallowed whole due to the stated reasons, modification of medicines may be considered necessary because of swallowing difficulties (Logrippo et al., 2017; Solberg et al., 2021) or, as in the case of children, inappropriate dosage forms and/or strengths of commercially available medicines (Bjerknes et al., 2017).

The Extent of and Reasons for Manipulation of Oral Solid Dosage Forms

Manipulation of solid oral dosage forms is common and occurs in different settings and for different reasons. Schiele et al. (2013) reported

that 59% of patients in a German general practice population, taking at least one OSDF for a period of four weeks or more, reported having modified their drugs to facilitate swallowing. A self-reported study done in Australian hospitals, found that modifications occurred at the bedside for 79% of responding hospitals (Nissen et al., 2009). Modification occurred for both adults and children, and the most common reason for modification was the inability to swallow the OSDF (82%). Other reasons were lack of the correct dose in commercially available products and the need for drug administration through, for example, nasogastric tubes. Furthermore, a Norwegian cross-sectional study carried out in hospital paediatric wards, found that 17% of administrations of oral medicines involved manipulation. Unacceptable dosage form, inappropriate strength, or a combination of these, were the most frequent reasons for manipulations (Bjerknes et al., 2017). A study performed in 19 Norwegian nursing homes, showed that crushing tablets occurred in all nursing homes. Difficulty swallowing was the most common reason for crushing tablets. Others were preventing tablets from being spat out, kept or hidden in the mouth, and the need to administer the drug through a probe (Wannebo, 2009). Solberg et al. (2021) recently reported that modifications were done in 56 (21%) of 273 dispensing episodes. In addition to swallowing difficulties, lack of understanding by the patient, routines, and the patient's own wishes were the most common reasons reported for modification. For a specific patient, both the formulation, size, shape, and surface characteristics of the tablet/capsule, may contribute to swallowing difficulties. Fear of patients choking on medication may also contribute to modifying oral medicines (Mc Gillicuddy et al., 2019).

Potential Consequences of Modification

The consequences of modifying OSDFs depend on the pharmaceutical design of the specific medicine (Anonymous, 2014; Logrippo et al., 2017). Most worrying are cases of modifying extended-release solid dosage forms, which might lead to the release of the total amount of the drug, possibly causing severe adverse effects depending on the nature

of the drug itself (Cleary et al., 1999). The consequences of manipulating gastro-resistant dosage forms depend on the reason for formulating a gastro-resistant dosage form in the first place. For chemically susceptible drugs, drug loss through degradation may occur, resulting in a lower amount of the drug being absorbed, reducing the pharmacological response (e.g., proton pump inhibitors). For drugs showing gastrointestinal side effects due to, among other things, local irritation, like NSAIDs, these effects might be more pronounced (Anonymous, 2014).

Manipulating immediate-release solid dosage forms by means of crushing or chewing, might not necessarily have an impact on their intended release profile. Such dosage forms are supposed to disintegrate rapidly, releasing the drug immediately in the stomach, and one could argue that crushing or chewing such dosage forms would accelerate the disintegrating process, resulting in earlier onset. Lippert et al. (2005) revealed no significant differences in the area under the curve (AUC) and the maximum concentration (C_{max}) of immediate-release telithromycin tablets, administered as either intact or crushed tablets, and thereby assessed both administrations as bioequivalent. Nonetheless, manipulating immediate-release solid dosage forms might be unacceptable due to drug properties rather than release profile, like unpleasant taste or safety issues handling the medicine (e.g., chemotherapeutic agents).

The appearance of OSDFs do not in general reveal the purpose of their design, but since the intake of certain dosage forms in an unaltered way is crucial for their intended mode of action, so is comprehensible written information on how to handle and administer such dosage forms for the success of the medical treatment.

The aim of the study underlying this chapter is to describe the extent and content of information and advice given relating to manipulation (e.g., crushing and dividing) of OSDFs in the Felleskatalogen®. The research questions were: To what extent is information on manipulation given in the monographs? What information concerning manipulation is given for immediate-release and modified-release preparations, respectively? Based on specific examples, what could be the implications of (not)

following the advice concerning manipulation of oral solid medicines given in the monographs?

In this study, OSDFs include all different types of tablets, capsules, granules, powder, gums, pastilles/lozenges as well as powder and granules intended to be dissolved or dispersed in water by the patient before administration.

Methods

We exported trade names of all pharmaceutical preparations available in Felleskatalogen® (www.felleskatalogen.no) on 4 March 2021, n = 2,555 monographs. Written consent was given by Felleskatalogen® to store and use the data for the purpose of this study. Data were further handled and analyzed using IBM SPSS version 27.0. and 28.0.

The monographs were screened to identify the total number of individual pharmaceutical preparations. Medicines available as two different dosage forms, for example both tablets and capsules, were counted as two preparations. Medicines containing the same active substances having different names, (e.g., Cozaar Comp® and Cozaar Comp Forte® by Organon, both containing hydrochlorothiazide and losartan), were registered as two different preparations. A total of 2,915 individual pharmaceutical preparations were identified, representing 41 different oral dosage forms, in addition to preparations not intended for oral administration.

As shown in Figure 1, we excluded oral liquid preparations, and preparations not intended for oral administration. Thus, a total of 1,387 monographs relating to OSDFs were included in the study. From 4 March until 22 July 2021, we reviewed the monographs of these OSDFs on www.felleskatalogen.no. The following variables were registered: the dosage form; whether the preparation had its "own" monograph in Felleskatalogen®, and if not, which monograph the reader was referred to; the recommendations given under "Administration" for the manipulation of drugs (e.g., advice on crushing, dividing, and chewing the drugs); and whether the reasons for the recommendations were given. Dosage forms were registered based on the descriptions in Felleskatalogen®. In the analysis,

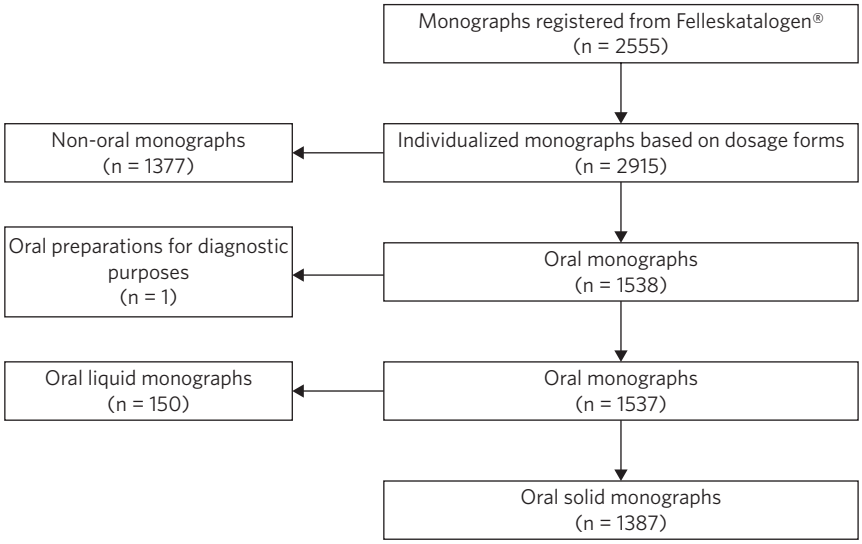

Figure 1. Flow Diagram Showing the Number of Monographs Registered in Felleskatalogen®. The monographs were reviewed to obtain the number of individual dosage forms. Monographs for non-oral medicines and oral liquid medicines were excluded

we categorized extended-release, delayed-release and gastro-resistant tablets, capsules, and granules as drugs with modified-release characteristics. All other drugs were categorized as immediate-release drugs.

We categorized the recommendations for medicines that "shall not", "should not" and "cannot be divided" as "cannot be divided". Medicines that "can be divided", "can be divided in two similar doses", "should only be divided once", "cannot be divided in two similar doses" and medicines for which different recommendations were given for different doses were categorized as "can be divided". For capsules, medicines were categorized in "shall not be opened", and "can be opened". For recommendations concerning crushing, medicines that "should not", "shall not" and "must not be crushed" were categorized as "cannot be crushed", whereas medicines that "should be" and "may (if necessary) be crushed" were categorized as "can be crushed". For chewing, medicines that "should not", "shall not" and "must not" be chewed were categorized as "cannot be chewed", whereas medicines that "can be" or "should be" chewed, were categorized as "can be chewed".

Results

Table 1 shows the frequency of different OSDFs in Felleskatalogen®, representing 33 different types of dosage forms. 1,200 (86,5%) of the preparations had dosage forms with immediate-release-characteristics, whereas 187 (13,5%) had modified-release characteristics. Of the 187 modified-release preparations 122 (65,2%) were tablets, 56 (29,9%) were capsules, and 9 (4,8%) were granules.

Table 1. Frequency of Different Oral Solid Dosage Forms in Felleskatalogen® (www.felleskatalogen.no)

Dosage form	Number of preparations (%)
Dosage forms with modified-release characteristics	**187 (13,5)**
Modified-release tablets	91 (6,6)
Gastro-resistant tablets	29 (2,1)
Gastro-resistant capsules	26 (1,9)
Modified-release capsules	30 (2,2)
Gastro-resistant and/or modified release granules	5 (0,3)
Others**	6 (0,4)
Conventional dosage forms with immediate-release characteristics	**1068 (77,0)**
Coated tablets	607 (43,8)
Conventional tablets	294 (21,2)
Hard capsules	133 (9,6)
Soft capsules	34 (2,5)
Alternative dosage forms with immediate-release characteristics	**132 (9,5)**
Powder or granules for liquid preparation (prepared by patient)	27 (1,9)
Orodispersible tablets (lyophilisates, "melting tablets")	27 (1,9)
Chewable tablets	17 (1,2)
Effervescent tablets	16 (1,2)
Dispersible tablets	9 (0,6)
Sublingual tablets	9 (0,6)
Granules	8 (0,6)
Lozenges	7 (0,5)
Others*	12 (0,9)
Total	**1387 (100,0)**

*Soluble tablets (n = 3), chewing gums (n = 2), powders (n = 4), granules in capsules to be opened (n = 1), pastils (n = 1), and dispersible/soluble tablet (n = 1).
**Gastro-resistant granules for liquid preparation (n = 3), gastro-resistant modified-release tablets (n = 2), modified-release granules for liquid preparation (n = 1).

Information and recommendations concerning administration varied largely between dosage forms and within similar dosage forms. We will further focus on information concerning modified-release tablets and capsules, and conventional immediate-release dosage forms. Table 2 shows the information and recommendations given on whether to swallow these drugs whole.

Table 2. Information and Recommendations in Monographs in Felleskatalogen® This relates to whether oral solid modified-release (tablets and capsules) and the conventional immediate-release dosage forms should be swallowed whole. Soft capsules are not included in the table

Dosage form/ To be swallowed whole?	No information N (%)	Can be swallowed whole N (%)	To be swallowed (primarily) whole N (%)	Should be swallowed whole N (%)	Shall be swallowed whole N (%)	N (%)
Tablets with modified-release characteristics	10 (8,2)	0 (0,0)	12 (9,8)	5 (4,1)	95 (77,9)	122 (100,0)
Capsules with modified-release characteristics	1 (1,8)	4 (7,1)	10 (17,9)	14 (25,0)	27 (48,2)	56 (100,0)
All coated tablets	297 (48,9)	1 (0,2)	97 (16,0)	79 (13,0)	133 (21,9)	607 (100,0)
Conventional tablets	227 (77,2)	3 (1,0)	25 (8,5)	13 (4,4)	26 (8,8)	294 (100,0)
Hard capsules	23 (17,3)	3 (2,3)	31 (23,3)	6 (4,5)	70 (52,6)	133 (100,0)

Of the 11 OSDFs with modified-release characteristics lacking information on whether to be swallowed whole, all had other specific recommendations on how to handle the drug. Recommendations were, for example:

- Should be swallowed with a glass of water. Shall not be chewed. Shall not be divided or crushed (Cortiment® modified-release tablets (budesonide, Ferring Legemidler AS))
- One gastro-resistant capsule is to be taken with cold or lukewarm water (not over 37°C) on an empty stomach, and at least one hour before the next meal. Shall not be chewed, and is to be swallowed as soon as possible after being put in the mouth (Vivotif® gastro-resistant capsules (typhoid vaccine, Emergent)).

Six of the 11 medicines with modified-release characteristics lacking recommendations to be swallowed whole, could, however, be divided, (e.g., Tegretol Retard®, carbamazepine, Novartis). Selo-Zok® modified-release tablets (metoprolol, Recordati) could also be divided. Yet, for 50, 100 and 200mg doses, dividing should only take place to make them easier to swallow. In comparison, dividing 25mg tablets results in two similar doses.

Information on whether the medicine should be swallowed whole, could be divided, crushed, chewed, dispersed in water, or sucked was lacking for all variables for 143 coated tablets (23,6%), 45 (15,3%) conventional tablets, and 11 (8,3%) capsules. This does not necessarily mean that no information was given on how to administer these medicines, as some mentioned that the drug was to be swallowed (but not, specifically, whole) and gave other recommendations which did not fit into these pre-defined categories. No OSDFs with modified-release characteristics were among these.

Table 3 shows information and recommendations on dividing, crushing and chewing oral solid dosage forms with modified-release characteristics and the conventional immediate-release dosage forms.

Only a few monographs explained the reasons for recommendations relating to modifying the medicine. One explicit reason given for the recommendation on why one should swallow the drug whole, was that the taste of the drug was bitter or bad. Another stated reason to swallow the drug whole, was an increased risk of side effects if the drug was divided, crushed, or chewed. Side effects could occur due to local effects, such as irritation of the gastric mucosa (e.g., Albyl-E® gastro-resistant tablets (acetylsalicylic acid, Takeda)), and discoloration of the teeth and mouth cavity (e.g., Vanquin® tablets (pyrvin, MEDA)), or due to increased systemic effects of the drug, such as an increased risk of bleeding caused by Pradaxa® capsules (dabigatran, Boehringer Ingelheim). For some drugs, dividing, chewing, or crushing tablets may result in rapid release and absorption of potentially lethal doses of the drugs, such as for Reltebon Depot® (Actavis) and OxyContin® (Mundipharma), both containing the opioid analgesic drug oxycodone in a modified-release dosage form. Furthermore, some cytostatic drugs, such as Sprycel® tablets (dasatinib,

Table 3. Information and Recommendations. This relates to dividing, crushing, and chewing oral solid modified-release (tablets and capsules), and the conventional immediate-release dosage forms. Soft capsules are not included in the table

Dosage form	N (%)	Dividing/opening*			Crushing			Chewing		
		No information	Can be divided**	Cannot be divided	No information	Can be crushed	Cannot be crushed	No information	Can be chewed	Cannot be chewed
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Tablets with modified-release characteristics	122 (100,0)	38 (31,1)	16 (13,1)	68 (55,7)	31 (25,4)	0 (0,0)	91 (74,6)	25 (20,5)	0 (0,0)	97 (79,5)
Capsules with modified-release characteristics	56 (100,0)	23 (41,1)	29 (51,8)	4 (7,1)	18 (32,1)	0 (0,0)	38 (67,9)	12 (21,4)	0 (0,0)	44 (78,6)
All coated tablets	607 (100,0)	351 (57,8)	154 (25,4)	102 (16,8)	419 (69,0)	60 (9,9)	128 (21,1)	496 (81,7)	0 (0,0)	111 (18,3)
Conventional tablets	294 (100,0)	93 (31,6)	175 (59,5)	26 (8,8)	222 (75,5)	49 (16,7)	23 (7,8)	262 (89,1)	8 (2,7)	24 (8,2)
Hard capsules	133 (100,0)	78 (58,6)	20 (15,0)	35 (26,3)	100 (75,2)	2 (1,5)	31 (23,3)	96 (72,2)	0 (0,0)	37 (27,8)

*For capsules, the presented data concerns opening the capsules.
**Includes preparations for which different recommendations are given for different strengths of the drug.

Bristol-Myers Squibb), were recommended to be swallowed whole to ensure correct dosing and minimize the risk of skin exposure. Similarly, Valganciclovir® tablets (valganciclovir, Accord; Sandoz), an antiviral drug, should not be divided or crushed as it is potentially teratogenic and carcinogenic.

Discussion

Different OSDFs and Recommendations Concerning Modification

We identified a great variation in OSDFs (Table 1) in Felleskatalogen®. As a consequence, recommendations concerning handling and administration of the medicines varied to a large degree. Some drugs are intended to be modified before or as they are administered, such as chewing tablets and orodispersable tablets. Others, such as medicines with modified-release characteristics are primarily intended to be swallowed whole. For OSDFs with modified-release properties, recommendations to swallow the medicines whole were more common than for OSDFs with immediate-release properties (Table 2). In addition, the monographs for these medicines generally contained recommendations to ensure their safe administration, and avoid potentially harmful modification. Modifying OSDFs with modified-release properties by crushing or chewing tablets, opening, or chewing capsules is of particular concern, as this may increase the risk of adverse effects (Cleary, et al., 1999), underdosing (for gastro-resistant medicines) and overdosing (for sustained-release medicines) (Anonymous, 2014). Approximately 20–30% (Table 3) of the monographs for OSDFs with modified-release characteristics lacked explicit recommendations as to whether these tablets or capsules should not be crushed or chewed. The phrase "to be swallowed whole" might be interpreted as a recommendation not to crush or chew the drug. Although OSDFs with modified-release properties require special caution regarding modifications, few rules of thumb exist for identifying whether a drug with a specific dosage form may or may not be modified, without checking information for the specific drug. Even though a large percentage

(78%) of tablets with modified-release characteristics *shall* be swallowed whole according to Felleskatalogen®, some may be divided, at least under specific circumstances, such as when both parts of the tablet are taken, or for specific strengths of the medicines.

The most common OSDFs in Felleskatalogen® were coated and conventional tablets. We would expect fewer restrictions concerning the modification of these medicines, compared to modified-release medicines. As shown in Tables 2 and 3, recommendations on modifying medicines were often missing for coated and conventional tablets. However, a significant number of tablets and capsules were recommended to be swallowed whole. There may be many reasons why it is preferable to swallow drugs whole, as presented in this study, thus decreasing the risk of local adverse effects, masking bitter taste, as well as avoiding contact with the skin, and to risk exposure to potentially carcinogenic and teratogenic medicines. Interestingly, the reasons for recommendations concerning modification were given in only a few monographs. For OSDFs where modification of the medicine could affect their properties, having explicit information available as to: a) whether a specific type of modification (e.g., crushing) of a medicine can be done, and b) what happens if the medicine is modified this way, may help prevent inappropriate or potentially hazardous modification of drugs.

Using and Interpreting the Available Information

For some health care personnel, crushing tablets may be a routine procedure on which they do not reflect (Wannebo, 2009). Lack of knowledge for both patients and health care personnel concerning modification of OSDFs, in combination with a lack of explicit information related to medicine modification, may result in reliance on informal information and the continuation of previous practices (Mc Gillicuddy et al., 2017b). Several studies have reported crushing of drugs with modified-release characteristics (Bjerknes et al., 2017; Nissen et al., 2009; Solberg et al., 2021; Wannebo, 2009). While recommendations concerning the modification of many OSDFs are available in Felleskatalogen®, this information has limited value to patients, carers or health professionals preparing

and administering the drugs do not seek the information, cannot find it or interpret it (Kirkevold & Engedal, 2010; Wannebo & Sagmo, 2013), or choose, for various reasons, to deviate from the recommendations.

To administer and modify an OSDF safely three factors are crucial. Firstly, the person responsible needs to check whether the medicine can be modified using reliable sources of information. Studies have shown that health care personnel do not always check for information before modifying and administering medicines (Karttunen et al., 2020; Kirkevold & Engedal, 2010). In a Finnish cross-sectional study (Karttunen et al., 2020), one-third of 492 nurses working in long-term elderly care, reported that they did not always follow the guidelines for preparing medication, and only 59% checked for information before crushing tablets. Furthermore, only 66% and 67% of nurses followed guidelines on not to crush enteric-coated and sustained-release tablets, respectively, although the SPC did recommend not doing so.

Secondly, when seeking information, one must know where to look. In Felleskatalogen® information concerning modification of medicines is now given under the same paragraph for all medicines and should be relatively easy to look up. As shown in this study, information is available for many OSDFs, whereas it is lacking for others.

Thirdly, the information – if there – needs to be easy to understand for the reader. Earlier studies have criticized information concerning modification of medicines in Felleskatalogen® in terms of both availability and understandability (Kirkevold & Engedal, 2010; Wannebo & Sagmo, 2013). These studies are quite old and may not reflect how this source is evaluated today. However, according to Table 2, many immediate-release drugs lack information on whether to swallow the drugs whole. On the other hand, many monographs stated that the drugs should be "swallowed" or "taken", often with a glass of water or fluid (results not shown). We do not know whether health care personnel interpret to be "swallowed" or "taken" significantly differently from "to be swallowed whole". Explicit, and unambiguous information is, however, preferable. Table 2 also shows that nuances exist between different monographs on whether drugs "should be (primarily)" swallowed whole, "should be" swallowed whole or "shall be" swallowed whole. These may not be considered or interpreted identically.

Consequently, the variation in phrasing might be confusing. Lack of descriptions of possible consequences regarding modifying OSDFs makes weighing potential risks and benefits of a specific medicine difficult.

Lastly, when looking up, finding, and interpreting information, this must still be applied to the specific patient. The need and the reasons for modifications vary largely between patients (Mc Gillicuddy et al., 2017a; Mc Gillicuddy et al., 2017b; Mc Gillicuddy et al., 2019). Administering the medicine may be considered more important than following recommendations concerning modification. Mc Gillicuddy et al. (2017a) found that modifications may be considered a "necessary evil " to meet individual patient's needs. A recent systematic review (Mc Gillicuddy et al., 2017b) highlighted the complexity involved in balancing the advantages and disadvantages concerning modification of oral dosage forms to individual patients, for health care personnel and patients making these decisions. Concerns related to the effects and safety of medicines being modified are only one of many issues involved in this decision-making process. For example, facilitating the administration of important medicines and overcoming concerns regarding choking or discontinuation of therapy, are others. In many cases, however, alternative forms may be available, including OSDFs as effervescent or orodispersible tablets or oral liquid dosage forms (Schiele et al., 2013; Thong et al., 2018). The use of a similar medicine from the same class might also be an option, as well as the discontinuation of unnecessary medicines (Anonymous, 2014; Mc Gillicuddy et al., 2017b).

In addition, even though tablets could be crushed from a pharmaceutical point of view, crushing and dividing tablets are not standardized procedures, being further complicated by for example, splitting techniques that affect drug loss (Gharaibeh & Tahaineh, 2020; Thong et al., 2018), or mixing crushed tablets or the contents of capsules into food or liquid before administration (Manrique-Torres et al., 2014).

Implications and Further Studies

Information on how to administer and handle OSDFs is available in Felleskatalogen® as well as other sources of information, such as the SPC and the package leaflet. Based on the apparently common practice

to modify OSDFs in Norway (Bjerknes et al., 2017; Solberg et al., 2021; Wannebo, 2009), information on whether a specific medicine should be swallowed whole, can be divided, crushed, chewed and/or dispersed in water before administration needs to be readily available, explicit, and preferably with explanations for the given recommendations, as well as the consequences for each type of modification. We are not familiar with any gold standard for the organization or phrasing of this kind of information to ensure its readability and understandability. Mullen et al. (2018) reviewed best practices for written patient-oriented medication information. They found that plain, behavior-oriented and explicit text, standardized format and typographic cues (e.g., headings and bullet points) could be considered best practice, however, outcomes differed significantly between studies, as did their design.

One way to increase the understandability of information relating to the manipulation of OSDFs, is to design a traffic light model comparable to the ones used for classification of drug interactions: "Green light" might represent medicines for which all kinds of modifications could be done without risking a loss or increase in effect; "yellow light" could represent medicines for which some modifications can be made, such as dividing the tablet in two to ease intake; and "red light" could represent medicines for which all modifications would risk the patient being deprived of its effect or experiencing adverse effects. Information included in such a model would need to be explicit. For example, for OSDFs with modified-release characteristics which cannot be modified at all, it should be specified that these can neither be crushed, divided, nor chewed, and that they must be swallowed whole. In Australia, the Society of Hospital Pharmacists of Australia (SHPA) has published a book called, *Don't Rush to Crush,* which gives answers to whether medicines can be crushed, dispersed, opened, and whether liquid formulations are available (SHPA, 2021). In Norway, Oslo University Hospital has developed the crushing/opening/dissolving list ("knuse-/åpne-/løselisten") which summarizes information on whether one may modify many OSDFs on the Norwegian market (Oslo Universitetssykehus, 2021). The list is to be used in combination with the guidelines for crushing/opening/dissolving tablets and capsules at the hospital, although explanations for the recommendations concerning each

specific medicine are not included. We are not familiar with to what degree this source of information is used by health care personnel outside the hospital.

Strengths and Weaknesses of the Study

We chose to use Felleskatalogen® as the source of information in this study, as this is a familiar and frequently used source of drug information for health care personnel handling and administering drugs in Norway (Johansen, 2019; Kirkevold & Engedal, 2010). Earlier studies have reported that nurses experience the information in Felleskatalogen® relating to crushing and dividing tablets as difficult to find and/or understand (Kirkevold & Engedal, 2010; Wannebo & Sagmo, 2013) However, these studies are quite old, and Felleskatalogen® has gone through major changes both in lay-out, as well as in content in recent years. Importantly, it is no longer available in book form. The monographs are based on the approved SPC, and has its own structure (Felleskatalogen, 2021a). Under the chapter "Dosing", a tag called "Administration" exists for all drugs with a few exceptions, including some parallel-imported drugs. This makes information and recommendations relating to manipulation readily available if you know where to look. We could have chosen to use the SPC and/or the package leaflets for information on how to administer drugs. Felleskatalogen® however, is based on the SPC. Our impression is that Felleskatalogen® is used more, and is easier to search than the SPC and the digital package leaflets. Felleskatalogen® might be more familiar to health care personnel than to lay people, and future research could compare information and recommendations relating to administration and manipulation of drugs in these sources.

Drugs were categorized as immediate-release and modified-release based on their description under the paragraph "Administration" in Felleskatalogen® only. Some drugs may have properties causing them to belong to both categories. Lanzo Melt® (lansoprazole, Pfizer), for example, is designed as orodispersible tablets, intended to dissolve rapidly in the mouth cavity, and could therefore be categorized as immediate-release tablets. The active ingredient lanzoprazole on the other hand

is particularly sensitive to gastric acid, which is why the tablet consists of drug-loaded microgranules with a gastro-resistant coating. Drug release from these granules happens as a delayed-release process (Felleskatalogen, 2021b).

We focused on oral solid dosage forms, and exclusively on the information and recommendation in relation to the manipulation of these. Other given recommendations, like procedures encompassing the use of beverages (amount/type) and concurrent food intake would be interesting, but were not within the scope of this study.

Conclusion

Information on modification of OSDFs is commonly available in Felleskatalogen®. As expected, information was more common for medicines with modified-release than immediate-release characteristics. However, recommendations regarding the modification of immediate-release dosage forms were surprisingly numerous. Moreover, the information was not unambiguous, and the reasons for the given recommendations, as well as the possible consequences of modifications, were rarely included. This may result in medication errors and possible harm to the patient.

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CHAPTER 6

Potential Safety Issues With Combined Use of Dietary Supplements and Medication – Focus on Interactions

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Abstract: The use of dietary supplements (DS) is widespread and tends to increase with age and female gender. DS use can in some situations represent a safety risk for patients. For instance, concomitant use of medication and dietary supplements, particularly herbal remedies, may cause clinically significant pharmacological interactions. The study underlying this chapter aimed to investigate the prevalence of potentially clinically significant DS-medication interactions in a general population of middle-aged women. The study is a questionnaire survey among Norwegian women born between 1943 and 1957. Data were collected from 2002 to 2006 as a part of the Norwegian Women and Cancer study (NOWAC). The participants listed all medications and all DS they had used during the previous week. The reported DS were checked for interaction potential in combination with medication, using the Natural Medicines database. The study population comprised 3,970 women, of whom 1,885 combined medication and dietary supplements. Overall, 630 (16% of the total population) used a DS-medication combination with a potential for at least one clinically significant interaction. Of these, 132 women used herb-medication combinations, 63 used combination(s) that represented more than two interactions, and three used combinations classified as a major health risk. There is considerable

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potential for clinically significant medication-supplement interactions in a general population such as the one described in the study. Although few of the identified interactions represent a major health risk, the findings indicate that health personnel should take supplements into account when assessing the safety of medication use among their patients.

Keywords: Dietary supplements, medication, patient safety, interaction, general population

According to Norwegian legislation, dietary supplements (DS) are nutritional products and substances: 1) intended to supplement the diet; 2) representing concentrated sources of vitamins and minerals or other substances with a nutritional or physiological effect, alone or in combination; and 3) sold in prepacked, dosed form designed for intake of small, measured amounts (*Forskrift om Kosttilskudd [Regulation on Dietary Supplements]*, Lovdata [Norwegian statutes in force], 2004). "Other substances" include herbs and other substances of so-called natural origin, for instance omega-3 fatty acids. This legislation is adopted from European legislation (EU directive, 2002).

Use of DS in Norway increased extensively from 1986 to 2004 (Waaseth et al., 2007). There was a slight decrease from 2006 to 2012 (Norwegian Food Safety Authority, 2013). The biannual NAFCAM surveys from 2012 to 2018 have shown a fairly stable prevalence in the use of natural remedies/herbs in Norway (Bergli, 2020). NAFCAM is Norway's national research center for complementary and alternative medicine.

International reports suggest that women use more DS than men, and most show that prevalence of use increases with increasing age, socioeconomic status and healthy lifestyle (Bailey et al., 2013; Kofoed et al., 2015; Li et al., 2010; Park et al., 2009; Touvier et al., 2006). A previous publication from the Norwegian Women and Cancer study (NOWAC) showed that in a general population of middle-aged women, 71% used some type of DS and the use was associated with socioeconomic, lifestyle and health-related factors, including medication use (Waaseth et al., 2019).

DS do not undergo the same detailed approval processes as medications. Thus, use of DS may be unsafe for many reasons. One can experience side effects from substances in the product or interactions can occur

between such substances and medications through combined use (Ronis et al., 2018). Similar effects can occur from non-declared content or contamination. For instance, heavy metal contamination may interact with medication (Anwar-Mohamed et al., 2009). Other reasons that use of DS may be unsafe include the risk of toxic reactions due to overdose, impact on diagnostic and perioperative procedures (Abe et al., 2014), and lack of necessary treatment due to some patients replacing medication with supplements. The last one is rare, however. Commonly, DS are used complimentary to evidence-based treatment, and mostly to improve overall health (Astin, 1998; Bailey et al., 2013; Salamonsen, 2013). Finally, it is difficult for both health personnel and DS users to find easily available and reliable information about DS safety (Owens et al., 2014; Risvoll et al., 2021).

Some patient groups are particularly vulnerable to unsafe use of dietary supplements. This is exemplified by persons with dementia who, in addition to the direct risks mentioned above, are affected indirectly due to cognitive decline (Risvoll et al., 2017). Risvoll et al. shows how this patient group receives far less assistance with their dietary supplements use compared with medication use, and that health personnel are uncertain regarding who should take responsibility for safeguarding such use (Risvoll et al., 2019; Risvoll et al., 2021).

High quality DS do not pose a large health risk when used alone, according to recommended dosage, and by healthy individuals. However, concomitant use of medication and DS, particularly herbal remedies, may cause clinically significant pharmacokinetic or pharmacodynamic interactions (Boullata, 2005; Reddy et al., 2021; Ronis et al., 2018; Tarirai et al., 2010). Pharmacokinetic interactions occur when a substance A (from medication or herb) changes the absorption, protein binding, distribution, metabolism or excretion of a substance B, thereby causing a changed concentration of substance B in the body. St. John's wort (*hypericum perforatum)* is an herb particularly known for its influence on the metabolism of medical substances through induction of liver enzymes (Tarirai et al., 2010). In Norway, legal sales of products containing St. John's wort are restricted to pharmacies because of the need for guidance in relation to the herb's interaction

potential. Pharmacodynamic interactions occur when substance A, directly or indirectly, interferes with substance B on its action site, thereby influencing the effect, but not the body concentration of substance B.

Through experiences from pharmacy practice and from the work on the previously mentioned publication from NOWAC (Waaseth et al., 2019), we have seen worrying cases of DS use. This can for instance be the use of two or even three different omega-3-supplements, representing a risk of over dosage of fat-soluble vitamins, or concomitant use of herbs and medication, which represents a possible interaction. Such cases indicate a potential health risk. They also suggest a lack of knowledge among the general population when it comes to what such supplements contain. The NOWAC study found concomitant use of DS and medication among 48% of the population, suggesting a potential for medication-DS interaction.

Compared with pharmaceuticals, the safety of DS is rarely investigated through traditional evidence-based research methods. Randomized controlled trials are resource demanding, and not a prerequisite for legal distribution of DS (Waaseth et al., 2007). Even products with marketing authorization as herbal medicines are not checked for safety beyond documentation of "long-established use" according to the EU directive (EU directive, 2004). Observational studies, using data from surveys and registries, therefore play an important role in describing DS use, and identifying safety issues related to this use, although such research also has its challenges (Arab, 2000). So far, most of the research on this subject has focused on prevalence of use and user characteristics (Li et al., 2010), or potential interaction mechanisms related to certain herbs and/or medications (Mouly et al., 2017; Tarirai et al., 2010). Few have attempted to quantify DS-medication interactions, and mainly among specific patient groups (Bush et al., 2007; Dergal et al., 2002; Firkins et al., 2018; Peng et al., 2004; Risvoll et al., 2017).

The study underlying this chapter aims to describe the prevalence of potentially clinically significant interactions between DS and medication use in a general population of middle-aged women, using data from the NOWAC study.

Material and Methods

This is a cross-sectional study among Norwegian women born between 1943 and 1957. Data were collected from 2002 to 2006 as a part of NOWAC.

Study Population

The Norwegian Women and Cancer study (NOWAC) is a nationwide, population-based cohort study with participants randomly sampled from the National Population Register, held by Statistics Norway (Lund et al., 2007). Since 1991, approximately 172,000 women have answered questionnaires on health, lifestyle and socio-demography.

From 2002 to 2006 approximately 50,000 women participated in the blood sample collection for the NOWAC biobank (overall response rate 71%). Participants (born 1943–1957) reported their use of medication and DS during the week preceding the blood donation and accompanying questionnaire. The women were invited in groups of 500. Data from eleven groups (5,500 invitees), randomly chosen, were electronically available at the time of analysis and comprise the basis of our study sample of 3,970 women (response rate 72%).

Use of Medication and Dietary Supplements

The participants listed all medication and all DS they had used during the previous week. In addition to the general question on DS use, the questionnaire included three specific questions on use of soy, cod liver oil and other omega-3 supplements. Information on dosage was not included as it was not collected for all participants, nor all products, due to slight differences in questionnaires for the various waves of data collection.

DS were mapped according to content based on manufacturer information, if available. Some were classified according to the reported product title (for instance, “calcium”, “antioxidant supplement”, etc.).

Medications were coded according to WHO’s ATC-classification (*ATC/DDD Index*. The WHO Collaborating Centre for Drug Statistics Methodology), and further categorized into groups relevant to different

types of interaction. A category either represents the mechanism by which the included substances interact: cytochrome P450 enzymes (CYPs)(Anwar-Mohamed et al., 2009; *Drug Interactions Flockhart Table*™; Zanger & Schwab, 2013); P-glycoprotein (*P-glycoprotein*; Wang et al., 2005); narcotics (*List of Narcotic Analgesics*); organic anion transporting polypeptides (OATPs)(Niemi, 2007; Shitara et al., 2013; Stieger & Hagenbuch, 2014); photosensitizing substances (Zhang & Elmets, 2020); QT-prolonging substances (*QTDrug Lists*); seizure threshold lowering substances (Buchanan, 2001; Hitchings, 2016; Nestor et al., 2010); CNS depressants (*Prescription CNS Depressants DrugFacts*) or stimulants (*List of CNS stimulants*); hepatotoxic substances (Björnsson, 2016); glucuronidation substrates (Kiang et al., 2005); or it represents a medication class, for instance antiepileptics or opioids (*ATC/DDD Index*. The WHO Collaborating Centre for Drug Statistics Methodology). The medication categories were not mutually exclusive as some substances occur in several categories.

Identifying Interactions

The registered content/substances from all reported, decipherable DS were checked for interaction potential in combination with medication, using the Natural Medicines database (Natural Medicines, accessed 2020) professional monographs. Natural Medicines is a not-for-profit database, primarily focused on the safety and effectiveness of natural products of all kinds. It is systematically updated, and potential literature sources are critically evaluated for relevance and validity. Interactions are classified according to a stop-light rating system, combining severity and likelihood of occurrence (Natural Medicines). In addition, the interactions are classified according to level of evidence: A) high-quality RCT/meta-analysis; B) non-randomized/observational studies; C) consensus/expert opinion; and D) anecdotal/animal/in vitro/theoretical evidence.

In our study, we defined clinically significant interactions as interactions of moderate to high severity and of possible, probable, or likely occurrence (Figure 1). These were labelled "potential" interactions, as they were based on self-reported use and the data material did not provide

information about clinical evidence of an actual interaction occurring. In addition, classification C or D in level of evidence was considered low-grade documentation.

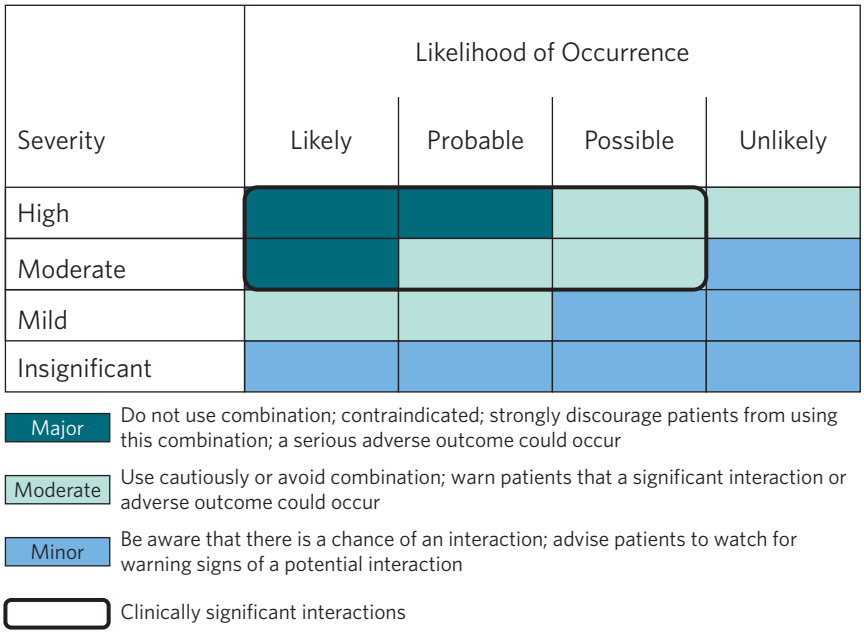

Figure 1. Classification of Clinically Significant Interactions
The figure is modified from the stop-light system for interaction severity and likelihood of occurrence (Natural Medicines). Reproduced with permission from Therapeutic Research Center, November 2021

We created a variable for each DS-medication or medication category combination with interaction potential identified by Natural Medicines. Interactions were further classified as potentially clinically significant or not (Figure 1). We counted the number of interactions and calculated the proportion of participants with a potential interaction. We also categorized the participants according to number of interactions identified (1, 2 and >2). One DS-medication combination may give rise to more than one interaction: a DS may interact through several interaction mechanisms due to mixed content, and a medication may belong to more than one medication group, it may for instance be both an OATP and a CYP3A4 substrate.

Analysis

Descriptive statistics (counts and percentage) were used to describe the number of potential interactions and proportion of participants with one or more identified interactions. We used IBM SPSS Statistics version 26 for the statistical analyses.

Ethics

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. NOWAC is approved by the Regional Committee for Medical and Health Research Ethics in North Norway (141/2008). Storage of data comply with the rules of the Norwegian Data Inspectorate and has an approved Data Protection Impact Assessment (DPIA) from UiT the Arctic University of Norway (ref. 743201, 16.11.2021). Written informed consent was obtained from all participants.

Results

The study population comprised 3,970 women, of whom 2,577 (65%) used medication, 1,824 (71%) used DS and 1,885 (47%) combined medication and DS use. Most of the women were postmenopausal (Table 1). The women reported a total of 463 different DS products. The content of 22 of these were not decipherable, and 64 participants used one (n = 59) or two such DS (n = 5).

Irrespective of documentation grade, the prevalence of potentially clinically significant DS-medication interactions was 44% (n = 823), that is the proportion of DS-medication users with at least one interaction identified (Table 2). When excluding interactions with low-grade documentation, the proportion was 33% (n = 630), which represents 16% of the total study population. Among these, 132 women (7%) used herb-medication combinations, and 63 (3%) used combination(s) that represented more than two interactions.

Altogether, 1,857 DS-medication interactions were identified, 591 of these were herb-medication interactions. The corresponding number of interactions after exclusion of those with low-grade documentation was 960 and 173 respectively. As shown in Table 3, herb-medication interactions are more

Table 1. Characteristics of the Study Population Overall and According to Use of Medication and Dietary Supplements (DS)*

	Total		No medication, no DS		DS, no medication		Medication, no DS		Medication and DS	
	N = 3970		N = 454 (11.4%)		N = 939 (23.7%)		N = 692 (17.4%)		N = 1885 (47.5%)	
Age, mean years (SD)	55.0	(3.9)	54.1	(4.1)	54.6	(4.0)	54.7	(3.9)	55.6	(3.8)
BMI, mean kg/m^2 (SD)	25.7	(4.4)	25.3	(3.7)	24.8	(3.7)	26.8	(5.0)	25.8	(4.4)
Number of medications, median (range)	1.0	(0–20)	0.0		0.0		2.0	(1–12)	2.0	(1–20)
Number of DS, median (range)	1.0	(0–12)	0.0		2.0	(1–12)	0.0		2.0	(1–9)
Smoking, n (%)	829	(20.9)	116	(25.6)	180	(19.2)	168	(24.3)	365	(19.4)
Menstrual status, n (%)										
Regular	487	(12.3)	84	(18.5)	146	(15.5)	85	(12.3)	172	(9.1)
Irregular	318	(8.0)	47	(10.4)	75	(8.0)	52	(7.5)	144	(7.6)
No menstruation	3126	(78.7)	313	(68.9)	711	(75.7)	547	(79.0)	1555	(82.5)

*Missing information was defined as non-use. 18 did not answer the question about medication use and 16 did not answer the questions about dietary supplement use.

Table 2. Number (%)* of Participants with Identified Potentially Clinically Significant Interactions Related to Dietary Supplements (DS) Use Among Participants Combining Medication and DS (n = 1885)

	Total		1 interaction		2 interactions		>2 interactions	
	N	(%)	N	(%)	N	(%)	N	(%)
DS-medication interaction overall#	823	(43.7)	330	(17.5)	243	(12.9)	250	(13.3)
Herb-medication interaction	299	(15.9)	154	(8.2)	83	(4.4)	62	(3.2)
Other DS-medication interaction	654	(34.7)	285	(15.1)	211	(11.2)	157	(8.3)
Excluding interactions with low-grade documentation:								
DS-medication interaction overall#	630	(33.4)	404	(21.4)	163	(8.6)	63	(3.3)
Herb-medication interaction	132	(7.0)	97	(5.1)	29	(1.5)	6	(0.3)
Other DS-medication interaction	547	(29.0)	380	(20.2)	121	(6.4)	46	(2.4)

*The percentages represent the proportion of participants who combine DS and medication, (i.e., 1,885).
#The overall numbers are not the sum (vertically) of participants with herb-medication and other DS-medication interactions. Some participants have both interaction types, and some have one interaction of one type and several interactions of another.

Table 3. Frequency of Potential Dietary Supplements-Medication Interactions, Excluding Interactions with Low-Grade Documentation

Herb	Medication	#	Non-herbal substance	Medication	#
Soy	Antidiabetics	1	Vitamin A	Hepatotoxic med.	68
	Antihypertensives	28	Vitamin B3, niacin	Antihypertensives	1
	Thyroxine	17	Vitamin B9, folate	Methotrexate	1
Fenugreek	Anticoagulants	1	Vitamin B6	Antihypertensives	8
	CYP1A2 substrates	11	Vitamin C	Estrogens	159
Ginkgo biloba	CYP1A2 substrates	2		Statins	42
	CYP3A4 substrates	2		Niacin	2
Ginseng	Antidiabetics	1	Vitamin D	CYP3A4 substrates	297
	CYP2D6 substrates	10		Diltiazem	1
	CYP3A4 substrates	32		Verapamil	1
	QT prolonging med.	8	Vitamin E	Anticoagulants	46
Grapefruit	CYP2C19 substrates	1		Statins	82
	Levothyroxine	2		Niacin	2
	OATP transporters	2*		Warfarin	3
	CYP2E1 substrates	4	Cr	Levothyroxine	9
	CYP3A4 substrates	17	Zn	Antidiabetics	1
Ginger	Anticoagulants	3		Tetracyclines	1
St. John's wort	CYP3A4 substrates	1*	Se	Statins	1
	P-glycoprotein substrates	1*	Mg	Bisphosphonates	2
Cassia	Antidiabetics	1	Ca	Aluminum salts	1
	CYP3A4 substrates	1		Bisphosphonates	5
	Anticoagulants	3		Levothyroxine	30
	Antidiabetics	1		Sotalol	1
Milk thistle	CYP2C9 substrates	3		Tetracyclines	2
Olive leaves	Antihypertensives	1		Tiazides	2
Capsicum annuum	Anticoagulants	3	Fe	Levothyroxine	11
	CYP3A4 substrates	7	Chlorophyll	Photosensitizing medication	8
Echinacea purpurea	CYP1A2 substrates	5			
	CYP3A4 substrates	4			
Total		**173**	**Total**		**787**

*Major risk of adverse outcome.
OATP: Organic Anion Transporting Polypeptides; CYP: Cytochrome P450.

often specifically related to liver metabolism and membrane transport than non-herb-medication interactions. Four of the herb-medication interactions, representing three of the participants (0.02% of 1,885 DS-medication combination users), were classified as major risk of adverse outcome according to the Natural Medicines database (Figure 1) and involved grapefruit and St. John's wort. One participant combined St. John's wort with clarithromycin, which represents a risk of reduced plasma concentration of clarithromycin due to induction of the liver enzyme CYP3A4. She also used a tomato extract, cod liver oil and a soy supplement. Two participants used a herbal mixture which included grapefruit, combined with levothyroxine, an OATP1B1 substrate. Due to the many herbs present in the herbal product as well as use of some other DS products, both women had several additional potentially clinically significant interactions identified, but these were all classified as low-grade documentation.

A complete list of identified DS-medication interactions is available on request.

Discussion

The main study findings are that among a middle-aged population of Norwegian women, 71% used DS and 47% combined DS and medication use. The prevalence of potentially clinically significant DS-medication interactions was 33% among the DS-medication users, 16% in the total study population. DS-medication combinations with a potentially serious interaction outcome were identified, but the prevalence was very low.

Other studies that have reported prevalence of DS-medication interactions, have found a variation from 5% to 40% (Bush et al., 2007; Dergal et al., 2002; Firkins et al., 2018; Peng et al., 2004; Risvoll et al., 2017). There are several plausible reasons for this variation: 1) varying study populations (elderly, particular patient groups (cancer, kidney, dementia)); 2) various countries/geographical regions with differing legislation and culture for DS use; and 3) varying methods and tools used to define DS or herbal use and DS-medication interactions.

The Norwegian study by Risvoll et al. (2017) is particularly interesting as it includes persons with dementia, a patient group who may be excluded from surveys either intentionally, or indirectly due to their cognitive status. Among 151 participants, 46% used DS and 11% had a potentially clinically significant DS-medication interaction. A similar Canadian study conducted at a memory clinic detected potential herb-medication interactions in 5% of the patients (Dergal et al., 2002). A survey among patients attending American outpatient clinics detected a substantial number of potentially adverse herb-medication (prescription) interactions (40% of the herb users), but did not uncover any serious adverse interactions after reviewing the patients' charts (Bush et al., 2007). Another American survey in primary care identified potential DS-medication interactions among 17% of the participants, while 1% had potentially severe interactions (Peng et al., 2004). A German study in oncology clinics found that 16% of the patients risked interaction due to combined use of conventional medication and so-called biologically based CAM (complementary and alternative medicine) (Firkins et al., 2018), but severity was not assessed.

The results from these studies, ours included, may be summed up as follows. There is a noteworthy potential for clinically significant interactions to occur between DS and medications, and the prevalence may be high or low depending on the type and number of medications used in the study population. Also, although there is a risk of seriously compromised health through combining DS-medication, the prevalence of interactions representing a major health risk is generally low.

Strengths and Limitations

The strengths of this study include a fairly large, nation-wide study population, random sampling of participants, and acceptable participation rate. NOWAC has been shown to be representative of middle-aged Norwegian women (Lund et al., 2003). We have used a comprehensive, quality ensured database for information on DS-medication interactions.

All information on medication and DS use was based on self-reporting. Participants were asked to list the products they used, and this may result in some level of underreporting. As we combined the

lists with specific questions on use of soy, cod liver oil and other omega-3 supplements, the risk of underreporting was somewhat reduced. Over-the-counter medication could be underreported, although the questionnaire did not specify prescription medicine. Validation analyses have been performed for frequently used medication groups (antidepressants and hormone therapy), and for vitamin D, all suggesting high validity with plasma concentrations as a reference standard (Brustad et al., 2004; Waaseth et al., 2008; Waaseth et al., 2020).

We have identified *potential* interactions, as we cannot know to which degree DS and medication use happened concurrently, beyond that they were used during the same week. Thus, there may be some overestimation of the prevalence of potential interactions. On the other hand, although unknown products or content comprised a small proportion of the DS use, some degree of missing information on use must be assumed, and consequently an underestimation of interaction prevalence. Neither for medication nor for DS did we know the dosage used or the timing of intake and cannot assess the seriousness of the identified interactions beyond what is stated in the Natural Medicines' professional monograph.

Our focus was on DS-medication interactions, and so we did not check for potential DS-DS interactions. Nor have we looked into interactions involving tobacco or alcohol consumption, although nicotine was included as a medication for those reporting medications used in nicotine dependence (N07BA). However, health personnel should be aware of these possibilities as well, and the professional monographs in Natural Medicines include such information.

Implications for Medication Safety in Municipal Health and Care Services

We identified a noteworthy prevalence of potentially clinically significant DS-medication interactions in a general population sample of middle-aged women. Some of these interactions had the potential to seriously affect the users' health. Health personnel need to be aware of potential problems regarding DS use and apply tools to identify them. Medication reconciliation procedures, as for example, the Integrated Medicines

Management (IMM) model (Scullin et al., 2007), should as a rule include questions regarding DS use, which should be asked actively. Patients tend not to disclose DS use to health personnel unless asked about it (Gardiner et al., 2015; Guzman et al., 2019). Regarding St. John's wort, sales are restricted to pharmacies particularly because of the interaction potential. The fact that we found a case of unsafe combination involving St. John's wort may suggest a lack of guidance from pharmacy personnel or that the product was bought illegally through other sales channels. Also, if the woman was already using St. John's wort when she got the clarithromycin prescription, this should have been detected at the doctor's office or at the pharmacy if health personnel in either setting had asked, "Which dietary supplements do you take?".

We have previously shown that DS use is more frequent among medication users, particularly when the reported medication suggests a chronic disease or condition (Waaseth et al., 2019), and particularly herbal supplements. The latter is noteworthy because herbs are the most worrisome DS due to the potential for pharmacokinetic interactions. The risk of interaction would necessarily increase with an increasing number of products used, both DS and medications, indicating a need to focus on elderly medication users. However, our material also shows that several, even severe, interactions may occur from a combination of just a few products.

The quality of online, public sources of information about DS is variable and generally lack safety information (Owens et al., 2014). Availability of reliable information about DS is also a problem for health personnel (Risvoll, 2021). How to relate to and interpret the detailed content in an otherwise reliable source can also be a challenge. Pharmacists should have a lower threshold for retrieving and interpreting such information, as they are trained in interaction mechanisms for medications in general. However, reliable databases are not readily available in community pharmacies. The regional medication information centers (RELIS) in Norway use Natural Medicines as the main source of information about DS-medication interactions. A subscription to this (or similar) databases and safety monitoring of consequences of DS-medication combination use, should be seen as an investment in quality health care by pharmacy chains, health authorities and policy makers (Skalli & Soulaymani

Bencheikh, 2012). Apart from databases, there are initiatives from clinical researchers in providing algorithms for the identification and management of DS-medication interaction within vulnerable patient groups, particularly cancer patients (Reddy et al., 2021; Ziemann et al., 2019).

According to European legislation (EU directive, 2002), all DS sold in a country shall be registered, or the regulatory food authorities shall have an inventory. As far as we know, it has not been a priority for Norwegian authorities to establish such a registry. Although it would not include information on interactions, it could be a great help in establishing the content of the various DS, which is a prerequisite for assessing the interaction potential of DS-medication combinations.

For pharmacists or other health personnel who feel they need an update on safety regarding DS use in general or DS-medication interaction specifically, there are good reviews to be found (Reddy et al., 2021; Tarirai et al., 2010), as well as digital courses. For instance, the National Institute of Health's National Center for Complementary and Integrative Health provide a course on DS-medication interactions (Gurley, 2014).

Conclusion

Pharmacological interaction with medications is one of several ways in which dietary supplements can adversely affect patients' health. There is considerable potential for clinically significant dietary supplement–medication interactions in a general population of middle-aged women. Whether this poses a serious health threat, could not be unequivocally established by the data material from NOWAC, though the probability of serious health risks seems low in this population segment. However, our findings indicate that health personnel should take supplements into account when assessing health risk and medication use among their patients.

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CHAPTER 7

Detecting Medication Errors and Adverse Drug Events: A Review of Current Methodologies

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Abstract: To establish the scope of harm related to medications, and thus design harm-reduction measures, healthcare organizations are required to measure medication safety events. This chapter will investigate methodologies for detecting adverse drug events and medication errors, analyze what type of events they detect, and discuss their advantages and limitations. We conducted a scoping review, and identified studies that compared at least two detection methods directly. The review resulted in 13 studies, of which ten were conducted in hospitals, and three were from the outpatient setting. Methods used to detect medication safety events were: incident reporting, record review, computerized surveillance, direct observation, and interviews. The detection rate of adverse drug events and medication errors varied substantially depending on the method. Incident reporting detected small numbers of events, but detected events that were not identified by other methods. Record review detected more adverse drug events than incident reporting, but missed whole classes of events, such as medication administration errors and omissions. Direct observation detected most medication errors. Computerized surveillance has promising detection abilities and can be less resource and time-intensive compared with record review, after the initial implementation. Small numbers of events were detected using any one method alone, that is, none of the methods can serve as a gold standard, and each method described has its place in monitoring medication safety. The literature supports a combination of methods to be used to detect adverse drug events and medication errors. The 10 studies in this scoping review that are from hospitals, are also described and discussed in the PhD thesis of the first author(Mulac, 2022). The scoping review, however, resulted in a low number of studies (n = 3) from the outpatient setting, which highlights the research and

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knowledge gaps of detecting methods for adverse drug events in municipal health and care services.

Keywords: adverse drug events, incident reporting, medication errors, medication safety, record review

Since the turn of the millennium, worldwide medication safety initiatives have been dedicated to reducing medication errors and adverse drug events (ADEs) in healthcare (Bates & Singh, 2018). WHO's campaign established international goals for reducing medication-related harm (Donaldson et al., 2017). On the local level, technology-based interventions such as electronic health records, automated dispensing cabinets or barcode medication administration were introduced (Mulac, Mathiesen, et al., 2021). To establish the scope of the problem, and demonstrate reductions in errors and adverse event rates, organizations need reliable detection tools. Yet, there is enormous variation in how, when and even if organizations and health professionals count adverse events and measure medication-related harm (Institute of Medicine 2007).

We argue that health professionals and health authorities need a better overview of the evidence and the vast number of methods for detecting ADEs. Our review will provide information about available approaches for detecting ADEs across levels of healthcare, and a discussion of the pros and cons of each approach based on the available evidence and research literature.

Background

A variety of tools and methods are utilized to measure the extent of ADEs. Depending on what is being measured, some methods are better suited for certain types of events than others. For example, some methods detect events regardless of harm, while others detect only harmful events – ADEs (Institute of Medicine 2007). Different approaches are needed to detect errors in research versus clinical practice. Different methods, or a variation of the same method, are utilized in inpatient versus outpatient care (Hanlon et al., 2001).

Overview of Detection Methods

This chapter builds on a literature review conducted in the PhD thesis of the first author. Parts of the text below (including Figure 1, parts of Table 1, and Table 2) are also included in the PhD thesis by the first author, which was published in April 2022 at the University of Oslo (Mulac, 2022). The thesis covers inpatient setting only and not findings from the municipality setting.

Methods used to detect medication safety events can be grouped into five categories: incident reporting, direct observation, record review, computerized surveillance, and interviews.

Incident reporting is frequently adopted by organizations to detect events recognized by health professionals. Analysis of events might identify system flaws. However, incident reporting systems alone cannot be used to measure incidence. They are simply a reflection of the safety culture in a given organization. High reporting rates may indicate an organization devoted to reporting and preventing errors and ADEs, rather than reflecting a truly high ADE rate (Larson & Saine, 2013). Contrarily, health professionals might not report errors if they are afraid of repercussions, hence low reporting rates may indicate an organization with an unhealthy safety culture or one that does not recognize the value of reporting in terms of preventing future events. It is estimated that only 5%–10% of all incidents are detected through incident reporting (Dabba et al., 2019). The limitations of incident reporting as the sole method of event detection are well documented (Erstad et al., 2012; Mulac et al., 2020). Incident reports are regularly collected within healthcare organizations in the Nordic countries, and also by national reporting systems in Denmark and Finland. The Finnish national incident reporting system, HaiPRo, is used in over 200 social service and healthcare organizations (Kinnunen-Luovi et al., 2014). The Danish Patient Safety Database is an incident reporting system that collects reports on adverse events from healthcare professionals in primary healthcare and hospitals, and also allows patients to report incidents (Christiansen et al., 2021). The Norwegian Incident Reporting System was established in 2012, however it was closed down in 2017 (Mulac et al., 2020). Incident reports are still reported on a local or regional level in Norwegian hospitals.

Direct observation of medication administration as a prospective method can detect the greatest numbers of medication errors. The method usually involves observation of medication administration by trained health professionals, frequently nurses and pharmacists, who compare administered medications to the prescribed medications. The additional value of this method is that it often highlights the contextual factors relating to a medication error, and reveals the causes of errors not discovered by other detection methods. Considering that observing over a long time is costly, observation is only recommended for in-depth studies or periodical monitoring. Also, the presence of observers is known to influence the health professionals being observed and consequently changes their behavior, something known as the Hawthorne effect (McCambridge et al., 2014).

Record review can be either untargeted (manual) or targeted. Manual record review involves a review of patients' complete health records, and thus is suitable for periodical review of a specific unit or institution. Targeted record review is less time consuming as it applies specific triggers/rules, such as: diagnostic codes (ICD-9 codes); symptoms (nausea, pain, new rash, vomiting); prescription of antidotes (naloxone, vitamin K); or triggers of laboratory abnormalities occurring in the presence of certain drugs (INR ≥6, serum glucose < 2.8 mmol/l) to identify records for review. Utilizing such triggers is considered to be an effective ADE detection method when applied as a two-stage review (Bates, Cullen, et al., 1995; Classen et al., 2011), such as the Harvard Medical Practice Study and the Global Trigger Tool, both of which involve a set of triggers to identify potential events (Hanskamp-Sebregts et al., 2016). The Harvard Medical Practice Study involves an extensive full chart review, and a number of questions in addition to triggers. Determining preventability is a standard, with no time limit per case. The Global Trigger Tool applies a recommended time limit per review (usually 20 minutes) for randomly selected records creating a sampling method that produces small samples over time, for example, 10 records from one population or institution, two times a month. It is not aimed at detecting every adverse event. The Global Trigger Tool is a promising, structured method for estimating and monitoring adverse event rates over time, and can be applied to the screening

of large populations, for example, national screening of all hospitals. In the first stage of this method, a health professional (e.g., a nurse) screens health records using specific criteria. In the second stage a physician validates the potential events identified in the first stage to confirm the adverse event. The Global Trigger Tool is more feasible and less time consuming than the Harvard Medical Practice Study, since it originally did not determine the preventability of the event (Griffin & Resar), although this has also been included in several studies (Hwang et al., 2014; Kennerly et al., 2013; Schildmeijer et al., 2013). By focusing on triggers within methods, the Global Trigger Tool has detected ten times more events than other ADE detection methods (Classen et al., 2011). Since its development in 2003, the Global Trigger Tool has expanded from small scale studies for quality improvement within organizations, to being used by hundreds of hospitals worldwide (Hanskamp-Sebregts et al., 2016; Hibbert et al., 2017). In the Nordic countries it has been on the rise in the last decade for monitoring adverse event rates (Doupi et al., 2015). Currently there are also initiatives to measure adverse drug events and harm using the Global Trigger tool in nursing homes in Norway (von Plessen et al., 2012).

Chart review using the trigger tool was developed as a manual method, intended for application by clinicians who review health records. With the increased introduction of electronic medical records and electronic prescribing, there may be even more effective ways to detect ADEs.

Computerized surveillance and automation provide prospective, active monitoring, and improve the efficiency of ADE detection, while decreasing the time and personnel resources. This method can monitor events in real time, and potentially limit patient harm through concurrent interventions. The implementation of computerized surveillance requires technological sophistication and an integration of comprehensive information sources from laboratories, radiology, microbiology, and pharmacies. ADE detection using computerized surveillance relies on numeric or coded medical data, including various clinical triggers, such as medication discontinuation, abnormal laboratory values, or transfer to an intensive care unit. Cases flagged by computerized surveillance are validated by dedicated surveillance personnel. The method can potentially detect greater numbers of ADEs if expanded by analyzing physician narratives or notes

using computer-based free-text searching (Bates et al., 2003). This additional adaptation facilitates detecting ADEs that would not be detected by triggers, for example, "drowsiness from morphine" (Stockwell & Kane-Gill, 2010). Text word searches add further challenges in identifying key phrases, and require adaptation to local synonyms, abbreviations, or language. These challenges can be overcome through natural language processing, pattern matching, and the development of algorithms through machine learning (Melton & Hripcsak, 2005). Additionally, computerized surveillance requires maintenance to increase the sensitivity of the rules to changing medical practice, such as the introduction of new medications or new indications for existing medications.

Strengthening the partnership of patients, their relatives, and health professionals is an important approach for promoting medication safety and identifying medication-related harm (Donaldson et al., 2017). Thus interviewing patients for symptoms related to medications has also been used in identifying potential ADEs (Erstad et al., 2012). Likewise, health professionals can be interviewed to see whether any incidents have occurred. This method can, for example, be performed by trained health staff during nursing shift changes (Institute of Medicine 2007).

Several studies have evaluated the ability of different methods to detect ADEs, usually involving chart review, incident reporting, and observation (Erstad et al., 2012; Hanskamp-Sebregts et al., 2016). With the digitalization of healthcare services, the focus has shifted from measuring event rates using manual methods to automated computerized surveillance, and methods that encompass contextual and human factors in the error environment (Govindan et al., 2010; Mulac, Mathiesen, et al., 2021; Rochefort et al., 2015b). Previous studies have focused on providing evidence for one specific method, such as a medical record review (Hanskamp-Sebregts et al., 2016), or compared several specific methods in order to address their differences in detecting ADEs (Rochefort et al., 2015a). Most studies reviewing methods of ADE detection originate within a hospital setting, yet medication-related harm also occurs in primary healthcare and across municipal healthcare institutions. The literature lacks a synthesis of available methods, which could guide researchers and health professionals in choosing the most appropriate

method, depending on the purpose for measuring and the setting. Our review addresses this gap.

This scoping review will provide information about available approaches for detecting ADEs across levels of care, and categorize the available evidence for each method.

Aim

The aim of this chapter is to examine methodologies for detecting adverse drug events and medication errors, analyze what type of events they detect, and discuss their advantages and limitations.

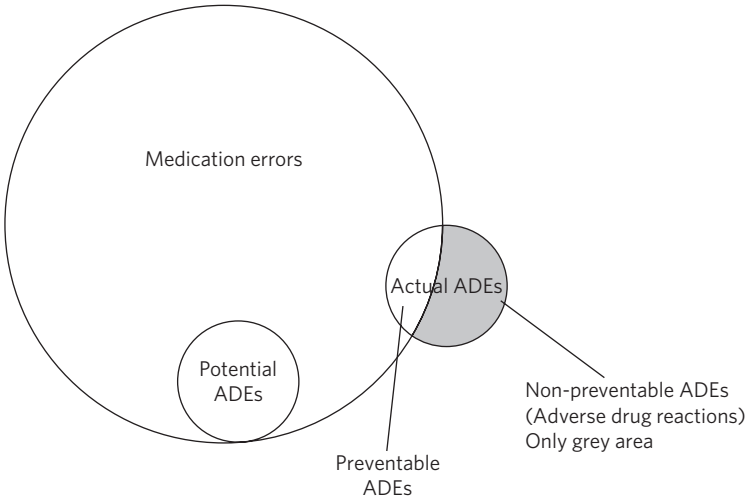
Methods

Terminology and Definitions

Box 1 Definitions of an adverse drug event and a medication error
An adverse drug event is defined as any harm caused by medication use (Nebeker et al., 2004). Medication error is defined as any preventable event that may cause or lead to inappropriate medication use or patient harm (NCC MERP, 2001).

In this review, we use the terms "incident", "event", "medication error" and "adverse drug event" (ADE) to describe medication safety events. These events vary in their preventability and harm. ADEs can be potential, meaning an event that has the potential to cause patient harm. Actual ADEs have reached the patient and caused some grade of harm (Bates, Boyle, et al., 1995). All potential ADEs are preventable, while actual ADEs can be preventable or non-preventable. Actual ADEs were considered preventable if they resulted from a medication error (e.g., liver damage caused by administering the wrong dose of paracetamol), or non-preventable if they did not result from a medication error (and were thus attributable to adverse drug reactions e.g., harm occurred at doses normally used in patients).

The correlation between medication errors and adverse drug events is somewhat tricky to separate, but important to distinguish. Figure 1 illustrates the terms "medication errors", "actual ADEs" (preventable/non-preventable) and "potential ADEs". Essentially, medication error does not necessarily imply harm. Only a small number of medication errors are actual ADEs, while all potential ADEs are medication errors. Which also means that, fortunately, only a small number of medication errors reach the patient and cause some grade of harm.



Figur 1. The Relationship Between Medication Errors and Adverse Drug Events. Adapted from Bates (1995). ADEs- adverse drug events. Duplicated from Mulac (2022)

Research Question, Literature Search and Study Selection

We conducted a scoping review (Arksey & O'Malley, 2005; Levac et al., 2010) to examine methodologies for detecting ADEs and medication errors, analyze what type of events they detect, and evaluate their efficacy. To answer the research question, we identified keywords and MeSH terms describing the fundamental concepts of medication errors, adverse drug events, and detection. We conducted the search in PubMed and EMBASE and included keywords: "adverse drug events", "medication errors", "medication safety" combined with operator OR. The above terms

were searched in combination with keywords: "detection", "measuring", "surveillance" with operator AND. One reviewer screened all titles and abstracts. Full text articles were retrieved and reviewed independently by two reviewers. Study inclusion was discussed to reach consensus. We manually searched the references of included studies for additional articles of relevance.

We included articles from inpatient and outpatient settings published until October 2021. A key inclusion criterion of studies was that they had used and compared at least two methods. The search was restricted to studies published in English. Studies that evaluated event detection of one single trigger criterion, "disease", "drug", "drug class" or "route of administration" were not included.

Where possible we extracted the positive predictive value (PPV) of the methods used. PPV is applied with studies involving triggers to express the ability of methods to detect adverse events, and is calculated by dividing the number of true positive triggers related to confirming AEs by the total number of positive triggers.

Results

Study Characteristics

The literature search identified 172 citations, which were reviewed for title and abstract. Of these we retrieved and reviewed 53 articles in full. We excluded 42 articles because they did not contain sufficient information regarding ADEs, did not compare at least two detecting methods, or because they involved individual triggers or medications. We additionally identified two articles from manually searching the references of included articles. Our analysis of 13 articles published from 1998 to 2018 is summarized in Table 1. Three studies (Field et al., 2004; Olsen et al., 2007; Weissman et al., 2008) involved outpatients, while the remaining studies involved inpatients. Two studies focused on pediatric patients (Ferranti et al., 2008; Maaskant et al., 2018), and one study focused on older persons (Field et al., 2004). We categorized the articles based on the types of methods used, types of medication safety events that were detected, and the efficacy of methods to detect events.

Table 1. Characteristics of the Reviewed Studies

Reference	Study design, setting and population	Event type detected	Results
(Ferranti et al., 2008)	Prospective over 14 months, pediatric inpatients of one hospital, 4711 patients	ADEs, medication errors	Computerized surveillance detected 78 ADEs, Voluntary reporting detected 93 ADEs,
(Field et al., 2004)	Cohort study over 12 months for older persons in the ambulatory setting, 31,757 per month	ADEs, preventable ADEs	In total 1,523 (100%) ADE identified of which 421 (28%) preventable ADEs. Per method: Provider reports: 11% of ADEs and 6% of preventable ADEs Hospitalizations: 11% of ADEs and 14% of preventable ADEs Emergency department visits: 13% of ADEs and 17% of preventable ADEs Computer-generated signals: 31% of ADEs and 37% of preventable ADEs Electronic notes: 39% of ADEs and 29% of preventable ADEs Incident reports: 4% of ADEs and 2% of preventable ADEs.
(Flynn et al., 2002)	Retrospective and prospective, 85,197 doses from 36 hospitals	Medication errors	2556 doses were compared for three methods: 457 medication errors detected (100%): Direct observation: 300 (66%) medication errors Chart review: 17 (3,7%) medication errors Incident reporting: 1 (0,2%) medication error
(Franklin et al., 2009)	Prospective and retrospective, surgical ward of one hospital during two 4-week periods, 207	Medication (prescribing) errors	In total: 135 (100%) prescribing errors detected Ward pharmacist alone: 48 (35%) prescribing errors Record review: 86 (69%) prescribing errors Ward pharmacist and record review: 7 (5%) prescribing errors Spontaneous reporting: 1 (1%) prescribing errors Trigger tool: No errors detected
(Franklin et al., 2010)	Retrospective pilot study, surgical ward of one hospital for two 4-week periods, 207 patients	ADEs, ADRs, medication errors	Trigger tool: 7 ADEs detected, 5 non-preventable ADEs (ADRs) and 2 medication errors Health record review: 5 medication errors

(Jha et al., 1998)	Prospective cohort, 21,964 patient days on 9 medical and surgical wards for 8 months	ADEs, preventable ADEs	In total: 617 ADEs and 86 potential ADEs detected Computer-monitor strategy: 2 potential ADEs; 275 ADEs of which 70 preventable Chart review: 23 potential ADEs; 398 ADEs of which 109 preventable Voluntary reporting (stimulated): 61 potential ADEs; 23 ADEs of which 9 preventable ADEs
(Kilbridge et al., 2006)	Prospective cohort over 8 months at two hospitals (one university and one community hospital) 33,206 patients 146,416 patient days	ADEs	Automated surveillance: University hospital: 520 ADEs detected Community hospital: 283 ADEs detected Voluntary reporting: University hospital: 144 ADEs detected Community hospital: 23 ADEs detected
(Maaskant et al., 2018)	Cross-sectional study, 369 patients, 4 pediatric wards at one hospital for 2 months	Medication errors, harmful medication errors (ADEs)	Multifaceted method: 242 medication errors detected, of which 33 harmful medication errors (ADEs) Record review: 27 harmful medication errors (ADEs) Incident reports: 5 harmful medication errors (ADEs) Direct observations and pharmacy logs: No ADEs detected Trigger tool: No harmful medication errors (ADEs) detected When trigger tool was modified (added pain, nausea/vomiting symptoms) 19 ADEs were detected.
(O'Leary et al., 2013)	Retrospective, 250 randomly selected patients	AEs, ADEs	In total: 66 (100%) ADEs detected Traditional trigger tool: 44 (67%) ADEs detected Enterprise data warehouse screening: 46 (70%) ADES detected
(Olsen et al., 2007)	Prospective, 288 patients discharged from one hospital	AEs, ADEs, medication errors	Active pharmacist surveillance: 30 medication errors Record review: 14 medication errors Incident reporting: No medication errors detected
(Tinoco et al., 2011)	Retrospective, 2137 patient admissions, surgical services of one hospital for 14 months	AEs, ADEs	In total: 195 ADEs (100%) Computerized surveillance: 102 ADEs detected (52%) Manual chart review: 96 ADEs detected (51%)

(*Continued*)

Table 1. (Continued)

Reference	Study design, setting and population	Event type detected	Results
(Weissman et al., 2008)	Random sample survey, 988 patients discharged from 16 hospitals	AEs, ADEs	Medical records review: 32 ADEs detected Patient interview: 135 ADEs detected
(Yun et al., 2012)	Retrospective, 30 wards, one hospital, for 14 moths	ADEs	In total: 1539 ADEs Spontaneous reporting: 1055 (66%) ADEs detected Ward rounds with chart review: 309 (20%) ADEs detected Clinical data repository: 229(14%) ADEs detected

AE = adverse event, ADE = adverse drug event, ADR = adverse drug reaction Built on Table 1 in Mulac (2022).

Method Characteristics

All studies have directly compared at least two methods. Ten studies used incident reports to measure the baseline. Incident reporting was voluntary spontaneous reporting within institutions for the majority of studies. One study used stimulated, confidential reporting (Jha et al., 1998) whereby the nursing and pharmacy staff were asked about possible events to report. The majority of studies used record reviews (n = 11), which involved a non-targeted and/or targeted review that utilizes triggers. The included studies varied considerably in the information sources used and the type and number of triggers. Computerized surveillance (i.e., automated detection method) was used in five studies (Ferranti et al., 2008; Field et al., 2004; Jha et al., 1998; Kilbridge et al., 2006; O'Leary et al., 2013). Using targeted triggers was common for all computerized detection methods, however the application of the triggers and the data sources used varied greatly. Two studies involved prospective pharmacist surveillance of prescription records (Franklin et al., 2009; Olsen et al., 2007), and two studies involved direct observation (Flynn et al., 2002; Maaskant et al., 2018).

ADEs and/or Medication Errors Detected

Some studies distinguished between preventable and non-preventable ADEs (Ferranti et al., 2008; Field et al., 2004; Franklin et al., 2010; Jha

et al., 1998; Maaskant et al., 2018; Olsen et al., 2007). Four studies detected adverse events in general and detected ADEs as a subgroup within these (O'Leary et al., 2013; Olsen et al., 2007; Tinoco et al., 2011; Weissman et al., 2008). Two studies detected medication errors alone (Flynn et al., 2002; Franklin et al., 2009).

Efficiency of Detection Methods

Targeted record reviews detected more ADEs than incident reporting (Jha et al., 1998; Olsen et al., 2007). However, this was not the case for all populations or event types. In a multicenter study on medication errors, targeted record review detected 3,7%, while direct observation detected 66% of medication errors (Flynn et al., 2002). In another study on pediatric patients, 33 harmful medication errors were detected as a baseline by a multifaceted method, while the trigger tool did not detect any harmful medication errors (ADEs) (Maaskant et al., 2018). When the trigger tool was extended for two additional symptoms (pain and nausea/vomiting), the tool detected 19 harmful medication errors. It is likely that the trigger tool was not properly adapted to the specific setting and pediatric population. In another study that evaluated prescribing errors in a surgical hospital ward, the trigger tool method detected only 2% of prescribing errors, while manual record review detected 83%, and pharmacist surveillance detected 24% of prescribing errors (Franklin et al., 2009). Targeted record review alone is, according to Franklin et al., not the method of choice to measure medication safety during prescribing (Franklin et al., 2009). Interviewing patients after discharge detected four times more ADEs than record review, and more serious events that were not documented in the medical record (Weissman et al., 2008). Computerized surveillance detected ADEs at a rate 3.6 times greater than incident reporting at a university hospital, and 12.3 times greater at a community hospital (Kilbridge et al., 2006). Similar results were found in the study by Jha et al., that detected ADEs with computerized strategies at a rate 12 times higher than incident reporting (Jha et al., 1998). When compared with record review, computerized surveillance detected similar numbers of ADEs

(O'Leary et al., 2013; Tinoco et al., 2011). In a study focusing on medication errors in pediatric patients, Ferranti et al. found that computerized surveillance did not detect drug omissions, meaning the detection was entirely reliant on incident reporting to detect this type of events (Ferranti et al., 2008).

There was generally a poor overlap between events detected with more than one source. Although incident reporting detected small numbers of events, these were not detected by other methods (Maaskant et al., 2018; Olsen et al., 2007). This applies for other methods as well. Tinoco et al. found that overlap between events detected by record review and computerized surveillance was 3% (Tinoco et al., 2011). Field et al. found that only 5% of ADEs were detected with more than one source when comparing multiple detection methods (Field et al., 2004).

PPV was calculated in three studies that used signals generating ways to establish the cost and productivity of the methods for detecting ADEs. In one study that evaluated ADEs in older patients in the ambulatory setting, the PPV for computer-generated signals was 7%, while it was highest for provider reports (54%) (Field et al., 2004). In the same study nearly three-fourths of the computer-generated signals were eliminated after prompting a record review. The overall PPV was low in a study that evaluated harm from medication errors, and the signals generated with a trigger tool led to reviewing the charts of 61% of patients while ADEs were identified in 3.4% of patients (Franklin et al., 2010).

There were substantial differences in time and resources required for utilizing the different methods. Jha et al. evaluated the time needed to conduct the different methods. Chart review was most time consuming requiring 55 person-hours per week, computer strategy required 11 person-hours per week, and voluntary reporting required five person-hours per week (Jha et al., 1998). Record review was also found to be resource intensive in other studies (Flynn et al., 2002; Franklin et al., 2010; Weissman et al., 2008). The main advantages and limitations of the reviewed methods are presented in Table 2.

Table 2. Advantages and Limitations of Detection Methods for Adverse Drug Events (ADEs) and Medication Errors. Duplicated from Mulac (2022)

Method	Advantages	Limitations
Incident reporting (voluntary and stimulated)	Detect events not detected by other methods Require minimal training of health professionals to report an event Identifies system failures, potential ADEs (non-harmful medication errors), omissions, medication administration errors that are not detected by trigger tools (targeted record review) Can identify ADE trends with sufficient data Stimulated reporting is likely to detect more events than voluntary	Detect small number of ADEs Underreporting Reporting bias: Healthcare providers report the most severe events Health professionals must be aware of an event to report Higher reporting rates do not indicate higher rate of ADEs, but a culture devoted to reporting
Record review: manual (untargeted) or triggers (targeted)	Utilizes readily available data Well adopted and commonly used Targeted review less time-consuming than manual review Detects more ADEs than incident reporting Effective to detect ADEs when applied as a two-stage review	Dependent on training and experience of reviewers Interrater reliability issues between reviewers Time and resource intensive: Best suited for periodical review Involve reviewing patients' complete written or electronic records Not effective in detecting latent errors, non-harmful medication errors Dependent on the rules/triggers to be adjusted to specific setting Many false positive signals Sensitivity and specificity of the trigger tools for ADE detection dependent on how the rules are applied and used in the given setting
Automated monitoring (computerized)	Can monitor ADEs in real time and thus potentially prevent harm Integrates multiple data sources Inexpensive after initial implementation, but needs maintenance to increase trigger sensitivity Identifies events associated with known areas of risk (high-risk medications) and harmful events	Applies for setting with full electronic records Costly to implement, requires software Integrating multiple data sources takes time (years) Vulnerable to programming errors Not effective in detecting latent errors, non-harmful

(*Continued*)

Table 2. (Continued)

Method	Advantages	Limitations
Direct observation	Prospective method Preferred approach for detection of medication errors and potential ADEs Provides data otherwise unavailable such as near misses, latent failures, contextual and human factors of the error environment Provides clues to error causes	Not suitable for detection of ADEs Require experience and training of observers (data collectors) in observation technique and appropriate medication knowledge Costly, recommended for periodical monitoring Observers' presence may affect the observed (Hawthorne effect)
Interviews (Patients, healthcare professionals)	Detect more incidents than record review or incident reporting Could be combined with discharge/medication review/reconciliation to optimize resource and time use Unique perspective (interviewing patients)	Only patients that are conscious and healthy enough can participate Time from the ADE occurred to interview affects detect rates, especially in discharged patients

Discussion

A comparison of different methods reveals that they vary in the number and type of events they can detect. This is best illustrated in a study performed in 36 hospitals and skilled-nursing facilities that compared three methods for medication error detection, and found that direct observation was more efficient and accurate than reviewing charts and incident reports. It is a well-established fact that chart reviews and incident reporting underestimate the true rates of medication errors (Meyer-Massetti et al., 2011; Westbrook et al., 2015), while the method that detects the highest number of medication errors is direct observation (Barker & Allan, 1995). Nevertheless, observation was least effective for detecting ADEs (Maaskant et al., 2018) when compared to other methods.

While known as a low-cost method that provides rich data within or across healthcare systems or nationwide, incident reporting detected the least number of ADEs, and is thus not suited to establish ADE rates.

Chart review has been the most effective method for ADE detection in the majority of studies, however, this requires a trained and experienced reviewer, and is resource intensive. The role of computerized surveillance in detecting ADEs is important, since it integrates comprehensive

information sources, and it can identify ADEs missed by clinicians more quickly and inexpensively than other methods. More importantly, there was a poor overlap between ADEs detected with record reviews, computerized surveillance, and incident reporting. The results of our literature review are consistent with prior studies, and confirm the need for complementary detection methods as a standard for measuring ADEs and medication errors.

Why Do Different Methods Detect Different Events?

Incident reporting is a valuable low-cost monitoring tool that detects all types of events, but in very small numbers. The incidents that were, however, detected with incident reporting overlapped minimally with ADEs detected by other methods, which argues the case for utilizing this method to detect additional events. This specifically concerns potential ADEs, and non-harmful medication administration errors that are not routinely detected through record review (Jha et al., 1998).Manual record review is more effective in detecting ADEs than incident reporting, but is too costly to be used routinely. Targeted chart review detects significantly more events than incident reporting, but has, for instance, not detected whole classes of incidents, for example, medication administration errors, prescribing errors, and omissions (Franklin et al., 2009; Franklin et al., 2010; Maaskant et al., 2018). The computerized method detected ADEs overlooked by a targeted chart review and incident reporting. The potential of the computerized method has not been fully exploited, and studies suggest that computerized surveillance would detect more events if integrated with information from physician notes (Tinoco et al., 2011). One study (Nwulu et al., 2013) reviewing triggers involving INR values over 6, found that the average time to intervention (for example a vitamin K-administration, a blood transfusion or both) after a trigger was generated was 6 hours. Through "real time" ADE detection the ability of the computerized method to potentially prevent harm must be recognized, and it may have a role in reducing the time to critical intervention. We believe that the capability of computerized surveillance to limit harm from ADEs should be further exploited.

Detecting ADEs in the Outpatient Setting

Our literature search yielded three outpatient studies: two conducted on discharged patients and one involving outpatients in the ambulatory setting. No studies involving nursing homes or long-term facilities were evaluated in this review, however, evidence from studies on outpatients suggests similar advantages and challenges with incident reporting, manual chart reviews and targeted chart reviews (Field et al., 2004; Hanlon et al., 2001). Studies that have assessed the trigger tools criterion for ADE detection in nursing homes (Boyce et al., 2014) (Handler & Hanlon, 2010; Kapoor et al., 2019) used data sources (laboratory, medication charts, pharmacy orders) similar to those used in studies from inpatient settings. There is less research on ADE detection in this setting, and more specifically, there is limited research on comparing ADE detection rates, using at least two methods, in nursing homes that could provide more information on the efficiency of ADE detection methods in this particular setting (Field et al., 2004; Honigman et al., 2001). The lack of competence and unexperienced staff have been raised as issues associated with medication errors in nursing homes (Bengtsson et al., 2021). Nurses, due to staff shortage, often delegate medication administration tasks to unlicensed staff, who are usually not familiar with the reporting systems and are less prone to reporting mistakes and errors (Leape, 2002). Elderly nursing home residents are more vulnerable to medication errors due to their age-related pharmacological changes and associated polypharmacy. Also, studies have shown that elderly are more frequently subjected to medication errors than other populations (Fialová & Onder, 2009; Mulac, Taxis, et al., 2021). Therefore, we should address the knowledge gaps on detecting and reporting medication errors and ADEs in outpatient settings in future studies.

Strengths

Studies describing computerized surveillance originate from the later 1990s, or even earlier in the USA, while the method has not been introduced on a large scale in European countries. Despite some of these studies having been conducted around 20 years ago (Field et al., 2004; Jha

et al., 1998; Kilbridge et al., 2006), we do not consider them to be outdated in light of todays' technological advances. The implementation of electronic medication administration records is in its infancy stage in the Nordic countries, while this technology was implemented in single frontier hospitals in the USA two decades ago. Therefore, we can value on the experience derived from these early established systems.

Evaluating ADE detection rates in studies comparing at least two methods suggests that ADEs might be more common than previously indicated in studies that used only one method for detecting events (Franklin et al., 2009; Jha et al., 1998).

Limitations

Because of the differences in the type and number of triggers across studies, it is difficult to discuss the exact detection value of the different methods applied to review health records. ADE rates are easier to compare between studies that apply similar triggers, such as comparing studies that have used the broadly recognized Global Trigger Tool (von Plessen et al., 2012). This however also involves challenges, as even this method must be adapted to local settings to increase efficiency and specificity, as well as to changes in medical practice over time (Field et al., 2004).

Box 2 ADEs and Medication Errors: Detection Methods Summary

- Healthcare organizations use different methods to detect adverse drug events: incident reporting, direct observation, record review, computerized surveillance, and interviews.
- The detection rate of adverse drug events and medication errors vary substantially according to the method used.
- The different methods detect different types of events, e.g., trigger tool strategies missed whole classes of events (medication administration errors, prescribing errors, omissions).
- Incident reporting detects only a small number of events.
- There is poor overlap in events detected by more than one method.

Box 2 (*Continued*)

- A complementary multi-method approach is a gold standard in monitoring and detecting adverse drug events.
- Computerized surveillance offers future potential benefits in detecting real time events and following up with concurrent intervention to limit patient harm.
- Research efforts should focus on developing effective adverse drug event and medication error detection methods for outpatient settings, and as well as seamless transitioning between hospitals and nursing homes.

Conclusion

This review of the pros and cons of current ADEs and medication error detection methodologies can assist and inspire stakeholders to choose the most appropriate methods relevant to their local, regional or national setting. We have discussed how the detection methods vary in their detection rates, cost, time, and resources required. We have exemplified the event types the different methods detect, the ability to detect preventable events, and their ability to limit harm.The low number of studies from the outpatient setting highlights the research and knowledge gaps of detecting methods for adverse drug events in municipal health and care services.

Few medication errors and adverse events are detected using any one method alone, that means that none of the methods can serve as a gold standard, and each method described has its place in monitoring medication safety. The literature supports a combination of methods to be used to detect the diversity of ADEs and medication errors.

One single method cannot detect and measure all medication errors and adverse events. Our discussion of how the current methodologies can detect and measure medication errors – their advantages and limitations – will hopefully expand the toolbox of stakeholders when they set out to learn from the past, and prevent future adverse drug events and medication errors.

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Part Three:

Healthcare Professionals

CHAPTER 8

Nurse-Led Interventions to Promote Medication Adherence in Community Care: A Systematic Review

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Abstract: The aim of this systematic review was to describe and assess nurse-led interventions to enhance medication adherence and clinical outcomes among adults in community care. PubMed, Medline, Embase, CINAHL, and CENTRAL were searched for relevant studies. Randomized controlled trials (RCTs) published 2011–2021 that tested nurse-led interventions with community-dwelling patients and quantitatively measured adherence were included. Adherence and clinical outcomes were analyzed descriptively. Seventeen RCTs fulfilled the inclusion criteria and were of acceptable quality. The studies varied in sample size, loss to follow-up rates, study subject ages, medical conditions, and pharmacotherapy. The nurse-led interventions were complex and multifaceted. Four (23.5%) and seven (41.2%) RCTs reported statistically significant effects of nurse-led interventions on medication adherence and clinical outcomes (e.g., blood pressure, quality of life), respectively, when compared with control arms. All studies had methodological quality limitations. In conclusion, low-quality evidence suggests that some nurse-led interventions may improve medication adherence and clinical outcomes in patients living in the community.

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Future research should focus on the effective components of interventions identified here, such as motivational interviewing, adherence aids, patient education and eHealth components, and include defined clinical endpoints, for example, hospital admissions, all-cause mortality, and cost-effectiveness.

Keywords: Nurse-led intervention, medication adherence, patient compliance, nursing, intervention studies, systematic review

Optimizing the benefits of pharmacotherapy depends on patients taking medicine as prescribed, a concept defined as medication adherence (hereafter adherence). Adherence involves the patient's agreement to follow prescription recommendations from the healthcare provider (Sabaté, 2003), and includes the timing, dosage, and frequency of medication administration. However, many patients are unable to follow the recommendations for the administration of their prescribed medicines. Poor adherence is associated with increased morbidity, mortality, and healthcare costs, and reduced effectiveness of treatment (Cutler et al., 2018; Sabaté, 2003). Poor adherence is also a risk factor for medication errors (Assiri et al., 2018).

Patient safety in primary care depends on medication management in domiciliary settings, where patients, their caregivers and healthcare providers, like nurses, are the key actors. Adverse drug events and suboptimal medicine management are important sources of ill-health and hospitalization (Jordan et al., 2021). Nurses increasingly take active responsibility for disease management and health promotion, and are often the professionals closest to patients. They are trained to deliver patient-centred care and liaise between patients and physicians. A review of studies on the impact of nursing on patients' outcomes concludes that deployment of well-trained nurses improves health outcomes for patients in primary care, and nurse-led care promotes patient satisfaction and medication adherence (Coster et al., 2018). A systematic review and meta-analysis including ten randomized controlled trials (RCT) on nurse-led interventions to enhance adherence to long-term medication for HIV, hypertension, depression, or arthritis, indicates that: all interventions improve adherence; counseling is frequently a component of successful interventions; multifaceted, tailored interventions are the most effective;

and patients benefit from continuous follow-up (Van Camp et al., 2013). Another systematic review of 11 RCTs and two controlled clinical trials, reports that, when compared with usual care, nurse-led interventions improve adherence among recently discharged older adults, with statistically significant effect estimates in eight studies (Verloo et al., 2017).

Existing evidence suggests that nurses are well suited to deliver interventions to improve medication adherence, and complex, tailored interventions including counseling are needed (Coster et al., 2018; Van Camp et al., 2013; Verloo et al., 2017). Despite the increasing body of evidence regarding adherence interventions, nurses' contributions in aiding community-dwelling patients to follow pharmacotherapy recommendations have received little attention. This chapter is based on a systematic review, aiming to: 1) describe and assess the impact of nurse-led interventions on medication adherence among adults living in the community; and 2) synthesize the interventions' effects on clinical outcomes.

Method

Study Design

A systematic literature review was conducted, according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Higgins et al., 2021; Moher et al., 2009).

Databases

The databases PubMed, Medline, Embase, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched for relevant studies by HS.

Search Terms

The search strategy was determined after team discussions, performing pilot searches, and consultation with a librarian. Key search terms relating to the PICO (Table 1) were combined using Boolean operators: *or* within the PICO elements, *and* between PICO elements.

Limitations

Limitations for the search were: English, Norwegian, Danish or Swedish as the publication language, published in the time period, January 2011 to October 2021, and in a scientific, peer-reviewed journal. The PubMed search included the following additional filters: abstract, full text, clinical study, clinical trial, controlled clinical trial, randomized controlled trial, and Danish, English, Norwegian, or Swedish language.

Inclusion and Exclusion Criteria

The population, intervention, comparison, and outcome (PICO) of the study were defined as in Table 1. An additional inclusion criterion regarding study design was that the studies reported original empirical data from an RCT, including cluster and stepped RCTs. Non-randomized study designs, including non-randomized and pseudo-randomized clinical trials, were excluded.

Table 1. The PICO of the Study, Including Search Terms

Element acronyms	Descriptor	Determinants	Search terms
P	Population	adult (≥18 years old) medication users in community settings, i.e., home health care, long-term care, sheltered housing, residential facilities	community health services (MeSH) or residential facilities (MeSH) or long term care (MeSH) or home health care (MeSH)
I	Intervention	nurse-led interventions, i.e., nurses play a key role in the intervention	nurses (MeSH) or community health nursing (MeSH) or "nurse-led"
C	Comparison	No specific criteria for the comparison	No search terms included
O	Outcome	medication adherence as study outcome, quantified using a subjective or objective medication adherence measure (Lam & Fresco, 2015)	medication adherence (MeSH) or patient compliance (MeSH) or "non-adherence" or "non-compliance"

Search results were exported to EndNote 20.2 software, and duplicates removed. First, the results were screened by reading the article titles and excluding articles that were not relevant, according to PICO and inclusion

criteria. Next, the study abstracts were evaluated, and non-relevant articles were excluded. Subsequently, the full-text articles were assessed for their eligibility. Finally, the reference lists of the identified studies were reviewed to retrieve additional relevant articles, resulting in the identification of one study. One reviewer (HS) performed the identification and screening of studies, and the initial assessment of eligibility based on full-text studies. In cases of uncertainty of relevance and acceptability, three authors read each article in full-text, and consensus on whether to include the article was reached by discussion.

Quality Appraisal

The quality of the included studies was assessed using the Cochrane collaboration's tool for assessing risk of bias in randomized trials across seven dimensions (Higgins et al., 2021; Higgins et al., 2011): 1) Random sequence generation (selection bias); 2) Allocation concealment (selection bias); 3) Blinding of participants and personnel (performance bias); 4) Blinding of outcome assessment (detection bias); 5) Incomplete outcome data (attrition bias); 6) Selective reporting (reporting bias); and 7) Other bias. RCTs with a high risk of bias in four or more dimensions were excluded.

Data Extraction and Knowledge Synthesis

Data were extracted using a pre-defined, standardized data extraction table, that included the following study characteristics: study author; year of publication; design; aim; study setting including country; number of study participants; description of the study population (P); intervention (I) and comparison/control (C) group; outcome measurements; results of intervention on medication adherence (O); and results of intervention on clinical outcomes (defined as measurable change in health, function or quality of health). One reviewer (HS) created a preliminary data extraction table with the summary of findings from the included studies. Then, all researchers reviewed the extracted results individually, making comments and corrections to the extracted content. Subsequently, the reviewers discussed the evidence and summarized the findings according to study characteristics.

We focused on synthesizing the nature and content of the interventions, and their impact on adherence and clinical outcome. The diverse nature of the studies with respect to study population, nurse-led interventions, and adherence outcome measurements did not allow meta-analysis. Hence, the results of this review are presented narratively.

Excluded Studies

After full text assessment of eligibility, 39 studies were excluded. Reasons for exclusion were: study design (e.g., pre-post design, non-randomized trial in 10 studies); study setting (e.g., hospital, in 9 studies); not a nurse-led intervention (n = 12); not presenting adherence results (n = 5); and poor study quality (n = 3, with a high risk of bias in ≥4 dimensions).

Results

Figure 1 shows the study flow diagram. The search strategy yielded 715 studies, of which 108 were duplicates. In total, 550 studies were excluded

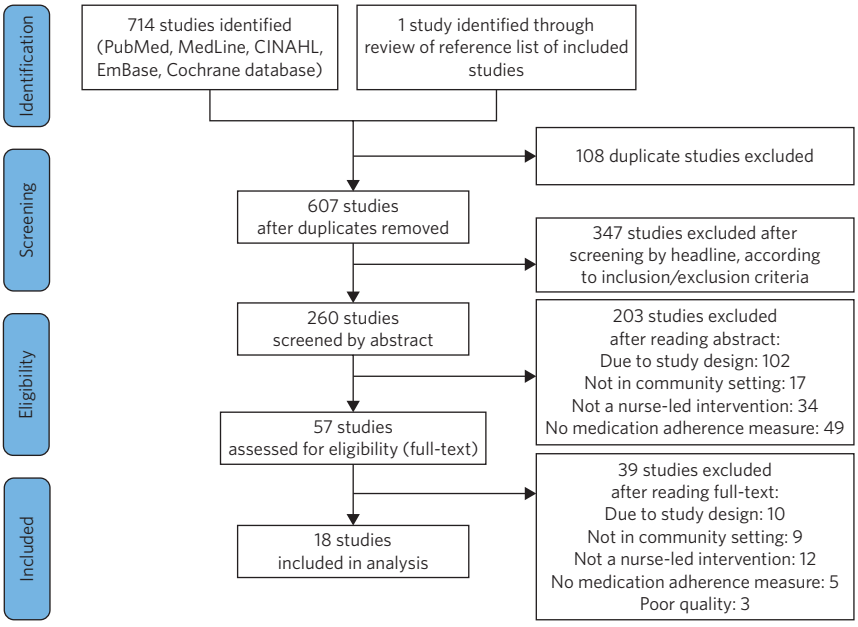

Figure 1. Study Flow Diagram

based on their title or abstract, and 39 studies were excluded following full-text review for eligibility. In total, 18 studies were included for analysis in this review.

Characteristics of Studies

Table 2 shows the characteristics of the included studies and the study sample. Two studies presented results from the same RCT (Blank et al., 2011; Blank et al., 2014), resulting in 17 RCTs to analyze. Study designs included two-armed (n = 14), three-armed (n = 3), cluster (n = 3), and pilot RCTs (n = 4). Clusters were determined by geographical location or health center (Amado Guirado et al., 2011; Lewis et al., 2016; Persell et al., 2018; Shen et al., 2021). The studies were conducted in 13 different countries, predominantly the USA (n = 5), and China (n = 4). Total study sample was 4,654 participants, with an average of 274 study subjects (standard deviation, SD 295) randomized to intervention or control groups. Overall

Table 2. Characteristics of the Included Studies and Participants

Study reference	RCT design	Country	Setting	N	Loss to follow-up (%)	Mean age (years)[a]	Condition[b]
Adeyemo et al., 2013	Two-arms	Nigeria	Community clinics and patients in own homes	698	154 (22.1)	62.6	Hypertension
Amado Guirado et al., 2011	Two-arms, cluster	Spain	Primary healthcare centres	996	128 (12.9)	63.4	Hypertension
Blank et al., 2011; Blank et al., 2014[c]	Two-arms	USA	Community HIV treatment sites and patients in own homes	238	135 (56.7)	43.6	HIV and mental illness
Chien et al., 2015	Two-arms	China	Community psychiatric nursing service and patients in own homes	114	4 (3.5)	28.7	Schizophrenia
Cicolini et al., 2014	Two-arms	Italy	Primary care centre and patients in own homes	203	5 (2.5)	59.1	Hypertension

(*Continued*)

Table 2. (Continued)

Study reference	RCT design	Country	Setting	N	Loss to follow-up (%)	Mean age (years)[a]	Condition[b]
Del Hoyo et al., 2018	Three-arms, pilot	Spain	Outpatient clinic and patients in own homes	63	3 (4.8)	40.5	Inflammatory bowel disease
Kolcu & Ergun, 2020	Two-arms	Turkey	Nursing homes	74	2 (2.7)	75.6	Hypertension
Liang et al., 2021	Two-arms	Taiwan	Home care	200	33 (16.5)	80.7	Chronic disease (any)
Ma et al., 2014	Two-arms	China	Community health centres and patients in own homes	120	14 (11.7)	58.8	Hypertension
Mayer et al., 2017	Two-arms, pilot	USA	Primary care clinic	50	11 (22.9)	38.2	HIV
McAlister et al., 2019	Two-arms,	Canada	Patients in own homes	361	8 (2.2)	65.2	Upper extremity fragility fracture
Persell et al., 2018	Three-arms, cluster	USA	Community health centres	920	126 (13.7)	52.7	Hypertension
Shen et al., 2021	Two-arms, cluster	China	Community health centres and patients in own homes	82	5 (6.1)	66.2	Coronary heart disease
Simoni et al., 2011	Two-arms, pilot	China	Patients own homes and hospital	70	0 (0)	36.0	HIV
Still et al., 2020	Two-arms, pilot	USA	Community clinics and patients in own homes	60	0 (0)	59.5	Hypertension
Usher et al., 2013	Two-arms	Australia	Community mental health services	101	0 (0)	NA	Mental illness (any)
Wakefield et al., 2011	Three-arms, single centre	USA	Medical centre and patients in own homes	304	58 (19.1)	68.7	Hypertension and diabetes mellitus

Abbreviations: RCT, randomized controlled trial; NA, not available; HIV, human immunodeficiency virus.
[a]Mean age of study participants at baseline in intervention and comparison groups combined.
[b]Health condition of study participants that was an inclusion criterion.
[c]Two articles published on the same intervention.

loss to follow-up was 686 study subjects (14.7%), ranging from 0 to 154 subjects. The mean age of the study subjects at baseline was 56.2 years (SD 14.4), and varied from 28.7 years (Chien et al., 2015) to 80.7 (Liang et al., 2021). The study sample was diverse in terms of health conditions, with hypertension most frequently represented (n = 8), followed by HIV (n = 3). Other health conditions were "mental illness", schizophrenia, inflammatory bowel disease, long-term diseases in general, coronary heart disease, diabetes mellitus, and upper extremity fragility fracture.

Characteristics of Nurse-Led Interventions

Table 3 shows an overview of the nurse-led interventions in the included studies. Overall, the nurse-led interventions were complex, with a variety of components that typically included personalized health or medication information (oral, written and/or digital), education, consultation, counseling and/or motivational interviewing performed by nurses in primary health clinics or home visits. eHealth components, that is information and communication technology in support of health education and/or health and medication management, were used in seven studies (Cicolini et al., 2014; Del Hoyo et al., 2018; Liang et al., 2021; Persell et al., 2018; Shen et al., 2021; Still et al., 2020; Wakefield et al., 2011). The eHealth intervention elements ranged in complexity, from relatively simple e-mail alerts (Cicolini et al., 2014) and apps (Del Hoyo et al., 2018), to a complex integrated tele-homecare program including a smartphone, blood pressure monitor, medication dispenser, glucometer and a necklace emergency call button (Liang et al., 2021). Adherence aids were used in six interventions (Blank et al., 2014; Del Hoyo et al., 2018; Kolcu & Ergun, 2020; Liang et al., 2021; Simoni et al., 2011; Still et al., 2020).

The interventions in 14 of the RCTs included strategies to change behavior, like motivational interviewing (n = 3), counseling sessions (n = 5), habit-based interventions comprising digital alerts and tools (n = 6), or adherence tools like pillbox organizers or reminder alarms (n = 6), and different combinations of these. Additionally, strategies to increase knowledge were used, like patient education on health and medicines, and psychoeducation (n = 13). In two studies, knowledge increasing

Table 3. Characteristics of the Nurse-Led Interventions and Synthesis of Intervention Effects on Adherence and Clinical Outcomes

Study reference	Aim of study	Intervention group (I)	Control group (C)	Outcome measurements[a]	Adherence results	Clinical outcomes
Adeyemo et al., 2013	To expand the evidence base necessary to guide hypertension treatment and control programs in Africa.	I1) Clinic-based nurse-led treatment with free of charge antihypertensive agent(s), facilitation of clinic visits and health education over 6 months. I2) like I1 and additional home visits by nurses	I1 compared with I2	1º: Pill count 2º: Biological assay with a urinary riboflavin tracer (participants instructed to take riboflavin daily combined with antihypertensive medication)	No significant effects on adherence	None measured
Amado Guirado et al., 2011	To evaluate the efficacy of a healthcare education program for patients with hypertension.	Personalized information provided by a trained nurse, and written leaflets, during 4 visits to healthcare centres (average 15 min duration) over 1 year.	Usual care	The Haynes-Sackett and Morisky-Green tests and pill counts measured adherence. BP and BMI.	No significant effects on adherence	No significant effects on BP or BMI.
Blank et al., 2011 Blank et al., 2014 [b]	To test the effectiveness of a community-based advanced practice nurses' intervention to promote adherence to HIV and psychiatric treatment regimens.	The PATH+ I: Preventing AIDS through Health for HIV Positive persons. A practice nurse intervention including weekly in-home consultations (psychoeducation, adherence measurements and tools) and coordinated medical and mental health services over 1 year.	Usual care	1º: Viral load CD4 cell count Pill-counts Health-related QoL	In the I arm 58% (N = 61) were at least 80% adherent at 3 months, 80% (N = 84) from 3 to 6 months, and 70% (N = 74) from 6 to 12 months. No data provided to report on significant effects between groups.	A significantly reduction in log viral load (d = –.361 log 10 copies per ml, p<.001) in I compared with C. No significant difference in CD4 counts or QoL between study groups.

Chien et al., 2015	To test and evaluate the effectiveness of an adherence therapy (AT) for outpatients with schizophrenia spectrum disorders, based on a motivational interviewing approach.	Nurse-led (community psychiatric nurses) motivational interview-based medication adherence therapy (AT) program. The AT (a 4-month program) consisted of 3 phases in which 8 sessions of 2 hours were held in-home every 2 weeks.	Usual care	1º: Adherence Rating Scale (ARS) Symptom severity, insight into treatment, hospitalization rate, functioning	Significant improvements in medication adherence (F = 7.45, P = 0.007) over 6 months follow-up, when compared with usual care.	Significant improvements in insight into illness and/or treatment, psychosocial functioning, symptom severity, number of re-hospitalizations, (F = 5.01 to 7.32, P = 0.008 to 0.030) when compared with usual care.
Cicolini et al., 2014	To test the efficacy of a nurse-led reminder program through email (NRP-e) to improve cardiovascular risk factors among hypertensive adults.	The NRPe I: included self-assessment of medication adherence, and educational programs on a healthy lifestyle. Email alerts (once per week for 6 months) from a nurse care manager. The email required read receipt, and if no response, the nurse phoned to press for reading.	Usual care, including self-assessment of medication adherence and educational program.	One question from the MMAS: "Did you take all your medications yesterday?". BP, glycemia, blood lipids	No significant effects on adherence	Mean systolic BP was 135 ± 8 mmHg in I group vs 143 ± 6 mmHg in C group (p<0.001). Mean total cholesterol was 205 ± 40 mg/dL in I group vs 218 ± 3 2 mg/dL in C group (p = 0.015).
Del Hoyo et al., 2018	To evaluate the impact of remote monitoring using a Web system, compared with standard care and telephone care on health outcomes and health care in patients with complex inflammatory bowel disease (IBD).	TECCU (24 weeks) in two arms: I1) Nurse-assisted telephone care, and written information about IBD and medications. I2) Web-based tele-management system with an app for digital platforms, and included questionnaires, advice, reminders, educational material, preventive measures, and tools for medication management	Usual care, including in-person visits to the outpatient clinic run by nurses	1º: % of patients in clinical remission. 2º: adherence by Morisky-Green index. QoL, adverse effects, satisfaction, social activities.	No significant effects on adherence	No significant effects on clinical outcomes

(*Continued*)

Table 3. (*Continued*)

Study reference	Aim of study	Intervention group (I)	Control group (C)	Outcome measurements[a]	Adherence results	Clinical outcomes
Kolcu & Ergun, 2020	To evaluate the effects of a nurse-led hypertension management program on QoL, adherence and hypertension management in older adults.	Nurse (who is also the researcher) performed 6 sessions of health education, 4 motivational meetings, institutional actions (e.g., distribution of adherence aids/ pillbox organizers), over 20 weeks.	Usual care	1º: BP measurements, MMAS-4 measured at pre-test and post-test (20 weeks) Hypertension therapy knowledge score QoL (SF-36)	Adherence rate was significantly higher in I vs C group (100% vs 64.9%, respectively: χ^2 = 15.77, p = 0,000)	Systolic BP was 118 ± 10 mmHg in I group vs 130 ± 15 mmHg in C group. QoL subscale physical component was 58.4 ± 13.9 in I group vs 44.3 ± 16.7 in C group.
Liang et al., 2021	To evaluate the effectiveness of an integrated nurse-led tele-homecare program for patients with a range of chronic illnesses and a high risk for readmission.	Integrated tele-homecare program (e.g., wireless transmission devices, including a smartphone, BP monitor, medication dispenser, and a necklace emergency call button, glucometer). The smartphone had an alarm for medication reminders. Continuous telemonitoring with nurses assessing patients' conditions. Nurses' home visits (content of care included assessment, patients' education, nutrition and medication consultation, and medication reminders) on discharge day, 3 and 6 months after discharge, and additional visits depending on individual needs.	Patients received discharge planning. Home-visits by nurses (content included assessment, checking vital signs, patient education, nutrition and medication consultation, and medication reminders) at 3 and 6 months after discharge	1º: mortality, readmission, number of ED visits 2º: Chinese version of the Medication Adherence Behavior Scale (C-MABS) Daily living activities Health status QoL	Adherence scores remained stable from initiation and to 3 and 6 months of follow-up. No significant effects on adherence	Mortality and ED visits were significantly reduced in I group compared with C group.

Ma et al., 2014	To test the effectiveness of motivational interviewing compared with the usual care for Chinese hypertensive patients.	Motivational interviewing counseling by trained nurses, 8 sessions of 30-40 min over 6 months, performed at-home or health centres.	Usual care, including information on hypertension and recommendations to improve adherence and lifestyle every 6 weeks	1º: Treatment Adherence Questionnaire for Patients with Hypertension (TAQPH) BP QoL	Adherence increased more in I group than C group (29.7 ± 3.5 vs 25.3 ± 3.1, respectively, p = 0.04)	Systolic BP was 141 ± 20 mmHg in I group vs 147 ± 20 mmHg in C group (p = 0.011)
Mayer et al., 2017	To preliminarily test the intervention "Life-Steps for PrEP" compared with an active, time and session-matched comparison condition, among men who have sex with men, initiating HIV pre-exposure prophylaxis (PrEP)	"Life-Steps for PrEP" I: a cognitive behavioral, counseling intervention over 6 months, including 4 nurse-delivered initial sessions and 2 booster sessions of about 50 min, based on Life-Steps, an ART treatment adherence intervention. Overall, the core components focused on medication adherence, sexual behavior, and problem-solving barriers to adherence.	Time and session-matched comparison condition comprised informational and supportive counseling (ISP) by a nurse on the same schedule as I	1º: Wisepill™ (electronic pill storage device, allows for real-time adherence monitoring), calculated a variable for each week that participant had at least 80% adherence. PrEP plasma levels (tenofovir)	No significant difference in adherence between study groups (for those who completed study visits).	None reported
McAlister et al., 2019	To compare the effectiveness of two interventions on long-term oral bisphosphonate adherence after an upper extremity fragility fracture.	C-STOP: Comparing Strategies Targeting Osteoporosis to Prevent fractures after upper extremity fracture. Participants initiating oral bisphosphonate therapy were randomized to two arms over 24 months: I1) A nurse study case manager educated and counseled patients face-to-face or by telephone (minimum 4 times) I2) multi-faceted patient and physician education intervention	I1 compared with I2	1º: adherence to bisphosphonate therapy at 12 months after enrolment. Self-report and pharmacy dispensing records. 2º: health-related QoL	No significant effects on adherence	No differences in QoL between patients who were adherent and those who were not. Any new fractions were not reported.

(*Continued*)

Table 3. (*Continued*)

Study reference	Aim of study	Intervention group (I)	Control group (C)	Outcome measurements[a]	Adherence results	Clinical outcomes
Persell et al., 2018	To test medication management tools delivered through a commercial electronic health record (EHR) with and without a nurse-led education intervention.	I1) EHR-based medication management tools over 12 months; involved medication lists, review sheets at visit check-in, lay medication information sheets printed after visits. I2) EHR+ nurse-led medication management support, involving e.g., medication reconciliation and review, education, and counseling sessions	Usual care	1º: Systolic BP 2º: medication management, including adherence using questions from the Patient Medication Adherence Questionnaire (PMAQ)	No significant effects on adherence	Systolic BP in the I2 group was not significantly lower compared with the C group, but was significantly lower compared with the I1 group (−5.6 mmHg, 95% CI −8.8 to −2.4 mmHg)
Shen et al., 2021	To investigate the effect of a nursing intervention based on Cox's interaction model of client health behavior to improve health outcomes and behaviors for secondary prevention of coronary heart disease.	Nurse-led routine health-education and a 12-week Cox's interaction model of client health behavior and routine health education (6 sessions à 60-90 min). Onsite, telephone and online interaction	Routine health-education	1º: self-management, physical activity, anxiety, sexual knowledge, ability to identify sexual health education needs, and adherence, measured by MMAS-8 2º: BP, BMI, LDL	The score on adherence in the I group was significantly higher than that in the C group ($t = 3.438$, $p = .001$).	Systolic BP was 128 ± 16 mmHg in I group vs 136 ± 12 mmHg in C group ($p<0.001$). BMI was 21.9 ± 2.3 kg/m^2 in I group vs 24.2 ± 4.0 kg/m^2 in C group ($p = 0.049$) LDL was 2.61 ± 0.4 mmol/L in I group vs 3.12 ± 0.55 mmol/L in C group ($p = 0.03$)

Simoni et al., 2011	To evaluate a nurse-delivered adherence intervention among HIV-positive outpatients initiating antiretroviral therapy.	A 30-min educational session, a pillbox organizer, and a referral to a peer support group. Additionally, participants could choose an electronic reminder device, three sessions of counseling either alone or with a treatment adherence partner, or both reminder and counseling. Counseling sessions delivered by one nurse. I of 13 weeks.	A 30-min educational session, a pillbox, and a referral to a peer support group	1º: Self-reported single-item question. EDM (MEMS®). 2º: CD4 counts and viral load	No significant effects on adherence	No significant effects on CD4 counts or viral load
Still et al., 2020	To explore effects of a community and technology-based intervention for hypertension self-management (COACHMAN) on BP control and health-related QoL in African Americans with hypertension.	COACHMAN I: a technology-based intervention for hypertension self-management. I included web-based education, home BP monitoring, medication management application (MediSafe), and nurse counseling, over 12 weeks. The nurses provided 3–4 sessions of informal counseling focused on medication adherence and BP monitoring.	Usual care, involving printed educational material on hypertension management, and training to use a home BP monitor.	BP The Hill-Bone Compliance to High Blood Pressure Therapy Scale. QoL MediSafe app results.	No significant effects on adherence	No significant effects on BP or QoL
Usher et al., 2013	To test the effect of a nurse-led intervention on weight gain in people with serious mental illness prescribed and taking second generation antipsychotic medication.	Received a 12-week healthy lifestyle booklet, weekly nutrition and exercise education, exercise sessions, and nurse support (nurse also the researcher)	Received a 12-week healthy lifestyle booklet	BMI Medication Compliance Questionnaire Medication side effects Health-related QoL	No significant effects on adherence	No significant effects on BMI or QoL

(*Continued*)

Table 3. (*Continued*)

Study reference	Aim of study	Intervention group (I)	Control group (C)	Outcome measurements[a]	Adherence results	Clinical outcomes
Wakefield et al., 2011	To evaluate the efficacy of a nurse-managed home telehealth intervention to improve outcomes in veterans with comorbid diabetes and critical need to control hypertension.	Nurse-managed home telehealth intervention over 6 months. Participants measured BP and blood glucose, and entered them into the telehealth device, and answered questions. High-intensity I: many questions based on a branching disease management algorithm. Low-intensity I: small subset of questions each day.	Usual care.	1°: systolic BP and HbA1c. 2°: adherence by the Self-Reported Medication Taking scale.	No significant effects on adherence	Results are presented as a change in outcome during I period. HbA1c decreased significantly in both I groups compared with C. Systolic BP decreased significantly for the high-intensity I compared with the other groups

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; BP, blood pressure; C, control; ED, emergency department; EDM, electronic drug monitoring; HbA1c, haemoglobin A1c; HIV, human immunodeficiency virus; I, intervention; LDL, low density lipoprotein; MMAS, the Morisky medication adherence scale; RCT, randomized controlled trial; QoL, quality of life.
[a]Primary (1°) and secondary (2°) outcomes are specified, if defined by the study authors.
[b]Two articles published on the same intervention.

strategies were the main intervetion components (Adeyemo et al., 2013; Amado Guirado et al., 2011), and one study used a knowledge strategy involving monitoring key clinical symptoms combined with education and advice (Wakefield et al., 2011).

Interventions appeared to be time-consuming, but time was not reported, and no economic analyses were located.

Effect on Medication Adherence

Table 2 shows an overview of adherence measurements used and the interventions' effects on adherence. Adherence was the primary outcome measure in 13 out of the 17 RCTs (72.2%). Both subjective and objective measures were used, including self-reported adherence scales or questionnaires, pill counts, plasma/urine levels of medication/tracer, medication event monitoring systems (MEMS), and electronic pharmacy refill records. The most commonly used measure was subjective self-reported adherence (n = 14, 82.3%). Two or more adherence measures were used in six studies out of the 17 (35.3%) (Adeyemo et al., 2013; Amado Guirado et al., 2011; Mayer et al., 2017; McAlister et al., 2019; Simoni et al., 2011; Still et al., 2020).

Of the 17 included RCTs, four (23.5%) reported a statistically significant effect of nurse-led interventions on adherence (Chien et al., 2015; Kolcu & Ergun, 2020; Ma et al., 2014; Shen et al., 2021). These interventions targeted behavior and knowledge. The intervention components in these RCTs were: motivational interviewing, pillbox organizers, patient education, and eHealth. Duration of the intervention ranged from 3 to 6 months, and involved antipsychotics, antihypertensive agents, and unspecified agents for treatment of coronary heart disease. A common feature of these four studies was that the nurses' contribution to the intervention was substantial, in terms of scope and time used on repetitive educational and/or behavioral intervention elements. For example, in the study by Shen and co-workers, the nurses provided six sessions over 12 weeks including health education and behavioral/skills, combined with participant interaction onsite (quizzes, seminars, simulation), regular telephone interaction, and continual online interaction via a social media platform (Shen et al., 2021). In the adherence therapy program described in Chien

et al. (2015), nurses provided two hours of in-home motivational interview-based adherence therapy every two weeks for four months.

None of the included RCTs had a negative impact on adherence measures.

Effects on Clinical Outcomes

Seven (41.2%) of the included RCTs reported a statistically significant effect of the intervention on clinical outcomes when compared with control arms (Chien et al., 2015; Cicolini et al., 2014; Kolcu & Ergun, 2020; Liang et al., 2021; Ma et al., 2014; Shen et al., 2021; Wakefield et al., 2011). Table 3 presents an overview of clinical measurements and outcomes of the included studies. The nurse-led interventions on patients living in the community reduced systolic blood pressure (BP) (n = 5) (Cicolini et al., 2014; Kolcu & Ergun, 2020; Ma et al., 2014; Shen et al., 2021; Wakefield et al., 2011), reduced body mass index (BMI) and/or cholesterol concentrations (Cicolini et al., 2014; Shen et al., 2021), and increased quality of life (QoL) (Kolcu & Ergun, 2020), among hypertensive patients. Statistically significant positive effects on symptom severity and reduced numbers of readmissions among outpatients with schizophrenia (Chien et al., 2015), reduction in emergency department (ED) visits among patients with multiple long-term conditions (Liang et al., 2021), and reduction in haemoglobin A1c (HbA1c) among patients with diabetes (Wakefield et al., 2011), were also reported.

Risk of Bias and Quality of Studies

Figure 2 shows the risk of bias (RoB) analysis results of the individual studies. All studies have a high RoB in at least one dimension, most commonly in blinding of participants and/or researchers (15 studies), since the nature of interventions rarely allowed for blinding. Of note, 12 studies gave no information on blinding of outcome assessment and were assessed as unclear RoB. All included studies are defined by the study authors to have an RCT design, however, in one study the randomization was insufficiently described and was assessed to have a high RoB (Amado Guirado et al., 2011). Additionally, the randomization procedure was described vaguely

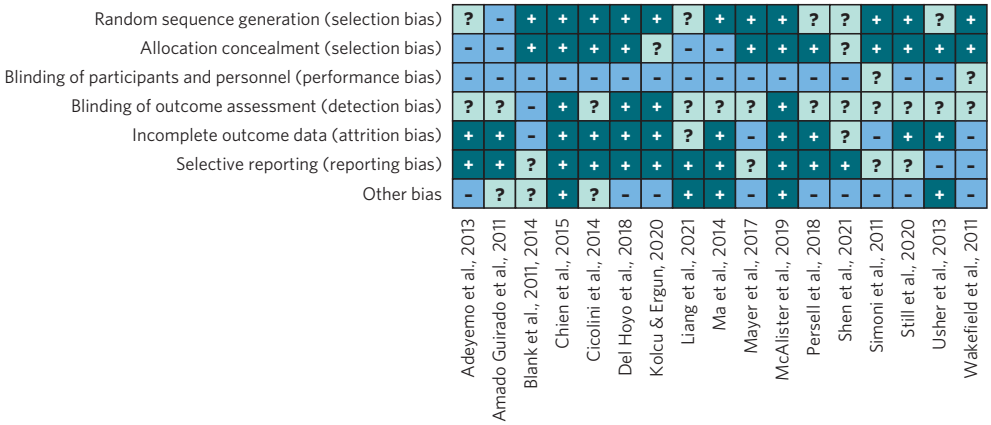

Figure 2. Risk of Bias (RoB) Analysis of the Included RCTs. +, Low RoB; ?, Unclear RoB; -, High RoB.

in five studies (Adeyemo et al., 2013; Liang et al., 2021; Persell et al., 2018; Shen et al., 2021; Usher et al., 2013), which were therefore assessed to have an unclear RoB. A high risk of attrition bias was detected in four studies (Blank et al., 2011; Mayer et al., 2017; Simoni et al., 2011; Wakefield et al., 2011), mainly due to high attrition (>20%) in combination with unbalanced attrition between intervention and comparison groups. A medium or lower overall attrition (<20%), but unbalanced between groups, was classified as an unknown RoB, concerning two studies (Liang et al., 2021; Shen et al., 2021). Most studies had a low risk of reporting bias (n = 11), and four studies had an unclear risk of reporting bias due to for example, not showing a study flow diagram or not giving detailed data on adherence (Blank et al., 2011; Mayer et al., 2017; Simoni et al., 2011; Still et al., 2020). Two studies had a high risk of reporting bias due to missing data on adherence outcomes, and/or study flow diagrams, and/or study participants' health characteristics (Usher et al., 2013; Wakefield et al., 2011). A high risk of other bias was detected in nine studies, due to low statistical power (small sample sizes, pilot studies), or unbalanced study participant groups likely influencing outcomes.

Figure 3 shows the cumulative risk of bias in the included studies, illustrating the overall quality of evidence in this systematic review. In total, a low RoB was observed in 45% of the dimensions, whereas a high RoB was observed in 30% of the dimensions.

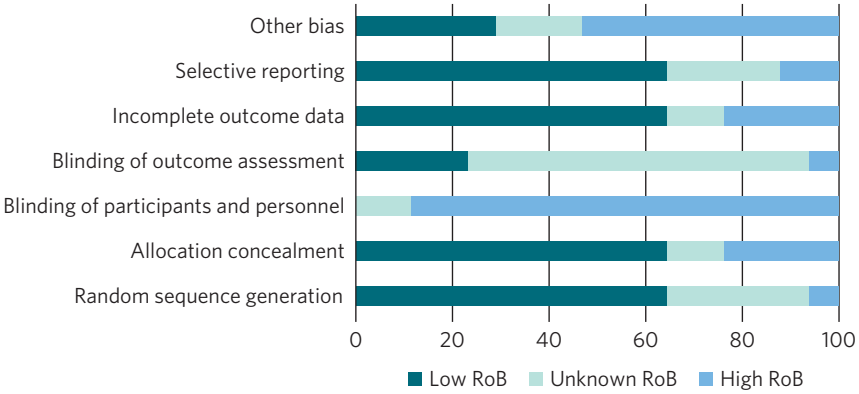

Figure 3. Cumulative Risk of Bias (RoB) Observed in the Studies, Given in Percentage.

Discussion

In this systematic review, we identified and assessed 17 RCTs describing nurses' involvement in aiding adherence and clinical outcomes. Interventions typically targeted adherence through behavior and/or knowledge of health and medicines, with components and combinations of motivational interviewing, counseling, education, adherence tools, and eHealth. Four (23.5%) and seven (41.2%) out of the 17 RCTs reported statistically significant effects on adherence and clinical outcomes, respectively, when compared with control arms. The interventions that improved adherence entailed substantial contributions from nurses, in terms of using several interventional components and the time used in the intervention. Diversity in design and conduct of the RCTs precluded any meta-analysis of the reported nurse-led interventions.

The extent to which patients adhere to the recommendations for prescribed medications, greatly impacts health and healthcare expenditure (Cutler et al., 2018; Sabaté, 2003). Hence, adherence served as a natural primary outcome measure for this review. Additionally, we synthesized nurse-led intervention effects on clinical outcomes, which might serve as an indirect measure of whether patients adhere to treatment. Furthermore, it is important to review existing research evidence on nurses' contributions to patients' health in a community setting, to pinpoint measures

that have been shown to be useful, and to highlight areas of interest and make recommendations for further research.

Of the 17 RCTs in this review, only four (23.5%) reported significant effect estimates on adherence, and concomitantly they reported significant effects on clinical outcomes. However, seven (41.2%) of the RCTs showed significant positive effects on clinical outcomes or surrogate endpoints, such as BP, BMI, HbA1c, and cholesterol-levels. One trial (Liang et al., 2021) demonstrated a reduction in ED visits, and one a reduction in re-hospitalization (Chien et al., 2015). The lack of statistically significant intervention effects might be attributed to insufficient sample sizes in some studies: five had fewer than 100 participants (Del Hoyo et al., 2018; Kolcu & Ergun, 2020; Mayer et al., 2017; Simoni et al., 2011; Still et al., 2020). However, some studies used continuous outcome measures, which can indicate a statistically significant difference with relatively small sample sizes. Adherence was a secondary outcome in four RCTs, hence the interventions were not primarily designed to enhance adherence. Furthermore, there are challenges in measuring adherence as there is no single gold standard measure, and a mixed-method approach is recommended (Lam & Fresco, 2015; Nguyen et al., 2014). Among the RCTs in this review, only six (35.3%) used a mixed-method approach, as recommended (Lam & Fresco, 2015). However, none of these studies detected statistically significant effects. Crucial in detecting intervention effects is quality in study design. This may have affected outcome measures in the RCTs in this review, as all studies had issues regarding risk of bias. Consequently, results should be interpreted with caution.

Two previous systematic reviews have investigated nurse-led interventions on improving adherence, focusing on discharged older adults (Verloo et al., 2017), and long-term medications (Van Camp et al., 2013). The latter review identified ten studies published from 2006 to 2011, where five studies reported significant effects on short and/or long-term adherence to long-term medications. In contrast to our review, Van Camp and co-authors reported odds ratios and pooled mean differences in adherence between intervention and control arms, revealing that nurses can enhance adherence in this population. However, the generalizability is

limited, since seven of the ten studies involved only HIV-positive patients (Van Camp et al., 2013). Furthermore, the review states that nursing interventions for tackling non-adherence must be multifaceted and tailored, with continuous efforts and follow-up of patients (Van Camp et al., 2013), a conclusion that is supported by the results of this review. This review endorses these conclusions: to ensure the correct and safe use of medicines, several strategies – multifaceted and multitargeted – are needed (Cross et al., 2020; Jordan et al., 2021; Khalil et al., 2017; Ryan et al., 2014; World Health Organization (WHO), 2017).

Verloo and co-authors reviewed 14 studies published between 1989–2015 that included nurse-led (n = 7) or nurse-collaborative (n = 7) interventions. The population primarily consisted of discharged older inpatients with cardiovascular diseases (n = 8), and post-surgical patients from hospital geriatric and internal medicine units (n = 4) (Verloo et al., 2017). Hence, the patients and contexts differed from this review. In further contrast, Verloo et al. detected a relatively high proportion of interventions that significantly increased adherence (57.1%, 8 of 14 studies) (Verloo et al., 2017). In line with our results, Verloo et al. describes heterogeneity between studies regarding design and type of intervention, and relative low quality of evidence (Verloo et al., 2017). Low quality of evidence in studies investigating adherence interventions has been described previously in several reviews, due to heterogeneity and the methodological limitations of the studies (Conn & Ruppar, 2017; Cross et al., 2020; Sletvold et al., 2020).

The overall effect of nursing on health outcomes in the community is of interest, and this review found that nurses can play an important role in patients' clinical outcomes, particularly surrogate markers, such as BP. To make an impact on patient-focused outcomes of pharmacotherapy, increased engagement among healthcare professionals, including nurses, is necessary, and may be facilitated by nurse-led approaches (Jordan et al., 2021). An overview of research evidence by Coster et al., indicates moderate evidence for nurses being able to produce health outcomes that are equivalent to those of doctors, for patients with long-term conditions, particularly in primary care (Coster et al., 2018). Furthermore, a meta-analysis found that modest but significant improvements in patient-centered

outcomes (knowledge of medications, QoL, physical functioning and symptoms) followed adherence interventions (Conn et al., 2016). This review adds to this evidence: in some trials, nursing-led adherence interventions contributed to improvement in patients' BP, BMI, HbA1c, and cholesterol-levels, when compared with controls in the community. In two trials, adherence interventions in primary care reduced the demands on secondary healthcare (Chien et al., 2015; Liang et al., 2021). Both these interventions were high intensity. Further research might consider investigating if intensity of interventions is associated with effectiveness of outcomes.

Strengths and Limitations

The major strength of this review is the systematic approach in all parts of the study, from search strategy, study selection, results extraction, to assessment of quality. Furthermore, we included studies covering adult patients with a wide age range, a variety of health conditions, and studies were performed in diverse community settings. Both adherence and clinical outcomes are reported, which might enhance the transferability of findings.

The main limitation of this review is publication bias, since we did not search for grey literature or unpublished reports. Furthermore, the evidence is limited to articles published between 2011 and 2021 and includes only adults (≥18 years old). This review is solely based on the results presented in the published articles, hence there was no contact with corresponding authors to provide additional information that could have improved the result synthesis.

In the study selection process, the exclusion of irrelevant studies through perusal of the titles and abstracts was done by one researcher only, which may have resulted in missing studies. However, the reviewer has substantial experience in relevance screening for systematic reviews (three peer-reviewed systematic reviews published in scientific journals the last four years), which is suggested to be an acceptable approach (Waffenschmidt et al., 2019). Single researcher evaluation of study quality may pose a risk of misclassification, and is a study limitation.

The diverse nature of the studies precluded a numerical analysis, and studies are reported narratively. The time spent on these interventions was not costed, and no economic analysis could be attempted. No studies indicated whether any nursing tasks were delegated or omitted to allow nurses to complete these interventions. Given the global shortages in the nursing workforce, the impact of interventions on all aspects of nursing care warrants attention.

Conclusion

This systematic review provides updated and expanded knowledge on the impact of nurses on the correct use of medications among community-based patients. Low-quality evidence, as assessed in line with GRADE criteria (Schünemann, 2013), suggests that nurse-led interventions may improve medication adherence and clinical outcomes in community care. Interventions are typically multifaceted, targeting adherence through behavior and knowledge strategies, and nurses may play a significant role. However, to increase confidence in the effectiveness of these interventions, further high-quality studies reporting clinical outcomes and cost-effectiveness are needed.

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CHAPTER 9

Pharmacist Involvement in Optimizing Medication Use in Nursing Homes

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Abstract: Nursing home residents have many comorbidities, for which medication therapy is the treatment modality most utilized. The extensive use of medications among these residents is beneficial, but puts these individuals at high risk of experiencing adverse drug events. To optimize medication use in nursing home residents, we have witnessed an increased pharmacist involvement. This review presents how pharmacists can be involved in optimizing medication use among Norwegian nursing home residents. The review is based on a literature search (PubMed), knowledge of Norwegian nursing home studies involving pharmacists, and fifteen years of work experience. A conceptual framework guided the knowledge synthesis regarding the different work tasks identified at the individual, healthcare, and system level. Pharmacists contribute on different levels to ensure high-quality medication use in nursing homes, which means involvement in multidisciplinary teams to identify and solve medication-related problems. Collaboration with other healthcare professionals and teaching them about medication management are examples on the healthcare level. Involvement on the system level includes developing medication management procedures, providing medication statistics, investigating costs, and facilitating tender rounds. Studies investigating hard endpoints in nursing home residents were not identified. Although pharmacists as healthcare providers seem to be expanding their role, municipalities and the healthcare system seem to lack a strategy about how and where this resource can be used most effectively. Developing job descriptions for pharmacists, and preparing the healthcare setting and nursing homes for future challenges, should be prioritized.

Keywords: interventions, nursing homes, medications, pharmacists

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Nursing homes provide 24-hour care to older adults with an increased need for medical attention, treatment, and care. In Norway, there exist 39,241 nursing home places, 9,090 short-term places and 39,241 long-term places (Statistics Norway (SSB), 2021). Persons in nursing homes are often referred to as residents, and the nursing home is usually their final place of residency before death. Reports state that the treatment of nursing home residents has become more advanced during the past two decades, and residents now have an even broader range of diseases and symptoms (Abelsen et al., 2014). For most of these illnesses, medicines are the most important treatment modality. Thus, extensive medication use in this population is frequent and expected (Thomson et al., 2009).

Since the mid 1990s the number of medicines that residents receive, on average, has increased from three to eight (Halvorsen et al., 2017). In 2010, 89% of nursing home residents used five or more medicines, while 46% used 10 or more, showing that polypharmacy is highly present (Soraas et al., 2014). The presence of polypharmacy is indeed beneficial for the residents, but could also lead to substantial risks resulting in deteriorating health and shorter life expectancy.

The nursing home staff are responsible for initiating and monitoring adequate medical treatment for their residents. For decades staff members have normally consisted of nurses, auxiliary nurses, and part-time physicians. While these healthcare team members have provided optimal treatment and end-of-life care, they have also faced rapid changes regarding new disease management, and more advanced use of medicines. In addition, other healthcare professionals, such as physiotherapists and pharmacists, have expanded their roles and become more active in nursing homes.

Provision of optimal treatment and care requires that team members receive adequate training, and update themselves on new treatment strategies and guidelines. Moreover, quality enhancement and continuous improvement require the primary care sector to establish quality management systems. There is considerable variation in how municipalities organize healthcare teams to manage medications within the nursing home sector. Studies support the need to bring pharmacists into multidisciplinary teams (Halvorsen et al., 2010). However, only a few municipalities in Norway have employed pharmacists, and the inclusion of

non-dispensing pharmacists in multidisciplinary nursing home teams is still anecdotal. In contrast, many hospitals have included (clinical) pharmacists as trusted multidisciplinary collaborators, as they possess profound knowledge about medicines.

Due to comorbidities and extensive medication use, nursing home residents can experience several medication-related problems that may potentially reduce medication treatment quality. A few pharmacist-led interventions have been tested to improve medication use among these residents. However, pharmacists also contribute to patient safety in other areas. A recent narrative review by Spinewine et al. concluded that pharmacist interventions in nursing homes effectively optimize medication use (Spinewine et al., 2021). However, the same review pointed out a limitation in the current literature to identify the most effective components, or specific disease and drug classes. Implementation of pharmacist services in nursing homes could represent an opportunity (Spinewine et al., 2021). However, ensuring high-quality medication for these residents requires a multifaceted approach, and interventions should target diverse levels.

This chapter presents and discusses pharmacists' interventions aiming to optimize the quality of medication therapy for residents, based on studies from the Norwegian nursing home setting.

Method

This literature review provided an examination of published articles on Norwegian nursing homes, and a selection of recently published international articles, identifying the nature and extent of pharmacists' involvement with nursing home patients. The literature review method is appropriate because it allows consolidation and summation, it finds omissions or gaps in the literature, and it builds knowledge from previous work (Grant & Booth, 2009). The review was based on a search in PubMed, using both medical subject headings (MESH) and free-text search. The two MESH terms "pharmacist" and "nursing home" combined retrieved 222 results. These 222 results were filtered using "article type review", resulting in 16 papers. From these 16

papers, it was decided to include two recently published papers (Lee et al., 2019; Spinewine et al., 2021), since they mirror how pharmacists work in Norway. Subsequently, the free-text search using the terms "pharmacist", "nursing home" and "Norway" resulted in 17 studies. Of these 17 studies, 12 were included in the review, based on their relevance to the Norwegian setting and the author's knowledge from working for more than fifteen years with medication therapy in older nursing home residents, either as an advisor or clinical pharmacist.

The knowledge synthesis, describing where pharmacists can play an active role to optimize medication use in nursing home residents, was conducted by applying a conceptual framework (Institute of Medicine, 2005) of four (three, see Figure 1) different levels: A) the resident (patient) level; B) the care team level; C) the system (nursing home) level; and D) the environment level. However, the fourth level (D) was considered to be beyond the scope of this study.

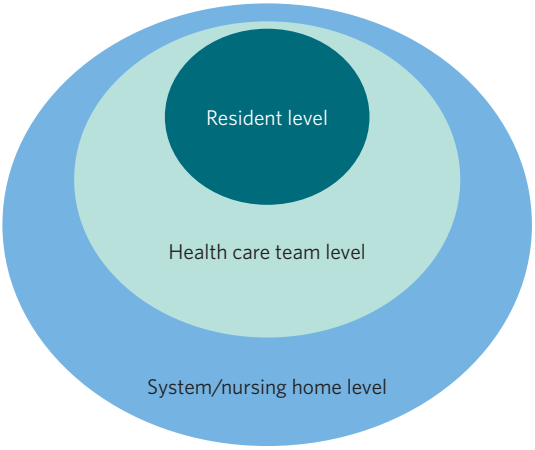

Figure 1. Framework Classifying Where the Pharmasist Could Play an Active Role to Ensure High-Quality Medication Use Among Nursing Home Residents

Results and Discussions

The results are based on 12 articles from the Norwegian nursing home setting, and two international articles mirroring how the author perceives how pharmacists work to improve the quality of medication

therapy in Norwegian nursing homes at the individual, healthcare and system level.

Individual Level

Pharmacist involvement in improving the quality of prescribing by performing medication reviews and assessing medication use among nursing home residents has been thoroughly studied. Since 2017, medication reviews on admission, and subsequently once yearly, have been required by law to achieve high-quality medication use among nursing home residents (Lovdata, 2021). However, a recent study concluded that only half of the residents received systematic medication reviews within the first month after admission, while 31% had not received this service within the first seven months (Hermann et al., 2021).

Medication reviews usually involve a four-step procedure including patient and medication history taking, systematic medication reviews, interdisciplinary case conference discussions, and pharmaceutical care planning (Halvorsen et al., 2019). While medication reviews result in a significant reduction in the number of medication-related problems, pooled estimates on hard endpoints, like falls, hospital admission and mortality, have been inconclusive, often explained by heterogeneity in studies. Nevertheless, physicians' acceptance rates of 70% regarding pharmacist recommendations show that pharmacists' medication reviews have a reasonable value in improving medication use among these residents.

Nursing home residents often have multiple chronic diseases and symptoms that fluctuate considerably. We have learned from medication review studies that overuse of inappropriate medication is prevalent among these residents. In addition, residents often receive too high doses, experience drug-drug interactions, and frequently use unnecessary medications. The unnecessary use of medications can be effectively reduced by deprescribing. Deprescribing constitutes safe reduction or removal of medications that are no longer indicated (Deprescribing.org, 2021). The concept of desprescribing has achieved growing interest, the goal of which is to reduce the medication burden or harm, and improve quality of life. Given the considerable number of unnecessary medications, making a

plan for deprescribing seems vital. Pharmacists often play an essential role in the process of identifying medications that could be deprescribed:

> I now see [the] drugs patients received all year through, for example one patient who received a drug for allergy. So this year [after the pharmacist visit] was the first year it was discontinued. And when I checked the medical records, it had been given each day for several years. (nurse, nursing home) (Halvorsen et al., 2011)

Individuals who move into nursing homes are also moving to their second to last, and last phase in life, that is the end of life. Although there is considerable variance, Norwegian nursing home residents on average live no longer than 24 months (Helsedirektoratet, 2017). The residents' short life expectancy questions the importance of continuing prophylactic therapy (e.g., use of statins or bisphosphonates). Moreover, indications for treatment are often no longer valid. Both scenarios should potentially encourage deprescribing. However, nursing home physicians who initiate deprescribing often find that residents or their next of kin feel that the healthcare system has given up on them. Thus, they become more reluctant to discontinue treatment. The feeling of standing alone when it comes to these decisions is indeed difficult. Through their own experiences, pharmacists see their involvement as helping to make such decisions, which thus helps to reduce the uncertainty of whether to discontinue treatment or not.

Healthcare Level

Due to age-related physiological changes and altered pharmacokinetics and dynamics in older adults, several medications are considered inappropriate for older nursing home residents. Since pharmacists are trained to assess the impact of such changes, scrutinizing medication charts by using explicit medicinal criteria has become more common. Although the Beers criteria (American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults, 2019; Meld. St. 28) and the START and STOPP criteria (O'Mahony et al., 2015) have been given most attention, the NORGEP-NH criteria

seem to be a more appropriate choice for Norwegian nursing home residents, especially as these validated criteria are based on nationally available medications (Nyborg et al., 2015). A few pharmacist-led studies have electronically identified the prevalence of inappropriate prescribing in nursing homes residents (Halvorsen et al., 2012) and older adults (Pagès et al., 2021). The findings of these studies are comparable to clinical studies, which also state that the use of inappropriate medications by these residents is highly prevalent. However, several of these studies have shortcomings, including lack of residents' clinical data and past medication history. Unfortunately, systematic use of these criteria in clinical practice is yet to come. Nevertheless, this method is regarded as beneficial in combination with medication reviews, since it systematically reminds pharmacists of medications representing potential risks for this population. Another possibility is that pharmacists use these screening tools to triage which residents should receive yearly medication reviews. In any case, identifying inappropriate prescribing is only a first step. The work of suggesting reasonable interventions that will ultimately result in improved quality of medication use remains to be done.

Performing explicit medication reviews and using information from criteria lists (i.e., medicines considered inappropriate for the elderly) have reduced inappropriate prescribing among these patients. Moreover, the drug-related problem framework established by the Pharmaceutical Care Network Europe has provided a rigorous structure to discuss suboptimal medication therapy (Pharmaceutical Care Network Europe (PCNE, 2021). The framework has been beneficial for many clinical pharmacists in promoting interdisciplinary collaboration with physicians and nurses, as it focuses on the residents' therapeutic problem instead of blaming the prescriber for misprescribing, or the nurses for mismanagement of medications.

The deliverance of high-quality medication services assumes that healthcare personnel have the right competence and training. The coordination reform of 2012 aims to encourage municipalities to take responsibility for their citizens, including nursing home residents. One of the objectives was to transfer tasks from hospitals to the primary care setting, such as home care services and nursing homes. In Norway, nursing

homes rely heavily on auxiliary nurses to care for their residents, but these healthcare professionals have minimum training in handling medication. Thus, to establish knowledge, skills and competence to administer medications to nursing home residents, they receive training from pharmacists. Staff education and supervision of students are essential aspects of pharmacists' contributions to ensure high-quality use of medicines (Lee et al., 2019). The result of this training is that auxiliary nurses can perform medication management and deliver medications to several thousand nursing home residents and receivers of homecare services daily.

System Level

Pharmacists must conduct clinical patient-centred work and gain experience to maintain patient safety for nursing homes residents. However, it is equally important to use this experience to develop high-quality medication management procedures. In nursing homes, pharmacists often develop and critically review medication management procedures. These procedures describe how medicines should be prescribed, dispensed, reviewed, and administered to residents. The importance of well-functioning procedures provides a safe working environment for healthcare workers, and preserves a positive experience for residents (Lee et al., 2019; Services & Conolly, 2016). Another essential task is to keep track of medication use both individually and overall. Pharmacists have a crucial role in monitoring overall medication use for these residents, delivering statistical analyses of differences in use and costs between nursing homes. Moreover, they should keep up with new treatment strategies and facilitate evidence-based practice by discussing new treatment alternatives within elderly care. This will ensure choosing the most appropriate medication therapy, providing the most value for money and minimising risk for residents.

At some nursing homes, nurses have the opportunity to administer medicines from a pre-approved medication list, so-called "as needed" medications. These medication lists include information about medications that nurses can administer to residents without first consulting

the physician, as a response to an acute change in diseases or symptoms. Pharmacists working at the municipality level, have closely collaborated with nursing home physicians and nurses to develop these lists, including medications for pain management, constipation and nausea. Although it is preferred to prescribe these medications to residents directly and keep use of such lists to a minimum, the situation with few doctors, especially in remote areas, could force municipalities to rethink how such lists could improve the quality of care for their residents.

Pharmacists' five years of university training provides them with profound knowledge on the use of medicines and especially drug-drug interactions. Pharmacists' involvement in developing databases that warn about dangerous medication combinations have minimized harmful drug-drug interactions. A study from 2010, using the Norwegian drug-drug interaction database, included 1,241 nursing home residents, and identified only 1.2% severe drug-drug interactions. At a glimpse, the identified prevalence seems relatively low, but medication combinations like these should be totally avoided, especially in frail old nursing home residents. Otherwise, the consequence could be fatal clinical outcomes.

Moreover, these databases rely on input from qualified personnel and seldom take into account pharmacodynamic interactions or changes in residents' pharmacokinetic parameters (absorption, first-pass metabolism, bioavailability, distribution, protein building, renal and hepatic clearance). In addition, they fail to identify planned beneficial synergistic effects of known drug-drug interactions. However, timely conducted analyses of drug-drug interactions and screening for inappropriate medications, can improve the quality of medication use in these residents.

This chapter has so far described different pharmacists' interventions with the potential to optimize the quality of medication therapy for residents in nursing homes at the individual, healthcare, and system level. A systematic review and meta-analysis by Lee et al. summarize outcomes of pharmacist-led nursing home studies performed on different levels. Outcomes include: the number of fallers; fall rates; mortality; hospital use and admission; quality of medication prescribing in terms of medication appropriateness and total medication use by residents; cost analysis;

adverse events; physicians' acceptance rates of pharmacotherapy recommendations; and others (i.e., quality of life, activity of daily living, mental health and depression). The pooled analysis demonstrated that pharmacists' services improved fall rates, and found a trend towards reduced mortality rates, hospitalization and admission rates.

In contrast, few Norwegian nursing home studies have investigated similar outcomes, except for residents' total medication use (Fog et al., 2017) and physicians' acceptance rates (Halvorsen et al., 2010). Instead, the vast majority of studies involving pharmacists have focused on increasing the quality of prescribing by identifying medication-related problems on the individual level (Bakken et al., 2012; Davidsson et al., 2011; Devik et al., 2018; Fog et al., 2017). These studies combined reveal a considerable number of medication-related problems in this population. However, as none of these studies have investigated hard endpoints, like mortality, falls, or quality of life, allocating funds to employ clinical pharmacists in nursing homes has so far not been prioritized by the municipalities. Instead, municipalities have been increasingly interested in employing pharmacists on the system level. A report from 2019, based on interviews with pharmacists, states that the first pharmacist was employed on the municipality level in 2009 (Toverud & Håkonsen, 2019). Today, around ten highly-populated municipalities have employed pharmacists. The pharmacists perform quite diverse tasks within these municipalities, from patient-oriented tasks on the home service/nursing home level, to administrative tasks on the system level. The pharmacists who hold these positions consider themselves pharmaceutical advisors for the municipality, but they also emphasize the importance of their presence at larger nursing homes. Pharmacists reported collaborating on different levels, most extensively with nurses, followed by physicians. In contrast, collaboration with other pharmacists was almost non-existent (Toverud & Håkonsen, 2019).

This literature review has limitations, as only one bibliometric database was searched, and only one author reviewed the selection of articles. Furthermore, the known weaknesses of the applied method include the absence of intent to maximize the scope of the literature review, and the possibility of bias due to the selection process of articles with the potential

of omitting relevant literature (Grant & Booth, 2009). Another limitation is that the review did not use a formal quality assessment template. Knowledge of how pharmacists work with optimizing medication use in nursing home residents is seldom published in research papers or reports. Therefore, pharmacists might be doing work to optimize medication use in nursing home residents, which this review could have missed.

Conclusion

Pharmacists contribute on different levels to optimize medication use in nursing home residents. Although pharmacists, as healthcare providers, seem to be expanding their role, municipalities and the healthcare system seem to lack a strategy in terms of how this resource can be used most effectively. Developing job descriptions for pharmacists, which prepare the primary healthcare setting and nursing homes for future challenges should be prioritized.

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CHAPTER 10

Patient-Centered Communication and Counseling to Ensure Patient Safety Through Correct Use of Medicines: Experiences and Challenges

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Abstract: In this chapter we discuss experiences and challenges regarding patient safety and correct use of medicines. Patient-centered communication and counseling are essential in order to achieve this. Incorrect use of medicines endangers patient safety, and can lead to medication-related problems, which again may have serious consequences for both the patient and society. Some of the most prominent pharmaceutical factors compromising patient safety are: communication challenges, language barriers, variety in health literacy, and self-care without guidance from a healthcare provider. The common theme for most barriers connected to incorrect use of medicines seems to be communication. It is therefore essential for healthcare providers to have good communication skills and be able to provide patient-centered communication and counseling of high quality. This may be the path

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towards optimizing use of medicines and ensuring patient safety. To improve patient-centered communication and counseling, teaching communication, as well as training courses, should be included in the curricula for healthcare providers, in addition to postgraduate training.

Keywords: patient safety, correct use of medicines, communication, counseling, pharmacy

Patient safety is fundamental to delivering quality essential health services. WHO's work on patient safety was launched in 2004 by the World Alliance for Patient Safety. The work has evolved since then. One example is strategic guidance and leadership to countries through the annual Global Ministerial Summit on Patient Safety, which aims to advance a patient safety agenda on the political leadership level, with the support of health ministers, high-level delegates, experts, and representatives from international organizations (WHO, 2019).

Incorrect use of medicines is a serious problem, which not only affects the patient but also the healthcare system as a whole. Medication errors, defined as "failure in the treatment process that leads to, or has the potential to lead to, harm to the patient", are expensive and cause unnecessary suffering among patients (Aronson, 2009). Medication errors are a leading cause of injury and avoidable harm in healthcare systems: globally, the cost associated with medication errors has been estimated at US$ 42 billion annually (Aitken et al., 2012). It can lead to medication-related problems, which may have serious consequences for individual patients. The occurrence of adverse events due to unsafe care is likely one of the 10 leading causes of death and disability in the world (JHA, 2018).

Reducing the risk of this is crucial and can be achieved through high quality patient-centered communication and counseling (Ryan et al., 2014). For successful implementation of patient safety strategies, like ensuring correct use of medicines, it is important to have clear policies, skilled healthcare professionals, and effective involvement of patients in their own care. Thus, quality health services should be effective, safe, and patient-centered.

What is the situation in Norway? In 2020, 69% of all Norwegians collected a prescription medicine from a pharmacy (Norwegian Institute of Public Health, FHI, 2021a). In addition, people use over the counter

medicines (OTC), herbs, vitamins, and minerals. There is also medication use in hospitals and nursing homes.

Only 20%–30% of medicines are taken as recommended. Although the research criteria may vary, there have been reports of incorrect prescriptions in 10%–25% of all cases. The previous medicinal product policy report indicated that 5%–10% of all acute internal medicine hospitalizations were the result of an incorrect use of medicines, and that about half of these hospitalizations might have been avoided (Department of Health and Care Services, HOD, 2015). In a study from Bergen, it was found that patients in nursing homes had an average of 5.5 medication-related problems caused by the use of on average 11.5 different medicines. A third of the medication-related problems were caused by unnecessary use of medicines (Halvorsen et al., 2010). One multicenter study of hospitals in Norway showed that more than 80% of patients had an average of 2.1 relevant medicine-related problems (Blix et al., 2004). The risk of medication-related problems increases with an increasing number of medicines. Many elderly patients have several illnesses and use many necessary medicines simultaneously. However, the literature also demonstrates that many patients use unnecessary medications, which also increases the risk of medication-related problems (Blix et al., 2004; Halvorsen et al., 2010; Viktil et al., 2006). This is especially unfortunate among older patients, who are particularly vulnerable to adverse reactions and other medicine-related problems (HOD, 2015).

The aim of the present study is to focus on the importance of communication and counseling to ensure patient safety in general, with examples from pharmacies regarding the correct use of medicines. We will identify challenges and describe the present situation based upon findings from the literature. Furthermore, we will discuss and conclude as to future approaches to what may be done, based on our experience and multiprofessional opinions.

Method

This study is based on the authors' experiences from their practice in pharmacies and the specialist healthcare services from the past several years to the present. A literature review was performed according to

Grant and Booth (2009). The authors' experiences have been valuable for recognizing the challenges in this area, and also for selecting keywords for the literature searches, which were not exhaustive but filtered through the following criteria. Articles from the last 15 years, with an emphasis on the last five years, have been included. Articles in English, published in international peer-reviewed journals, were chosen. Among the selection criteria, we included the following search terms: patient safety, communication, pharmacy, hospital pharmacy, health literacy, OTC. The literature search was performed from July to November 2021, including open searches on Google and Google Scholar, and more specific searches in Pubmed. We also included articles from the authors' own archives related to the topic. Articles written in Norwegian, or from non peer-reviewed journals, or older published studies were excluded.

The included articles covered the main experiences and challenges, relevant to patient-centered communication and counseling, defined by the authors. To describe Norwegian conditions primarily, it was necessary to include reports and documents from the authorities. A total of 57 studies were included.

Results and Discussion

Communication

The included studies show that many of the challenges presented in the introduction can be avoided if the communication, or more precisely counseling, is more focused. Counseling is, in Brown et al. (2016), defined as an "individualized process involving guidance and collaborative problem solving to help the patient better manage their health problems" (Brown et al., 2016).

Communicate originates from *communicare*, which is latin and means "to share". Interpersonal health communication deals with imbalanced and complex power positions between the patient and healthcare personnel. In past times, this relationship, especially the doctor-patient relationship, was authoritarian and often about biomedical issues. Now, communication is more individualized and focused on each patient (Higgs et al., 2014).

The communication process between a patient and a provider is well illustrated in Figure 1 in Fieldman-Steward et al. (2005).

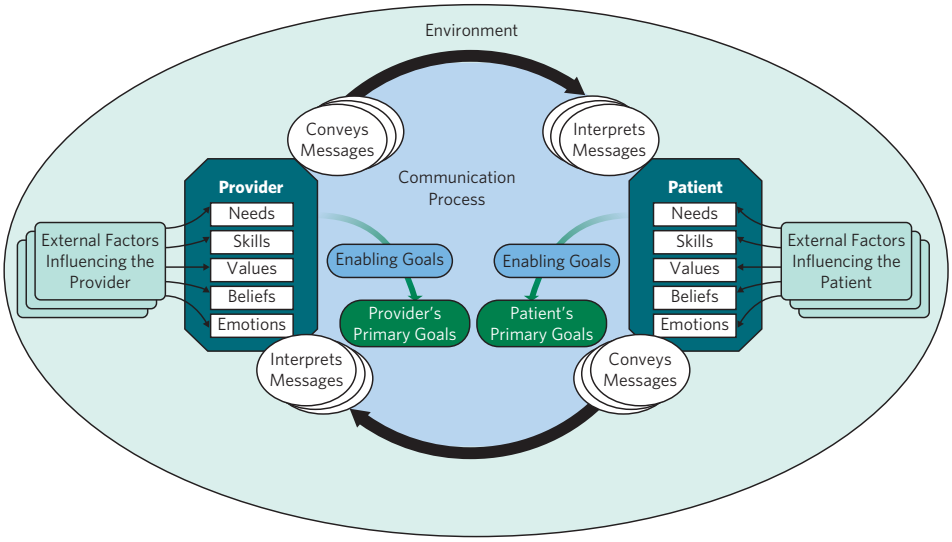

Figure 1. The communication process model of Fieldman-Steward et al. (2005, Figure 1)

This model focuses on the individual's goals in the communication and discussion process, and describes which factors are important for how the communication process proceeds (Feldman-Stewart et al., 2005). The framework includes four key components, with a focus on elements that can be modified. The first component is the focus of the interaction: each participant's communication goals. The second component consists of the participants themselves: each with five key attributes that determine, in part, how they address their goals. The third component is the communication process: each person both conveys and receives messages, and the messages themselves can be verbal, non-verbal, or silent. The communication process is iterative and extended in time, with one act having an impact on following acts. Finally, the fourth component is the environment in which the communication occurs, both the immediate physical setting and the context beyond. Important aspects of the environment, identified as external factors, affect the communication process through their impact on the participants' attributes. The framework builds on classic communication frameworks to which it adds unique elements. Some of these unique elements include the prominent role of the participants' goals and the distinct recognition that messages are conveyed through silence.

There are many models for assessing patient/healthcare provider interaction. One of them is the four habits model (FHM) (Frankel & Stein, 2001; Stein et al., 2005). This model is a relationship-centered framework for assessing healthcare provider communication skills with patients during medical interviews and encounters. The key concept in this model is: Patients don't care how much you know until they know how much you care. The four habits of clinical communication are: 1) invest in the beginning; 2) elicit the patient's perspective; 3) demonstrate empathy; and 4) invest in the end. The goals of the FHM are to: 1) establish rapport and build trust rapidly; 2) facilitate the effective exchange of information; 3) demonstrate care and concern; and 4) increase the likelihood of adherence and positive health outcomes (Frankel & Stein, 2001; Stein et al., 2005).

Communication Challenges

Healthcare professionals usually communicate with patients orally or through written information. There are, however, several challenges connected to both oral and written (health) communication.

The literacy rate in Norway is 100% (Burton, 2020), but to be able to read and write does not necessarily mean that one is capable of understanding written or oral health information. Being able to perform self-care requires a certain level of personal health literacy.

Personal Health Literacy

Personal health literacy is defined as "the degree to which individuals have the ability to find, understand, and use information and services to inform health-related decisions and actions for themselves and others" (CDC, 2021). This kind of literacy also includes the ability to understand and follow advice given by healthcare professionals.

From 2019 to 2021 a survey was conducted to assess health literacy in the Norwegian population. The results showed that a significant proportion of the population face a variety of challenges in dealing with health information (Le et al., 2021a). People on levels 2 and 3 are presumed to

possess sufficient health literacy based on the concept of "the patient's health service", a policy introduced by the government in 2014 in order to give patients more choices, and thus influence in their health questions (HOD, 2014). Thus, users of the health service must possess the knowledge and skills to "make choices" and "actively take part in decisions" concerning their own health (Le et al., 2021a). People on level 1 are not presumed to possess sufficient health literacy for the Norwegian patient's health service. Of the study population, 20% were on the highest level (level 3), 46% were on level 2, and as many as 34% were on level 1 (Le et al., 2021a).

Language

In 2021, immigrants constituted 18.5% of the population in Norway (SSB, 2021). Public information about healthcare services is available mostly in Norwegian, sometimes English, but rarely in any other language. In addition to a foreign language, most immigrants encounter a different culture, and a different kind of "health language" – making communication more challenging. Even for native Norwegians, healthcare professionals' "health language" can be challenging to understand.

A scoping review published in 2018 (Yeheskel & Rawal, 2019) mapped out the literature on the *patient* experience of individuals with limited English proficiency. Sixty qualitative and mixed-method studies published between 2007 and 2017 revealed four major themes: (1) communication, language barriers, and health literacy; (2) relationships with healthcare professionals; (3) discrimination and intersection with other dimensions of identity; and (4) cultural safety. To overcome language barriers the literature says that patients preferred language-concordant healthcare professionals or the use of interpreters. Failing this, patients resorted to using nonverbal communication to express themselves. In addition, language barriers left some patients feeling vulnerable, disempowered, and frustrated in the healthcare setting.

Digital Health Literacy

An increasingly important public website is helsenorge.no, where quality-assured information about medical self-care is to be found – that is if one knows how and what to search for.

Digital health literacy can be expressed through:

- Competence in searching for digital health information
- Possession of general digital skills
- Readiness to adopt digital healthcare services

The health literacy survey found that women claimed to have a higher skill level than men in searching for digital health information, and those with an education above upper secondary school claimed to have a higher skill level than those with less education. Furthermore, the group over 65 years of age self-reported a lower skill level than other groups (Le et al., 2021a).

We can therefore conclude that, when it comes to medical self-care, the possession of general digital skills and competence in searching for digital health information is much needed.

Understanding Written Information

As stated earlier, OTC packaging is supposed to contain enough written information for the general public to be able to know how to use the medicine. However, not every patient reads the patient information leaflets (PILs) and the safety information. In addition, PILs are still difficult for many non-professionals to understand (From, 2013). A Danish study from 2013 on prescription medications showed that 70% of patients always read the PILs. Patients were mostly interested in reading about the side effects of drugs (77%), effects, use and storage (50% – 30%). But as many as 38% of patients had problems reading and understanding the text (Horwitz et al., 2009). A small Norwegian study from 2011 on the use of OTC painkillers showed that older people wanted to read the PILs but had difficulties doing so due to the font size, and that younger people didn't read the

PILs because they thought the information was not relevant (Halvorsen, 2011). OTC painkillers in Norway are equal to the ones sold by prescription, but in smaller packages. However, many believed that the OTCs are less "dangerous" than the prescribed ones especially since they are also available outside pharmacies (Halvorsen, 2011).

Patients' Ability to Communicate with Healthcare Professionals

The health literacy survey from 2019–2020 (Le et al., 2021a) looked into Norwegian patients' ability to communicate with healthcare professionals – meaning being able to actively engage in a dialogue with healthcare professionals in order to make good decisions concerning health. Only 12% appear to experience challenges. However, the results indicated that:

- Those with a long-term illness claimed to have weaker skills than others
- Those with an education above upper secondary level claimed to have higher skills than those with less education
- Some people in the 18–24 age group may face challenges when interacting with healthcare professionals

The earlier mentioned health literacy survey also investigated health literacy in five immigrant populations in Norway. This study demonstrated that a larger proportion of immigrants are at lower levels of health literacy compared to the general population. (Le et al., 2021b).

Based on the studies and our (the authors') experiences communicating with foreign-language patients, we conclude that healthcare professionals must speak clearly, use the right words, and maybe use other tools, such as visual information.

Some studies have been performed regarding pharmacists communicating with foreign-language patients, and they show that language and cultural barriers may affect pharmaceutical service and patient-centered communication (Chang et al., 2011; Cleland et al., 2011;

Håkonsen et al., 2014; Schwappach et al., 2012). A qualitative face-to-face study involving Scottish pharmacists revealed a number of barriers to providing optimal care to migrants from central/eastern European states, such as: communication (information gathering and giving); confidentiality when using family/friends as translators; the impact of patient healthcare expectations on communication and length of the consultation; and frustration with the process of the consultation. Several barriers were specific to the migrants from these countries, but most of the barriers seemed pertinent to any group with limited English proficiency (Cleland et al., 2011).

A Norwegian focus group study consisting of ethnic Norwegian community pharmacists providing pharmaceutical care, who were in daily contact with non-Western immigrants, showed that language and cultural barriers, like body language and clothing, affected how much effort was exerted in order to provide this service, although the pharmacists knew that the patients needed drug counseling. They were all uncomfortable with situations where family or friends acted as interpreters, especially children (Håkonsen et al., 2014).

A Norwegian study published in 2021 investigated experiences and perceptions of Arabic and Kurdish people living in Norway, in terms of the medication information they received in the pharmacy. Overall, they were satisfied with the pharmacy service. However, their preferences in relation to medication information were not met. They had several suggestions for communication facilitators that could expedite medication information: simplified prescription labels, written information, pictograms, mobile phone apps, interpreters, and bilingual staff (Sletvold & Nguyen, 2021).

The results from the above-mentioned studies may be transferred to everyday life and meetings between patients and other healthcare professionals. Thus, as a healthcare professional it is important to realize that oral information is not necessarily the best way for all patients to receive information or knowledge. This information is often given to the patient in a stressful situation, and it is therefore of particular importance that it can be repeated or read later on by the patients themselves or their relatives or caregivers.

Ensuring Patient Safety After Discharge From Hospital: Experiences From Specialist Healthcare

At discharge from hospital, insufficient transfer of medication information is a common challenge (Cochrane et al., 1992; Coleman, 2003; Glintborg et al., 2007; Kripalani et al., 2007). After discharge, home-dwelling patients are expected to manage their medicines themselves, and adequate counseling is important for self-efficacy in relation to medication management (Náfrádi et al., 2017). In a study performed in Australia, pharmacists and patients were asked what made the pharmacist–patient conversations effective. The overarching theme or shared goal resonating from the participants' interviews was that patients need to be confident in managing their medications at home. To facilitate this, patients focused mainly on pharmacists' delivery of medication information and interpersonal behavior. For the pharmacists, building rapport was important, but they also emphasized patients' understanding of their medications, and their level of engagement, as indicators of patients' confidence in self-managing their therapy (Chevalier et al., 2018).

A Norwegian study from 2017 looked into patients' needs for medication information after discharge from hospital, including the patients' perception and appraisal of the information they received at discharge. The results from interviewing 12 patients showed that information should focus on empowering the patients throughout the hospital stay, and not only at discharge. The informants used various strategies for coping with their use of medicines, influencing their self-efficacy in relation to medicine management. They gained information in several ways: by receiving information from healthcare professionals, through observation, and by seeking it themselves. Some thought they could have been better informed about adverse reactions and how to manage life as a user of medicines. Others felt they did not want or need more information (Svensberg et al., 2021). This is also shown in other studies (Borgsteede et al., 2011; Kusch et al., 2018).

The National Center for Epilepsy, Oslo University Hospital, serves the most refractory patients with epilepsy from the whole country. Over

the years, different approaches to improving patient-centered communication have been utilized. As part of the service, a close follow-up of pharmacological treatment is a cornerstone. Therapeutic drug monitoring of all antiseizure medications is a tool to optimize treatment for the individual patient (Johannessen Landmark, Fløgstad, Baftiu, et al., 2019; Johannessen Landmark et al., 2020). It relies on close collaboration between the clinicians, nurses and pharmacists at the hospital, and pharmacologists at the laboratory for clinical pharmacology. The use of therapeutic drug monitoring in a clinical setting serves as a tool for improved understanding of drug exposure, and factors contributing to variability between and within patients: adherence, withdrawal, and interactions (Johannessen Landmark, Fløgstad, Syvertsen, et al., 2019; Syvertsen et al., 2019). This tool has also been used in direct communication with patients and their treating clinicians for improved health literacy and understanding of the importance of routines for drug intake and possible consequences (Johannessen Landmark, Fløgstad, Baftiu, et al., 2019).

Some years ago, a multi-professional pharmacology team was established, with the primary aim of optimal treatment with antiseizure medications for the individual patient: education of colleagues; information to patients and relatives; focusing on patient safety issues. Another practical task has been the participation of a pharmacist, attending the out-patient clinic along with the neurologist, for improved communication about medications. Furthermore, a digital e-learning course on the use of antiseizure medications, and written information on the website of all the different drugs available, have been developed and implemented. These are among the most popular sites within Oslo University Hospital.

In several studies the patients' perspectives on challenges in epilepsy and their treatment were elucidated. Patients were interviewed with a focus on their perspective regarding adverse effects and adherence to medications, first as a project in clinical pharmacy (Mevaag et al., 2017), then as a larger-scale questionnaire (Henning, Johannessen Landmark, et al., 2019; Henning, Lossius, et al., 2019). Finally, the questionnaires were utilized in routine screening for adverse effects, adherence issues and other factors related to living with epilepsy.

These studies demonstrate that, through various interventions and focusing on different aspects of the treatment of refractory epilepsy, a patient-centered emphasis as well as a multi-disciplinary approach will hopefully continue to achieve improved treatment and care of this vulnerable patient group.

Ensuring Patient Safety at Community Pharmacies: Experiences of Communication About Prescribed Medicines

In general, Norwegian pharmacies have a monopoly on distributing prescription medicines to the public. Even though community pharmacies are private, they are part of the Norwegian healthcare system, and cooperate with other healthcare personnel to ensure patient safety and the correct use of medicines, and to help patients take care of their own health. The three main goals are to:

- Ensure that patients receive medicines of high quality in the correct form, dosage, and quantum
- Ensure that medicines are available throughout the whole country
- Ensure that patients receive high quality information and guidance that ensures correct use of medicines

In the report to Stortinget (Norwegian Parliament) No. 28 (2014–2015) (HOD, 2015) *White paper on medicines correct use – better health*, it is stated that pharmacies have an important role in providing advice on the correct use of medicines. The pharmacy is a low-threshold healthcare service. Pharmacists or pharmacy technicians provide advice on how to use prescription or OTC medicines. The quality of the counseling is of great importance to safeguard patient safety. Thus, being up-to-date and having good communication skills are of great importance to ensure the correct use of medicines and thus, ensure patient safety.

Since 2000, the number of pharmacies has more than doubled, they have longer opening hours, and sell a wider range of health-related products. The general public also seek advice for treating a range of minor illnesses.

The law specifies requirements as to how the pharmacy should be designed. A number of pharmacies are small, which is challenging when personal conversations take place between staff and customers seeking advice. Discretion and lack of privacy is a challenge when delivering professional pharmacy services, especially regarding elderly patients (Mamen et al., 2015). Studies from Australia and Denmark have revealed that a lack of discretion is one of the main reasons that pharmacists do not offer these services and patients do not receive them (Latif et al., 2013; Patwardhan & Chewning, 2009). Our experiences indicate a need to improve these factors. It is important to examine the culture of the pharmacy and the pharmacy manager's interest in communication. Studies have revealed that this may explain the variation among pharmacies in terms of their degree of communication (Kaae et al., 2014).

Employees in pharmacies are authorized as healthcare personnel: pharmacists (holding a bachelor's or master's degree in pharmacy), and pharmacy technicians (three-year high school specialty). They have combined theoretical and practical training on how to advise customers on when and how to handle minor ailments, and can adjust their advice to each particular customer based on symptoms, age, gender, and health condition.

Patient counseling is important on all levels of the healthcare services, and this requires good communication skills. What kind of communication skills are important in patient counseling? Several researchers have looked into this and found that they can be divided into content skills, process skills, and perceptual skills. All are important. Table 1 exemplifies

Table 1. Communication Skills for the Role of the Pharmacist (Hargie et al., 2000; Hyvärinen et al., 2010)

Various forms of skills	Details
Content skills	Discussion of the name and indication of the medicine, explaining the dosage, if forgetting a dose, what will happen, when will the effect appear, discussion of side-effects, exploring the patients' beliefs about medicines
Process skills	Building rapport, explaining, questioning, active listening, nonverbal communication, advising, opening, closing, assertiveness, disclosing personal information, persuading, emphatic responding
Perceptual skills	Pharmacists' belief about the patient and the illness, clinical and professional judgement decisions, awareness of professional confidence, and external distractions

the skills for the pharmacist role within each of these three categories (Hargie et al., 2000; Hyvärinen et al., 2010).

As mentioned before, information on the patient's medicines is of great importance to patient safety. Because pharmacists possess extensive knowledge about medicines (administration, dosage, effects, side-effects, storage, interactions, and important factors for correct use), the pharmacist is in a position to play an important role in patient counseling (Hämmerlein et al., 2007). In addition to being a medicine expert, the pharmacists see patients with a chronic disease probably more often than their physician does. These patients often see their physician just once a year, while the pharmacist meets the patient at least four times a year, when they pick up their prescribed medicines.

However, from our own experiences, we believe that pharmacists, as well as other healthcare personnel, should be more conscious of and focus on dialogic patient-centered communication. Several studies have examined this issue. A review of counseling practices, in relation to prescription medicines in community pharmacies, revealed a variation in counseling rates from 8% to 100%, depending on the research methods used. The type of prescription also influenced the rate. Higher rates were found in counseling consumers with new compared to regular prescriptions. Information on directions for use, dosage, medicine name, and indications was given more frequently than information on side effects, precautions, interactions, contraindications, and storage (Puspitasari et al., 2009). A newer study from the Netherlands described the information exchanged between pharmacy staff and patients on prescribed medication at the community pharmacy counter. When dispensing first prescriptions, pharmacy staff provided most information on instructions of how to use the medication (83.3%), the form of the medication (71.4%), and treatment duration (42.9%). Topics for repeat prescriptions (such as the effects of the medication and the incidence of observed adverse effects) were rarely discussed. Pharmacy staff rarely encouraged patients to ask questions. In only 10% of the new prescriptions and in 5% of the repeat prescriptions did the pharmacist try to involve the patient (van Dijk et al., 2016). A Norwegian study among elderly patients showed that the general practitioner (GP) was the main

source of drug information. As many as 50% of them were not informed about the medicines when picking them up at the pharmacy. However, 56% wanted to know more about their medications (Mamen et al., 2015). In a Danish observation study, 26% of the encounters had no communication about medicines (Kaae et al., 2013). The aim of a Swedish study was to determine the content and time disposition of patient–pharmacist communication during the dispensing of prescribed medicines. They found that 11 seconds (median) was spent on medical issues like user instructions, 72 seconds (median) on non-medical issues like availability of the medicine, and 88 seconds was spent in silence (Olsson et al., 2014).

Some studies have revealed that pharmacists use patient-centered communication to a low degree, for example low patient involvement, and low exploration of the patients' needs (Greenhill et al., 2011; Kaae et al., 2012; Latif et al., 2011). One review has shown that a patient-centered focus was found in eight of 32 studies (Murad et al., 2014). Some of these studies indicate that the pharmacists forget or do not think, to explore the patients' needs, understanding and knowledge of their medicines, while another review reveals patient-centered focus in several studies. For patient safety reasons, it is important to inform patients about administration, side-effects, interactions, and important factors for correct use. However, just as important is motivating the patients to adhere to their medicines to promote good health. Thus, the patient's preferences have to be explored, in order to provide the patient with medical information to help them make the right decisions. Patients have to be honest about their needs and concerns. A patient-centered encounter contributes to the patients' trust in healthcare personnel, not only the pharmacy personnel, which in turn will increase adherence and patient safety.

To improve patient-healthcare personnel communication, teaching and training is of great importance. A study performed with hospital doctors demonstrated that a 20 hour course using the four habits model showed an improvement in communication skills among these doctors (Fossli Jensen et al., 2010). A review from 2021 has also looked into how pharmacists can develop patient-pharmacist communication skills (Kerr

et al., 2021). They conclude that educational interventions that promote reflection are particularly useful.

Ensuring Patient Safety for Self-Caring Patients

WHO defines self-care as "the ability of individuals, families, and communities to promote health, prevent disease, maintain health, and to cope with illness and disability with or without the support of a healthcare provider" (WHO, 2021).

There is a growing global trend for consumers to self-medicate with non-prescription medications, also called over the counter (OTC) medications, for common ailments (Benrimoj et al., 2008). Shifts in consumer preferences towards self-care and self-responsibility for health (Benrimoj et al., 2008), and the emerging trend towards "down-scheduling" of prescription medicines to non-prescription status (Global Self-Care Federation, 2004) are two factors associated with this development. Community pharmacists are the most accessible healthcare professionals to the public, and their competence is important to ensure the correct use of OTC.

When a member of the general public experiences symptoms of disease or illness, their response on how to treat the symptoms is often based on personal experience and advice from family or friends. A very common source of advice is to seek information on the internet, in these days referred to as "Dr. Google" or on the vast variety of public and private websites with health information. Depending on the severity of the symptoms, people also seek help at the emergency ward, or from a family doctor, or, if the symptoms are minor, they treat the symptoms through self-care or seeking advice at a community pharmacy.

Risks Associated With the Top Selling OTCs

Total OTC sales in 2020 were ca. NOK 3.5 billion (FHI, 2021b), and the leading indications were pain, fever and common cold. Use of nasal spray to treat nasal congestion has been rising steadily, and two thirds are sold

outside pharmacies (FHI, 2020). The number of people addicted to these types of nasal spray is, according to otolaryngologists, increasing (Hauge & Nordahl, 2019), and many healthcare professionals support restrictions to availability. It is hard to communicate information about safety concerns, and that continuous use beyond the recommended maximum 10 days leads to addiction and a constantly blocked nose.

Sales of paracetamol are second on the OTC list. A Norwegian study showed that 30% of female and 13% of male adolescents aged 13–19 use OTC analgesics weekly (Jonassen et al., 2021). Daily use of paracetamol, even in small doses, can give rebound headaches (Fischer & Jan, 2021). There has also been an increase in paracetamol intoxication, especially among young females (Soldal, 2017). In Sweden, non-prescription paracetamol tablets are, since 2015, no longer sold outside pharmacies due to the high increase in paracetamol intoxications (Sandstedt, 2015).

Remedies for smoking cessation (nicotine replacement therapy, NRT) are also high on the OTC sales list. The percentage of daily smokers in Norway has, however, decreased considerably from over 40% in the 1970s to 12% in 2016 (WHO, 2020). For some people, addiction to nicotine in cigarettes has been replaced by NRT addiction (Borup et al., 2015).

Supplements and Herbal Remedies in Self-Care

Many people use supplements and/or herbal remedies, instead of, or in addition to medicines as self-care. A Norwegian study from 2013 showed that among the 381 patients who participated, 44% used herbs (e.g., blueberry, green tea, garlic, aloe vera, echinacea) and among those using conventional drugs regularly, 45% used herbs concomitantly (Djuv et al., 2013).

It is a safety concern that herbal remedies often lack documentation of quality, efficacy, and safety, for example drug interactions. However, some interactions are known, for example NOMA recommends patients to refrain from herbal remedies containing ginkgo-biloba, ginseng, ginger and St. John's wart one to two weeks before surgery, as these could have an effect on bleeding during an operation (SLV, 2016).

Norwegian Governmental Strategies on Self-Care

The Principle of LEON

Since the 1970s, the principle of LEON has been the gold standard in the Norwegian healthcare system (Helsedirektoratet, 2016). The principle was introduced by the World Health Organization (Helsedirektoratet, 2010), and LEON (in Norwegian: Laveste Effektive OmsorgsNivå) means that patients with medical complaints are to be treated at the lowest care level possible.

Minor ailments are generally defined as medical conditions that can be reasonably self-diagnosed and self-managed with such things as over-the-counter medicines (OTCs; non-prescription medicines). People should in general manage self-care for minor ailments themselves before contacting the family doctor/public healthcare system. In Norway, a number of medicines are available without prescription, at grocery stores, kiosks, and fuel stations, as well as in pharmacies.

Reduction of Healthcare Costs

Norway has a universal, nationalized healthcare system that in 2021 was regarded as one of the best in the world (Schneider et al., 2021). It is also among the most expensive in Europe, primarily financed from public funds (WHO, 2020). A major pro of self-care is that it reduces strain on the public health system, and that patients pay the full cost for medications. Almost half of total medication costs are paid out of pocket: OTC (9%), non-reimbursable prescriptions (37%), and patient co-payment (3%). Remaining medication costs are funded by the authorities: reimbursable prescriptions (29%), medication in hospitals, and to some extent nursing homes (22%) (LMI, 2021).

Patient Safety for Self-Caring Patients in Pharmacies

Norwegian pharmacies have a monopoly on distributing prescription medicines to the public, but pharmacies also function as a place where

patients have healthcare personnel to turn to when experiencing minor ailments.

People often need assistance in determining whether there is a need for self-care at all, whether there are suitable self-care remedies, or whether the severity of the ailment requires the person to contact the emergency ward or family doctor, dentist, veterinarian etc.

If not stated otherwise, OTCs should only be used continuously for 7–10 days. Health personnel should always make sure that OTCs are not used longer than recommended. If the minor ailment persists, the pharmacy staff should refer the customer to other healthcare personnel if necessary.

There are some exceptions to the drug distribution monopoly of pharmacies, one being that grocery stores, kiosks and fuel stations can sell a number of OTCs categorized as suitable for self-care by the Norwegian Medicines Agency. OTC packaging and the inserted patient information leaflets should contain enough written information for the general public to use the medicine in an effective and safe manner.

Employees in grocery stores, kiosks and fuel stations are not allowed to give any medically related information or advice to customers regarding the self-care medication assortment. There is an age limit of 18 years, and customers may purchase one package only at one encounter. If people choose to buy their medicines in a pharmacy, there is no official age limit and few limitations regarding quantity, because the employees are trained healthcare personnel.

Criteria for OTC Status and Different Categories

It is important that self-care is done in a safe way so that a minor ailment does not turn into a severe condition needing hospitalization.

Whether a medicine is allowed OTC status or not is usually decided by the Norwegian Medicines Agency (NOMA) and some of the criteria NOMA assess are (SLV, 2021):

- Low general toxicity and no relevant reproductive toxicity, genotoxic or carcinogenic properties
- Low risk of known serious adverse reactions in the general population in normal dosages

- Very low risk of unknown serious reactions
- No interactions with commonly used medicines which can produce serious adverse reactions
- Condition or symptoms for indicated use can be assessed correctly by the patient
- Can be used without medical supervision, hence no parenteral medications
- Risk and consequences of incorrect use are low and harmless

Based on the above listed criteria for OTC status there are now three different categories of OTCs in Norway:

1. Most OTCs are available in pharmacies, grocery stores, kiosks, and fuel stations
2. Some are only available in pharmacies, but to be found in the self-selection area, such as combinations of paracetamol/caffeine, or aciklovir/hydrocortisone
3. Two products are (presently) kept behind the counter and the customer is given oral guidance: Viagra Reseptfri™ (sildenafil) and Duraphat™ (sodium fluoride)

Conclusion

The included articles, in addition to our own multi-disciplinary experiences, indicate that incorrect use of medicines endangers patient safety and may have serious consequences for both the patient and society. The common theme of most barriers connected to incorrect use of medicines seems to be communication. It is therefore essential for healthcare providers to have good communication skills, and to be able to provide patient-centered communication and counseling of high quality. This may be the path towards optimizing use of medicines and ensuring patient safety. To improve patient-centered communication and counseling, teaching communication, as well as training courses, should be included in the curricula for healthcare providers in addition to post-graduate training.

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CHAPTER 11

A Tool to Ensure Appropriate Drug Use and Maintain Patient Safety When Administering Pro Re Nata Medications: Healthcare Providers' Experiences With Medicine Lists in Sheltered Housing for Older People

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Abstract: Residents living in sheltered housing may need assistance with the administration of medications, including medications used as needed. Healthcare providers can then administer medications based on the resident's medication list. The aim of this study is to expand our understanding of how healthcare providers utilize medication lists in managing pro re nata medications. Based on a secondary analysis of qualitative data, we found that medication lists are important tools to ensure appropriate medication use, and to maintain patient safety in sheltered housing. The results show that the interviewees expected updated and unambiguous medication lists in order to safeguard uniform practice, and maintain confidence in the administration of pro re nata medications. However, they often experienced ambiguous medication lists, putting a strain on quality of care. To manage updated medication lists and provide safe administration of pro re nata medications, the

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interviewees asked for closer collaboration with general practitioners, in which case medication reviews could be a solution.

Keywords: Residential care facilities, as-needed medication, aged, medicine list, Norway

The aim of this chapter is to expand our understanding of how healthcare providers utilize medication lists in medication management, focusing on managing pro re nata medications. Medications used as needed, also referred to as pro re nata medications (PRNMs), are given as a response to symptom(s) that occur, without the need for regular medication. In long-term care services these medications are given based on healthcare providers' professional judgment (Stokes et al., 2004). Residents living in residential aged care services have on average four PRNMs on their lists (Lenander et al., 2018; Stasinopoulos et al., 2018), however, the use of PRNMs varies (Stokes et al., 2004). A variety of different PRNMs seems to be included on the medication lists of many sheltered housing patients, while those used the most are mild painkillers and laxatives (Stasinopoulos et al., 2018).

When living in residential aged care services some residents get help with their medication management. Healthcare providers then have the responsibility to ensure correct treatment. Medication management is the process involving judging the patient's situation and need for medication, including all steps from prescribing to administration and evaluation of use (Regulations on medication management for services and health professionals providing healthcare, 2008). Studies show that the healthcare provider's role is significant in terms of PRNM management (Murray, 2017; Rønningen et al., 2013). Registered nurses have the overall responsibility for medication management in sheltered housing, however, the task may be delegated to other healthcare providers, such as nursing assistants. The head of the unit is responsible for delegating medication administration, and for verifying that providers have the competence required to carry this out (Regulations on medication management for services and health professionals providing health care, 2008).

Sheltered housing is part of long-term residential care for older people in Norway; by law the residents live in their own apartment and healthcare is provided by home healthcare (Daatland et al., 2015; The act on municipal health care services, 2011). In Norway, general practitioners (GPs) are responsible for providing general healthcare for the sheltered-housing residents including prescribing medications. The GPs are by law (Regulations of general practitioners in the municipalities, 2012) entitled to keep an updated medication list available at all times to the healthcare providers at the sheltered housing. The GPs are seldom colocated at the sheltered housing, and one location might communicate with several GPs, depending on which GP follows up each resident. Healthcare providers are not allowed to administer medications that are not on the medication list (Regulations on medication management for services and health professionals providing healthcare, 2008).

Inappropriate polypharmacy is a major public health challenge, and a threat to patient safety. Older people living in sheltered housing are particularly at risk (Davies & O'mahony, 2015; Payne & Avery, 2011; World Health Organization, 2019). Polypharmacy generates the use of PRNMs (Dörks et al., 2016; Stasinopoulos et al., 2018), however, PRNMs may not significantly increase the medication burden (Stasinopoulos et al., 2018). Drug-related problems (DRP), such as side effects, inappropriate use, and errors are threats to patient safety, and may reduce quality of life, cause morbidity, death, and increase healthcare costs (World Health Organization, 2017). Inadequate medication lists are an obstruction to safe medication management (Tariq et al., 2013), especially when patients are transferred between levels of care, when medication lists are of utmost importance in ensuring appropriate medication use and maintaining patient safety (Manskow & Kristiansen, 2021). The current systems in Norway for maintaining medication lists are perceived as fragmented, complex, risky, time-consuming, and causing uncertainty (Manskow & Kristiansen, 2021). Lack of communication and information flow across levels of healthcare, in relation to medications in use, causes medical errors (Frydenberg & Brekke, 2012; Manskow & Kristiansen, 2021). A patient's current medication list can potentially affect medication safety and quality of care when the information is not correct (Berland & Bentsen, 2017;

Devik et al., 2018; Manskow & Kristiansen, 2021). In addition, safety issues and adverse events are shown to be under-recognized for PRNMs, according to a systematic review (Vaismoradi et al., 2018)

The importance of medication lists in medication management led to this study with the aim of expanding knowledge on how healthcare providers utilize medication lists in medication management. The following research question guided the study: What are the experiences of healthcare providers regarding medication lists in sheltered housing for older people, when administering pro re nata medications?

Methods

This chapter is based on a secondary analysis of qualitative data (Heaton, 2008; Ruggiano & Perry, 2019). Data were collected from two studies focusing on pro re nata decision making, by using focus groups or individual in-depth interviews, respectively (Nilsen et al., 2020, 2021). The first author conducted the two primary studies, and is well acquainted with the data material and the data gathering context.

The focus group study aimed to describe factors affecting PRNM management in sheltered housing, while the individual in-depth study aimed to expand knowledge on healthcare providers' experiences relating to decision making for PRNMs. All interviewees were licensed to administer PRNMs. The sample is described in Table 1.

A secondary analysis used existing data collected for a previous study, analyzed to explore new questions (Heaton, 2008; Ruggiano & Perry, 2019). The approach used in this article was to analyze data from the parent study that appeared crucial, and which were not sufficiently focused on in the original articles (Ruggiano & Perry, 2019). An amplified analysis in which the two datasets were combined for purposes of secondary analysis was used (Heaton, 2008). The focus of the secondary analysis was to explore healthcare providers' experiences related to the residents' medication lists.

The secondary analysis was performed by using systematic text condensation (Malterud, 2012). This is an iterative four-step process, searching for similarities and differences in the data material. In the first step,

Table 1. The Sample: Interviewees' Characteristics

	Focus group study	**In-depth interview study**
Context	5 interviews 5 sheltered housing 4 different municipalities (mid Norway)	8 interviews 5 sheltered housing 5 different municipalities (mid Norway and east Norway)
Number of interviewees	22 (3–6 in each group)	8
Gender	Female n = 22 Male n = 0	Female n = 8 Male n = 0
Education	Registered nurse n = 11 Social educator n = 1 Nurse assistant n = 8 Apprentice in health and social work n = 2	Registered nurse n = 4 Nurse assistant n = 4
Average years of work experience as healthcare provider (min-max)	14,3 (1–32)	17,5 (2–30)
Average number of years employed in this housing (min-max)	10,5 (1–30)	12,9 (1–22)
Number of residents in the sheltered housing	15–35	10–60

both authors read the transcripts, and preliminary themes were identified and discussed. Secondly, the transcripts were coded according to these themes by identifying units of meaning, and the main themes were adjusted. In the third step, the units of meaning were arranged into subthemes, and a condensate was made of each theme and subtheme. In the last step, an analytic text was synthesized based on the condensates of each theme and subtheme.

Both authors frequently discussed the steps to ensure the interpretation of our findings. Disagreements were discussed until agreement was reached. Throughout the whole process the authors returned to the transcripts to make sure their analysis was in line with the whole. The authors are pharmacists with supplementary experience. Both have experience with qualitative methods, and work experience from pharmacies and universities. Additionally, the second author is presently working as a municipal pharmacist. The authors have no clinical experience from sheltered housing.

Ethical Considerations

Ethical issues have been raised surrounding the use of secondary analysis (Heaton, 2008; Ruggiano & Perry, 2019). These issues relate particularly to obtaining informed consent from interviewees for retaining data, sharing data, and re-using data for another purpose than the original one. Written consent and approval from the Norwegian Centre for Research Data (NSD) [reference 57803] were collected for both of the primary interview studies. New consent or approval for this secondary analysis was not obtained. This could be considered to be a limitation. The strength of a secondary analysis is, on the other hand, that it relieves the burden for interviewees, and heads of units who collaborated with us, to identify, access, and recruit research participants. The research question guiding this secondary analysis is close to the original studies' research questions.

Results

The analysis showed that healthcare providers experience the resident's medication list as a tool for ensuring appropriate medication use, and for maintaining proper patient safety, but also to help them feel confident in their actions when managing medications. An updated list was perceived as essential to safeguard uniform practice, and when communicating with other healthcare personnel and residents. However, encountering outdated and unrevised medication lists was common. In these situations, healthcare providers had to rely on their experience and thorough knowledge of the resident to guarantee appropriate medication use. To be able to maintain proper patient safety when handling incorrect lists, the healthcare providers said they requested medication reviews. There appear to be differences between different sheltered housing locations regarding how updated the lists are, and how healthcare providers collaborate with the prescriber, revealing how well the list works as a tool for the healthcare provider. The analysis identified the medication lists functioning as a tool for the healthcare provider within two main themes, with two subthemes, respectively, as shown in Table 2.

Table 2. Overview of Results: Main Theme, Themes and Subthemes

Main theme	Theme	Subtheme
Resident's medication list as a tool	Tool to ensure appropriate medication use	Ensure uniform practice
		Communication tool
	Tool to maintain patient safety	Influence distribution of responsibility
		Initiator of medication reviews

Tool to Ensure Appropriate Medication Use

The medication list is actively used as a tool in everyday practice, because it provides the basis for the scope of the healthcare worker's practice. A reconciliated medication list with unambiguous PRNMs was said to safeguard more uniform practice, since it limited the available options. Lists containing several PRNMs, especially with the same indication (e.g., pain), could create insecurity and thus differences in practice. The interviewees were skeptical to medication lists left unchanged for several years, and also to when new medications were added without old ones being removed. They also spoke of PRNMs not being removed when the indication was no longer present, influencing their professional judgement. "The lists contain pro re nata medications they no longer use … Maybe we do not always assess whether to administer or not. They just get it." (Interview (I) A, registered nurse)

When facing complex and ambiguous medication lists, assessing the resident was more demanding, and therefore susceptible to variations related to persons and resources. In contrast, some interviewees followed the medication list strictly, and thus always administered the PRNM when asked. The argument given was that the GP had assessed a need, and it was not within the healthcare provider's scope to question this decision.

In addition to thorough knowledge of the resident, confidence, competence and experience were mentioned as necessary skills when dealing with medication lists of uncertain validity. This was particularly the case when the resident was cognitively impaired or struggling to communicate. The interviewees therefore questioned whether appropriate medication therapy could be performed when residents with ambiguous

medication lists were handed over to new employees or temporary staff. The majority of the interviewees emphasized the importance of not interpreting the medication list literally, but of actively using their observational and medication knowledge skills in guiding their decisions when navigating in this arena. One example was a resident who had been prescribed both a laxative and an anti-diarrhea medication as PRNM. Here proper competence was decisive in ensuring appropriate medication use. "We do have residents prescribed both Lactulose and Imodium as pro re nata (laughter), and who were administered both simultaneously." (Focus group (FG) A person (P) 6, nurse assistant)

The medication list was also used as a starting point for dialogue and communication when interacting with the resident, their next of kin, or between healthcare providers or other healthcare professionals. Knowing that the medication list was updated and in line with the resident's need was important to ensure confident reasoning. The interviewees spoke of residents who knew very well which medicines they were prescribed, and therefore perceived themselves as entitled to have them administered when requested. These could be elderly residents able to consent, yet with a predominance of psychiatric or addiction issues. These situations were described as challenging.

> You have to assess … your own security … when handling, for example, drug addicts who can act unrestrained, those who are demanding. You do not fight or wage war or sacrifice your health for a blister card of oxazepam. Then you open the lock and say, "Here you are, go home and enjoy", even though you know you shouldn't. (FGE P1, registered nurse)

Residents who are eloquent and able to consent, who plead their right to be administered their PRNMs, were difficult to argue against when the medication in question was on the list. In these situations, the healthcare provider may doubt what the GP had communicated to the resident, and whether this deviated from what had been communicated to them. They also experienced an expectation by some residents to receive PRNMs every day at fixed times. In these situations, they used the medication list in discussion with the resident in order to explain the rationale behind PRNMs. However, in the aftermath of such a discussion, if the resident

no longer requested the medication in question, they wondered whether the resident had not dared to ask for it. The interviewees were conscious of their position and appurtenant power, and therefore articulated a fear that a resident might repress a request despite having a need.

> We have had situations where the resident has been at war with us because of a tranquilizer, especially one person rang the alarm constantly and demanded medication … Such discussions can be intense. (FGC P1, registered nurse)

Tool to Maintain Patient Safety

An ambiguous medication list was perceived as an assurance for both resident and healthcare provider. The healthcare providers expressed concern as to whether the GPs had full control over their patients' medication lists, since they often experienced GPs not following up their responsibilities. Therefore, they said they had to step up beyond their legal liability, and take responsibility for the lists' validity, creating a shift in responsibility between nurse and GP. The majority of the interviewees said that following up the medication lists was the responsibility of the GP, however, there were nurses who claimed their profession also possessed a certain responsibility through their knowledge of the patient and their needs. "It's kind of our responsibility also if the medication list is very long.… I think it is the general practitioner's responsibility." (FGB P2, registered nurse, and P3 nursing assistants, in discussion) The GP seldom knew the resident as well as the healthcare providers. The nurses therefore often took the initiative and contacted the GP to cease medications that were never used, and in this way contributed to validating the list. This also included switching medications from regular to pro re nata, and vice versa.

The interviewees also substantiated their skepticism to the list's content by pointing out that the resident had used the same medication in the same dose for several years. Through their knowledge of the resident, they questioned whether the medical indication was still relevant.

The nurses also experienced variations in interest when contacting the GP about medication lists. Some of them were described as closing their ears, forcing the healthcare providers to use their own judgement

navigating through unambiguous medication lists. Others experienced the GP as asking for advice, giving the impression of wanting the nurses to decide. The interviewees understood to some extend the GPs' struggle to stay updated, since they were aware that different journal systems in primary and secondary care do not communicate.

Despite the urge to cease medications without indications, the interviewees admitted to not always being very eager to remove medications from the list. One interviewee said they were reluctant to remove strong pain killers from the list in case the resident once again suffered severe pain and a prescriber was not available. They justified this choice by the fact that GPs are often inaccessible, and they were confident that the resident would tolerate the medication due to prior use.

> I often think that if they use something strong, I am sure it is wrong, but that it is ok that it is on the list in case something happens. … so for example, someone breaks an arm or something, … I then let it be on the list, even though the arm is healed … It should be removed, I know that." (FGC P1, registered nurse)

"Regular medication reviews are important to improve patient safety." This was stated by many of the interviewees, since reviews ensured that medication lists could be trusted, and contained only medications the resident really needed. The number of GPs the healthcare providers in the different sheltered housing locations had to relate to varied greatly. In some municipalities, there was even a shortage of GPs. How close each GP followed up their patients also varied. There were units that had regular meetings with the GPs. This direct contact led to healthcare providers feeling confident in the medication list being updated and in line with the resident's needs.

> It's really good that we have started with the annual report and doctor's rounds. … We take blood samples in advance and perform a real check. Then the general practitioner can assess whether these are the right medications. It is a reassurance, both for us and the resident. (IF, registered nurse)

To have such a doctor's round was, however, the exception. The main rule was to be forced to communicate with the GP through e-messages or phone, something that could be frustrating, since they were not able to

discuss the resident's consecutive needs to the same extent. They felt they had to wait patiently for an answer, if it came at all.

Many of the interviewees expressed a desire for regular medication reviews. Those who experienced regular drug reviews claimed it was economical, and did not take much time. They perceived the GPs to be of the same opinion, and therefore appreciated this follow-up of their patient.

> Medication reviews are important I have to say … because there are many who are listed with an awful lot of medicines … They have reduced the number of medications. They now use what they need and nothing else. (IC, registered nurse)

Discussion

PRNM prescriptions and administration may increase efficiency of care since they allow frequent and intermittent medicine use, without having to contact the prescriber for new prescriptions. Nurses' involvement in decision making and patient care may therefore increase (Haw & Wolstencroft, 2014). The premise for optimal use of PRNM is, however, that prescriptions must be monitored continually to ensure appropriate medication use (Barr et al., 2018). The main results from this study show that reality may not agree with the premise. Medication lists are important tools for the healthcare provider, ensuring appropriate medication use and maintaining proper patient safety. The interviewees in this study expected updated and unambiguous medication lists, contributing to uniform practice and improving confidence when communicating with residents, next-of kin, or colleagues about the administration of PRNM. However, the nurses more often experience ambiguous medication lists, which result in a perceived shift in the distribution of responsibility between nurses and GPs, resulting in nurses requesting regular medication reviews.

Quality of Care Under Pressure

Our findings present evidence for quality of care being put under pressure when medication lists are not continually monitored, creating insecurity

among healthcare providers, and also affecting patient safety. Ambiguous and unrevised drug lists lead to non-uniform practice, which depends too much upon each healthcare provider's experience and competence, in addition to their knowledge of the patient, also known as relational continuity (Haggerty et al., 2013). This is in line with a systematic review on patient safety and PRNM prescriptions and administration, which indicated that safety issues and adverse events were under-recognized for PRN administration and prescription (Vaismoradi et al., 2018). PRNM widens the healthcare provider's scope, and increases their involvement in decision making (Haw & Wolstencroft, 2014). However, when these issues are not dealt with, insecurity results. In this insecure situation, healthcare providers were found to regard their responsibilities being stretched beyond their legal liability.

Our interviewees worried about safe practice when managing PRNMs from incorrect and outdated medication lists. Medication management consists of several steps, and medication errors can occur at each step (Carayon et al., 2006; Odberg et al., 2019). The importance of updated and correct medication lists for patient safety is emphasized in patient safety programs (The Norwegian Directorate of Health, 2020; World Health Organization, 2017). Medication lists are known to be important tools to ensure appropriate medication use and maintain patient safety when patients are transferred between healthcare services levels (Manskow & Kristiansen, 2021). Here inadequate medication lists are an obstruction to safe medication management (Tariq et al., 2013). Our findings show that even for patients not being transferred between levels of care, the nurses' uncertainty affects their ability to provide safe practice, and is also perceived as a threat to patient safety. This is because insufficient information causes stress and risky workarounds with a perceived risk of errors (Manskow & Kristiansen, 2021). Our study shows, however, that correct medication lists are also of utmost importance as a tool for healthcare providers in everyday care in the unit. To achieve appropriate medication treatment, access to the required information when needed is essential. Obstacles to safe practice and the risks to patient safety when medication lists not are updated are also known from other studies (Lindblad et al., 2017; Manskow & Kristiansen, 2021).

Our study indicates that the medication list was the basis for communication with the resident when assessing the need for PRNM. The interviewees mentioned residents who knew very well which medicines they were on, and when managing PRNM for this group, they felt more confident reasoning with them if they had updated lists. Patients use medication lists as a communicative device (Seidling et al., 2019), and patients are an important source of information about medications actually in use (Kim et al., 2018). In patient-centered care, involving the resident in decision making is central, and if the resident is able to communicate, the list could be a starting point for discussing why and which PRNM to use. Patients' right to be involved in decision making is essential in today's healthcare services, and should be positive for patient safety (Longtin et al., 2010; World Health Organization, 2017). Patients, involved in shared decision making, state that they are more satisfied with decisions and experience fewer conflicts, even when there is no evidence that shared decision making correlates with patient safety (Shay & Lafata, 2015). Our results show, however, that this is challenging in practice, such as when patients' demands are in conflict with the nurses' professional views. This was the case particularly when patients requested PRNM at a set time every day, and the nurses ended up discussing the concept of PRNM with the patient. A uniform medication list, containing only those medications thought to be in line with the patient's needs, could then help to avoid such situations. This practice was, however, not uniform, since there were interviewees who claimed it was not their task to assess whether to give medicine or not. The concept of PRNM indicates that the GP has already verified the patient's need for the medicine. When residents have the cognitive capacity to communicate about their medication use, they will be able to correct a medication list if healthcare providers discuss this matter with them. On the other hand, when healthcare providers must make decisions solely based on the list, an updated list becomes even more important.

The healthcare providers have a crucial role when it comes to making PRNM decisions (Murray, 2017; Rønningen et al., 2013). If medication lists consist of several medications that have allegedly stopped, the healthcare provider's judgement requires more competence. Medication

management will then not be straightforward, and the risk of medication errors increases. Systems independent of the individual healthcare provider are therefore important in avoiding errors, and are important for secure medication management (Kohn et al., 2000; Reason, 2000).

Collaboration With the General Practitioner

Updated medication lists were perceived to be important in maintaining adequate patient safety. The distribution of responsibility between the GP and the nurse was said to be affected when the lists were not reconciliated, that is perceived as not in line with the resident's needs. In order to solve these challenges, the healthcare providers wished to establish closer collaboration with the GP. A regular systematic follow-up including the GP, such as a medication review, was therefore preferred by the healthcare providers.

Interviewees in this study experienced GPs as not following up their responsibilities, forcing the healthcare providers to step up and take more responsibility for the medication list. Going beyond their responsibilities in medication management in order to cope in everyday work life has also been found in other studies (Devik et al., 2021; Odberg et al., 2019). Studies involving physicians have found that they regard themselves as responsible for the medication list, but how they perceive this responsibility varies (Hammar et al., 2014; Rahmner et al., 2010).

How close the GP followed up their patients varied in our study, from those interviewees experiencing doctors' rounds, to those being forced to communicate with the GP through e-messages or phonecalls and patiently having to wait for an answer. In Norway, interprofessional medication reviews are not fully established in primary care. Since 2013 the legislation for GPs states that for patients prescribed four or more drugs, the GP should perform medication reviews, if this is perceived as necessary from a medical point of view (Regulations on general practitioners in the municipalities, 2012). However, this requires that the GP either regularly meets with the patient, or accepts clinical input from other healthcare personnel, which was desired by our interviewees. Even though the nurses in our study requested medication reviews, they

experienced being without power to initiate them. This echoes a recent qualitative study of nurses' experiences, which showed that nurses felt they have the knowledge and will to participate in interprofessional medication reviews (IMRs), but little authority (Devik et al., 2021). In that study the nurses' knowledge and good intentions for improvement met resistance in interprofessional collaboration, especially from physicians, resulting in the nurses perceiving their role as lonely and without authority. They perceived their own professional and moral responsibility to be overriden by the physicians, who expressed the nurses' initiatives for IMR as interfering with the physicians' tasks. The nurses in our study, however, did not express an explicit wish to participate in the medication review, as much as they just wanted it done. Those who experienced close collaboration with GPs viewed the collaboration as economical and not taking much time. There were, however, organizational differences between the sheltered housing locations represented in this study, where some had to relate to several GPs, complicating the issue. Studies of healthcare services in sheltered housing are rare (Melby et al., 2019). Studies from nursing homes show that a physician who is well integrated in the nursing home has a great impact on the healthcare service, and is a support for other healthcare providers (Melby et al., 2019). Having a physician allocated to the sheltered housing, like in nursing homes, may ease the healthcare provider's burden following up medication use in sheltered housing.

The interviewees felt it was time-consuming and exhausting to navigate without a correct medication list. Medication reconciliation and medication reviews were therefore believed to be important both to improve patient safety and ease their own workday. The literature shows several reasons why medication reconciliation should be prioritized, in line with some of our findings (Rose et al., 2017), such as, a substantial potential to improve patient outcomes, avert crises and readmissions, in addition to initiating deprescribing. IMR are shown to reduce drug-related problems and improve quality of prescribing in primary healthcare (Modig et al., 2016). When new medications are added to the list, and there is never a review, the result is confusing lists. Moreover, the longer residents live in sheltered housing the more PRNMs they will supposedly

get (Dörks et al., 2016). This highlights the importance of updated medication lists to maintain safe everyday practice.

There are, however, no rules without an exception. To make everyday work as feasible as possible, the nurses admitted to not always taking their time to nag the prescriber to update the medication list. They spoke of using medications, which supposedly should have been removed from the drug list, for new indications, which they did reflect upon as being a potential threat to patient safety. When drug lists were not updated, it was possible to use medications without consulting the GP. They justified this practice with the knowledge that the resident previously tolerated the drug in question. However, they did not reflect on this practice in terms of the possibility that the resident's health may have changed since last time, or the risk of drug-drug or drug-disease interaction. Another study, from Norwegian nursing homes, also found that deviation from guidelines in medication management was a conscious choice, adjusting the practice to fit the circumstances (Solberg et al., 2022).

Conclusion

Healthcare providers in this study experience drug lists to be important for daily practice. The lists are used as tools to maintain appropriate drug use and maintain patient safety when administrating PRNMs in sheltered housing. Several of the healthcare providers experience today's practice as being put under pressure to achieve the goal of safe management of PRNMs. The interviewees in this study want closer collaboration with the GP to cope with their experienced challenges, such as systematic medication reviews. Medication reviews could contribute to updated medicine lists, and at the same time contribute to closer collaboration between healthcare providers in sheltered housing and the GP.

Implications

Based upon the findings in this study, there is a need to connect the GP closer to the sheltered housing to ensure that medication lists work as appropriate tools for healthcare providers. At present, legislation is an

obstacle. However, the authorities need to consider whether sheltered housing should follow the same legislation as nursing homes, where one prescriber is responsible for all residents. In addition, systematic interprofessional medication reviews are resource intensive. We therefore suggest a division of labor, in which nurses in sheltered housing take the responsibility to identify candidates for medication review, based upon their knowledge of the resident, and an updated assessment of the resident's clinical status. The nurses choose residents for whom they perceive the medication list does not operate as an appropriate tool, and substantiate their choice through a comprehensive geriatric assessment of the resident. A request for medication review could then be communicated to the GP, who thereafter is responsible for arranging a medication review together with the nurse.

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CHAPTER 12

Challenges in Obtaining and Sharing Core Patient Information in Norwegian Nursing Homes and Home Care Services: A Qualitative Study of Nurses' and Doctors' Experiences

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Abstract: In Norwegian nursing homes and home care services, medication information and other core patient information (CPI) is usually registered and stored in separate digital systems not connected to each other. This may pose a threat to medication safety and quality of care in municipal health and care services. This study explores how nurses and doctors in Norwegian nursing homes and home care services experience access to and exchange of CPI before two new national solutions, the Shared Medication List and the Summary Care Record, are implemented in Norway. We used a qualitative research design with semi-structured individual interviews with nurses (n = 17) and medical doctors (n = 6) from home care services and nursing homes in six Norwegian municipalities. Data were coded and analyzed following an approach based on grounded theory. Our participants reported having extensive experience of various challenges related to accessing and sharing CPI. Five main challenges emerged from our data: 1) excessive time consumption;

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2) frustration; 3) uncertainty; 4) dependence; and 5) complexity and risk. Our participants thought that these challenges posed a risk to patient safety and quality of care, and they were especially concerned about medication information in patient transitions between levels of care. Our study shows that nurses and medical doctors face substantial challenges, because they lack seamless, up-to-date digital solutions able to share CPI across healthcare services. The ongoing national implementation of the SML and SCR should address these challenges directly, and closely evaluate their impact on patient safety and quality of care.

Keywords: core patient information, health professionals, medication information, primary healthcare, shared medication list, summary care record

To ensure quality of care and patient safety, it is vital that core patient information is accurate and easily available (Eden et al., 2016). In this chapter we use "core patient information" (CPI hereafter) to denote all critical and important health and treatment related information about patients, such as medication lists, prescriptions, diagnoses, allergies, etc. (Dyb & Warth, 2018).

Medication errors are linked to substantial financial costs worldwide (Kierkegaard, 2013), and are considered the third leading cause of death in the US (Institute of Medicine Committee on Data Standards for Patient Safety, 2004). During the 5 years following the release of the WHO's Third Global Patient Safety Challenge, "Medication Without Harm", report in 2012, WHO aimed to reduce medication-related harm by 50% globally (Donaldson et al., 2017). Patient safety is the foundation on which all other aspects of quality of care are built, and is indistinguishable from the quality of healthcare services (Institute of Medicine Committee on Data Standards for Patient Safety, 2004; Institute of Medicine Committee on Quality of Health Care in America, 2001).

The everyday work of health professionals typically involves the use of many different digital and manual sources[1] to obtain CPI. CPI is normally stored in several digital systems within the different healthcare organizations and units (hospitals, nursing homes, home care services, pharmacies, GPs etc.), and a significant challenge is that the different

1 Digital sources: electronic health records (EHR), summary care record (SCR). Manual sources: paper, medicine list, phone, fax, face-to-face.

units use different systems, unable to share data across the healthcare services (Frydenberg & Brekke, 2012; Kierkegaard, 2013).This causes poor communication and information flow within and between services, and can lead to potentially harmful medication errors (Remen & Grimsmo, 2011). The lack of interoperability can also lead to ineffective care coordination and transitions of care (Samal et al., 2016). Health professionals' perspectives on improving information exchange reveal several challenges, such as ineffective communication, poor medication management and technical factors (Bengtsson et al., 2021; Sarzynski et al., 2019).

Keeping in mind this context, Norwegian authorities are currently working to implement several large national eHealth solutions, two of which are the summary care record (SCR) and the shared medication list (SML) (Helsenett, 2018; The Norwegian Directorate of eHealth (NDE) 2018). The implementation of the SCR in primary healthcare (nursing homes and home care services) was initiated in the first municipalities in late 2019/early 2020 and a full national rollout is expected in 2022.[2] The implementation of the SCR is a necessary and important step towards a national SML (expected national implementation in 2023–2025[3]). The SML is currently being piloted in the Bergen municipality. Bergen is Norway's second largest city, with a population of 285,601 as of 1 January, 2021.[4]

A recent Norwegian study explored doctors' use of and trust in the SCR, and reported that doctors used only the pharmaceutical summary (one of six functions in the SCR), and primarily for just a few subgroups of patients: unconscious patients, elderly with polypharmacy, and patients with substance conditions (Dyb & Warth, 2018). Studies from the UK on the functionality and impact of the SCR, reported that health personnel regarded it as supporting better quality of care with the potential to prevent medication errors (Greenhalgh et al., 2010; Jones et al., 2017).

2 https://www.helsenorge.no/en/summary-care-record/kjernejournal-for-safer-healthcare/
3 https://www.ehelse.no/programmer/program-pasientens-legemiddelliste
4 https://www.bergen.kommune.no/omkommunen/fakta-om-bergen/befolkning/folkemengde-per-1-januar-2021

FACT BOX

The summary care record (SCR) is the first national digital solution in Norway for the exchange of updated core health information, accessible regardless of where treatment is provided.[a] The SCR contains critical information, a pharmaceutical summary, appointment history (hospitals), patient data (relative, GP) and self-reported information. The SCR is expected to have a huge impact on patient safety and quality of care, especially in emergency situations or situations in which the patient (or relative) cannot provide this information. The SML and the SCR are interconnected, as nurses and nursing home MDs will be accessing the SML through the SCR interface.

[a] https://www.helsenorge.no/en/summary-care-record/kjernejournal-for-safer-healthcare/

The study underlying this chapter is part of the larger national longitudinal study "The Summary Care Record and a Shared Medication List in Norwegian Nursing Homes and Home Care Services" (2019–2025). In this chapter our aim is to present in-depth knowledge on how nurses and medical doctors (MDs) in nursing homes and home care services *experience* the access to and exchange of CPI in the context of current digital and manual sources, pre SCR and SML.

Methods

Research Design

We used a qualitative research design based on a stepwise-deductive-inductive (SDI) approach (Tjora, 2010). One of the core elements of SDI is that the researcher should be open-minded and unbiased, and let issues and themes "emerge" from the material. We used the SDI approach to explore how health professionals experience everyday access to and exchange of CPI in primary healthcare *before* the implementation of the SCR and the SML. In line with our methodological orientation, we tried to approach the material without any fixed ideas or expectations, and we were determined to allow findings to emerge freely from the material. We conducted semi-structured interviews, using an interview

guide[5] covering the following themes: 1) access to critical and relevant patient information; 2) access to medication information; 3) collaboration with other parties; 4) decision support; and 5) expectations for the SCR and SML. Participants were encouraged to talk freely about their experiences, thoughts and perspectives, and were able to influence the direction of the conversation. As interviewers, our job was to make sure that all themes in our interview guide were covered.

In this chapter we focus exclusively on access and exchange of CPI in nursing homes and home care services, and therefore only discuss findings from interviews with nurses and nursing home MDs, and cover only these themes: 1) access to critical and relevant patient information, and 2) access to medication information (see Table 1).

Table 1. Excerpt from Interview Guide

Theme 1: Access to critical and relevant patient information
How do you proceed to obtain critical and relevant information about the patients?
How do you consider the quality of the different information sources?
How do you experience the process related to obtaining critical and relevant patient information?
Theme 2: Experiences with current access to an overview of the patients' medications
How do you go about getting an overview of which medicines a patient is using?
What are the challenges today in relation to the limited opportunity to share medication lists, seen from your role and perspective?
How do you register and communicate changes in the medicines a patient uses?

Recruitment, Research Sites and Participants

For recruitment, we contacted the heads of health and care services in nine different Norwegian municipalities by email and phone, and provided them with information about the national study and an invitation to participate. The selection of municipalities was based on the following criteria:

5 Prior to the study, the interview guide was piloted on two colleagues (one nurse and one MD) with relevant clinical experience.

- Municipalities had to be in the process of implementing the SCR and SML
- All three main suppliers of EHR systems in Norway should be represented
- A spread of small, medium and large municipalities
- Different parts of Norway should be represented (geographical spread)

Seven out of nine municipalities agreed to take part in the study, and two declined due to lack of available resources at that time. For one of the seven included municipalities, planned interviews were postponed due to unexpected circumstances. After careful consideration, we concluded that data saturation was achieved through the six included municipalities. To secure experiences from different sites within the primary healthcare services who had not yet implemented the SCR, we chose to include nurses from both home care services and different nursing home contexts (long-term, short-term, and intermediate). We also recruited MDs working in nursing homes to obtain their experiences as well, as both nurses and MDs in these organizations lack access to the SCR. A contact person within each of the six municipalities helped to coordinate and recruit participants of both genders working at the sites mentioned above, having two or more years of experience as a nurse or MD at the site, and having experience using EHR systems for obtaining CPI. All participants received information on the study aims, funding and roles before the interviews. We hereby present findings from interviews with nurses (n = 9) and MDs (n = 6) employed in nursing homes (long-term, short-term, and intermediate[6]) and nurses from home care services (n = 8), a total of 23 participants.

6 Intermediate departments are organized through the municipal health services in Norway. Intermediate means between the specialist (hospitals) and municipal health service. Patients admitted to intermediate departments require more advanced treatment than the municipal health services are able to offer before returning to their own home or home care services, such as medical treatment or physical rehabilitation.

Data Generation and Analysis

The authors (USM, TTK) conducted all interviews with the participants at their workplaces from November 2019 to March 2020. Most participants were interviewed individually, with the exception of four, which we interviewed in pairs for practical reasons. The interviews lasted between 30 to 60 minutes, were digitally recorded and transcribed by a professional transcription service. Written informed consent was collected from all included participants.

Analysis and data coding were performed by both authors, in line with the SDI approach (Tjora, 2010), oriented towards identifying emergent issues and themes through an open inductive reading of the material. All transcripts were first coded in detail using NVivo 12 software. For the present study, we created 283 individual nodes covering access to and exchange of CPI. In the second step, the nodes were grouped into a coding tree consisting of five recurring themes: excessive time consumption, frustration, uncertainty, dependency, and complexity. In order to ensure rigour and continuity surrounding the empirical data, our open inductive reading, coding and grouping, we maintained a constant focus and dialogue to ensure that all of the themes we created both faithfully represented what was actually being said by the participants, and were general enough to cover all of the included nodes (Manskow & Kristiansen, 2021; Tjora, 2010; Trondsen et al., 2014). In line with the logic of the SDI approach, we constructed our categories, themes and concepts based on patterns that emerged from the empirical data.

Ethical Considerations

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Data Protection Officer at the University Hospital of North Norway (Project no. 02417, ref.: 2020/2856). Ethical considerations, such as information on anonymity and confidentiality, voluntary participation, informed written consent, and information about publication were explained to all participants, and all participants signed a written consent before the interviews. The data material was anonymized and handled securely according to the recommendations of

the local data protection officer. All methods were carried out in accordance with relevant guidelines and regulations.

Results

Nurses and MDs in primary healthcare generally experienced the task of obtaining and sharing CPI as a significant challenge, especially related to patients' medication information. One main pattern that emerged from our material was that the participants regularly experienced situations where access to CPI was limited, and where professional tasks had to be performed without having all relevant information at hand. When analyzing the material, we found that the participants typically described experiences of five sorts: 1) excessive time consumption, 2) frustration, 3) uncertainty, 4) dependency, and 5) complexity and risk. In the following sections, we explore these experiences in more detail.

Excessive Time Consumption

The participants reported that when access to CPI was limited, excessive time consumption was a common consequence: "I spend 40% of my workday getting information" (Nurse). In terms of both losing time designated to core tasks as well as "stealing" time from other health professionals, one MD stated, "Not only does it cost me time, but it costs the specialist and GP time as well". One of the main reasons for excessive time consumption was said to be the lack of adequate digital solutions for sharing CPI across health services, which hindered information access.

> [It is] difficult with systems that do not communicate and retrieve all the information. It is not easy. It does not come automatically, and we have to search for the information. (MD)

Some participants also reported that pre-existing time shortages could result in new problems, for example when nurses lack the time to obtain medical records with an updated medication list for new patients:

> We have a busy time schedule, and you may not be able to do things as fast as you should. The patient arrives and then it may take a week before you realize that you need to obtain a medical record. (Nurse)

Also, most participants mentioned that they spend a lot of extra time gathering core information about new patients:

> I spend a lot of unnecessary time calling around to find the right person and the right department in the hospital for information about a patient. (Nurse)

As illustrated above, the participants reported considerable time consumption, that is time spent searching for CPI, and that this was viewed as "excessive" by the participants.

Frustration Over Systems That Do Not Communicate

The participating nurses and MDs reported several types of situations that caused frustration. Frustration was often directed towards "systems that do not communicate" across sections and levels of the healthcare system, obstructing information flow. Frustration was also triggered partly by excessive time consumption and by difficulties in meeting the expectations of patients and relatives.

> Yes, it is time consuming, so you simply get frustrated, over and over again. And the patients ask what is going on, so you feel that you are in a pinch, really, with both patients and relatives. I feel that I have to chase after information. (Nurse)

Lacking or incomplete discharge summaries[7] from hospitals were one of the primary causes of frustration, especially among nurses. According to our participants, discharge summaries were often not fully approved at the time of discharge from the hospital. Many patients therefore arrive at primary care services before updated CPI about them is available to the responsible health professionals.

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7 A discharge summary is the main source of standardized clinical information between healthcare services, and a vital information source for health professionals involved in a patient's treatment and care.

> We are kind of helpless when we receive a new patient without any information available. (Nurse)

> It is very stressful to receive a patient without having the necessary papers …. If you have not received the discharge summary by electronic message before the patient arrives, you may have no idea what kind of medication the patient should have …. So, if vital examinations need to be performed and at certain times, you need to have control. (MD)

The participants in our study reported that hospitals are aware of the problem, and that there is a formal agreement in place between the hospitals and primary healthcare services that the discharge summary must be approved and available before a patient is transferred, in order to avoid situations like the one mentioned above. However, as one nurse put it, "These agreements are constantly broken", and this was perceived as a source of frustration.

Uncertainty Caused by Lack of Information

Many participants reported that limited access to necessary CPI tended to make them feel uncertain. One type of situation where our participants reported this was when they had to handle a multitude of different information sources to obtain sufficient CPI.

> We had to call around and were sent to different people for [core patient] information. So, we felt that when we finally did receive information, we were a bit in doubt as to whether we had received everything. (Nurse)

Health professionals also feared that their own uncertainty would affect the patients and possibly even cause harm, especially within psychiatric care. A psychiatric nurse explained how she feared that her own uncertainty could affect the patients:

> I don't know whether it's bad for the patient. But, within the psychiatric services, it creates uncertainty, which is not good for patients. It is better that we know everything and can tell them, "This is how it is, and this is what we are going to do". (Nurse)

Both nurses and MDs reported that when they received an incomplete discharge summary from the hospital, their work with the patient would be characterized by an unhealthy combination of feelings of increased responsibility and constant uncertainty until the final summary arrived. They would not know whether important corrections had been added to the final summary before the hospital doctor actually signed and approved it:

> Yes, it happens that they have written "not approved", and we are completely dependent as recipients to follow up and wait until we receive the final [approved and complete] discharge summary. And then we have to check whether there are any corrections from the pre-approved version. So, it puts a very heavy responsibility on the nurses in the ward. (Nurse)

As mentioned in the "time consumption" section, our participants reported delays ranging from one day to over a week before receiving a final and approved discharge summary from the hospital. In the meantime, considerable time and resources were devoted to obtaining updated CPI about the patient through other sources (phone, e-messages, patient). The patient's relatives also served as an important source of CPI, as one nurse said, "We have very little critical patient information in fact. So, you have to ask the relatives and, well, more or less interview them".

Dependency on Others

Both nurses and doctors reported that they often depended on GPs, hospital doctors, the patient or caregivers to confirm or provide access to correct CPI before they could proceed with their own tasks. This was challenging for nurses in home care services as well as in intermediate departments when receiving newly discharged patients from the hospital. As one MD stated:

> So, we do not have an overview of this: blood tests, medication lists, and things like that. Then we send an e-message to the GP, and then we have to wait too. And sometimes we need an answer right away. (MD)

One intermediate care nurse stated:

> And then, if the patients have not had previous healthcare services from the municipality, we have much less information, and are even more dependent on information from the hospital. Then there are the patients who are admitted for emergency care, where we depend on information from the GPs. (Nurse)

Our participants often needed to contact either the GP or treating doctor at the hospital for supplementary CPI about a new patient. In many cases, however, these GPs or specialists did not have the time to provide feedback during working hours, and the responsible nurse or MD had to spend a lot of time waiting for the information needed for the treatment and care of patients.

Complexity and Risk to Patient Safety

Complexity and risk in the information flow between primary healthcare and the hospital were seen as major challenges in everyday work, and were reported as posing a risk to patient safety. One doctor stated that "the information flow is highly vulnerable and critical between healthcare levels". As the available digital solutions did not allow sharing patient information across services, patient information often had to be obtained manually by phone or digitally through e-messages. Obtaining CPI thus became a more complex and riskier task.

Another challenge for some participants was the huge amount of information in the EHR and discharge summaries, which they experienced as "information overload" to some degree. They perceived an increase in complexity and risk in cases where they were unable to identify and retrieve necessary CPI. One nurse stated the following: "[The discharge summary] is often four or five pages, so it is a challenge to determine which information is relevant for us".

Another nurse stated the following:

> The discharge summary needs to be thoroughly read by the nurses, because we can't expect the MDs to read 25 different patient summaries in detail, since there is a high turnover of patients in our short-term department. If we don't

> catch the most important information, there is a risk that something will happen to the patient and their condition might get worse. (Nurse)

Our participants desired a more readily available, structured and easier system, both in terms of the local EHR systems and the ability to share CPI.

Discussion

Our results indicate that nurses and MDs in Norwegian nursing homes and home care services have extensive experience of situations where inadequate access to CPI affected patient safety and quality of care. Our participants regularly linked these challenges to absent or inadequate digital solutions for accessing and sharing CPI across healthcare services. This complements a qualitative study of clinicians' perspectives, that revealed multiple areas in which the lack of interoperability led to ineffective processes and a lack of data in care coordination and transitions (Samal et al., 2016).

Another main challenge was excessive time consumption. This finding complements a 2020 review of nurses' time use *after* the implementation of health technology, that shows how nurses, after implementation, use more time documenting but less time administering medications, and that this in sum enables more time with the patient (Moore et al., 2020). Our findings complement this review by documenting how actual health professionals in Norwegian nursing homes and home care services experience their time use *before* the implementation of the SCR and SML.

Another finding was that limited access to CPI caused uncertainty about the correctness of the information at hand. This finding complements a cross-sectional study from the U.S. that evaluated the completeness and timeliness of information transfer and communication between a hospital and a post-acute care facility (PAC). The study reported that nurses and clinicians at the PAC experienced substantial deficits in content and timeliness of health information exchange (Jones et al., 2017). Another study from Sweden reported that both human limitations and technical deficiencies could lead to medication errors and patient harm (Bengtsson et al., 2021). Our findings complement both these studies, by

documenting how problems concerning information timeliness and correctness are experienced by actual health professionals in a Norwegian nursing home and home care setting before the implementation of the SCR and SML.

A similar problem was the frequent incomplete or delayed approval of discharge summaries from hospitals. As with the abovementioned limited access to CPI, this was also perceived as a major source of uncertainty. In addition, it was linked to frustration, and dependency. This finding complements Samal et al., who claim that the completion of structured discharge summaries before discharge from hospital should be one of the main targets for quality improvement (Samal et al., 2016). We complement Samal's point about discharge summaries and quality improvement, by showing different ways in which incomplete discharge summaries are experienced by actual health professionals in a Norwegian nursing home and home care setting before the implementation of the SCR and SML.

E-messages were commonly used in communication between nurses, MDs and general practitioners (GPs) in our study, to clarify a patient's medications and/or the need for observation. Some participants experienced quick answers from the GPs, although many reported that it could take days or even weeks to receive an answer to a question or clarification. Two Norwegian studies explored the impact of electronic messaging on patients in patient transition, and concluded that the introduction of e-messages, as well as information and communication technology, can support the work of nurses in the transition situation and benefit patients (Hellesø et al., 2016; Melby et al., 2015). Our study provides important nuances to these previous studies, as e-messages have certainly eased communication challenges, especially between GPs and nurses in home care, but limitations concerning CPI access and exchange is still a main issue and source of frustration and uncertainty among nurses and MDs.

In our study, both nurses and doctors reported that they often had to handle unnecessarily complex situations resulting from limitations in the access to and exchange of CPI, and that they considered this complexity as a threat to patient safety. This finding is in accordance with previous Norwegian studies reporting how inadequate information exchange poses a threat to patient safety, since fragmented patient information and

poor communication with and between services can lead to potentially harmful medical/medication errors (Frydenberg & Brekke, 2012; Remen & Grimsmo, 2011). Our results also complement a qualitative study from the US, which explored nurses' perspectives on improving information exchange between hospitals and home healthcare, and revealed the following challenges: ineffective communication, technological factors, poor medication management, and different patient factors (Sarzynski et al., 2019). Our findings complement these studies by documenting how challenges are experienced as an increase in complexity by actual health professionals in Norwegian nursing home and home care settings.

Considerations of Methodology and Design

We used a qualitative research design to obtain in-depth knowledge on the experiences of nurses and MDs in relation to obtaining and sharing CPI in their everyday work. This approach was chosen in consideration of our aims for the main study. We did not aim to provide a final and conclusive answer to our research question, but to explore the research topic in depth (Malterud, 2001a, 2001b). A recent review of factors for the success and failure of eHealth interventions supports our approach to perform in-depth studies of the workflow(s) that an intervention is intended to support, and to evaluate the clinical processes involved (Granja et al., 2018). By providing in-depth knowledge on health professionals experiences before SCR and SML implementation, we provide a context for our planned follow-up studies after implementation. Our research also contributes to the realization of the Norwegian eHealth strategy, which states that research-based knowledge on the intersection of health, technology, organization and society is a key tool for decision making and shedding light on the effect of eHealth interventions (The Norwegian Directorate of eHealth (NDE), 2018).

Our study is limited in terms of a relatively small number of participants and only six municipalities, meaning that we are not able to state how *widespread* the identified perceptions are among health professionals in Norwegian nursing homes and home care services. However, the research design enabled in-depth mapping and understanding *actual*

nurse and MD experiences of the challenges in obtaining and sharing CPI. By aiming for balance among large, medium and small municipalities from both urban and rural parts of Norway, we have also tried to secure breadth in our findings. As such, our included participants and municipalities may serve as a cross section of the Norwegian primary care services. The identified challenges may be similar and transferrable to other countries planning new national eHealth implementations, especially those with a health and social care system similar to that in Norway.

To comply with research ethics rules concerning personal information and the privacy of participants, we were not directly involved in the recruitment process. We contacted each municipality through its healthcare authorities to establish a good and solid relationship for the main national study, and had a local contact person handle the initial recruitment in each municipality. All participants were able to withdraw from the study with no explanation needed, and recruitment was voluntary. All in all, we assess the risk of participation bias to be low in this study.

Conclusion and Future Research

Equipped with accurate and updated CPI, health professionals can act with precision and confidence as participants in complex and fine-tuned co-operation, oriented towards the delivery of health services tailored to a patient's needs. Our results show that having access to accurate and updated CPI is not always the case in primary healthcare in Norway. The current digital solutions limit an effective utilization of health sector resources, and digital interaction is not fully prevalent. In Norway, most nursing homes and home care services do not yet have access to a summary care record (SCR), although the implementation process and the use of SCR have now started in some municipalities. The shared medications list (SML) is at present being piloted in one municipality in Norway, and a full national rollout is planned in 2023–2025. In this situation, our chapter provides important new insights into how the present challenges are experienced by nurses and MDs in nursing homes and home care services in six municipalities in Norway. We found that accessing CPI was

widely experienced as challenging among the participants. It was linked to frustration, uncertainty, unnecessary time-consumption and complexity, and was perceived as a threat to patient safety and to quality of care. Based on our findings, we contend that future eHealth initiatives aimed at improving quality and safety in healthcare must address these challenges in accessing CPI directly, especially in the critical phase of patient transition between levels of care. The knowledge presented in this chapter will serve as a baseline for the longitudinal main study on the implementation of SCR and SML in Norway. Our findings will enable monitoring the effects, limitations and possibilities of ongoing and planned national eHealth initiatives. The next steps following this pre-study of SCR and SML implementation will be to investigate the experiences of nurses and MDs *during* and *after* the implementation of the SCR and SML in the same six municipalities.

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CHAPTER 13

Work Interruptions as a Source of Knowledge When Nurses Administer Medicines in Nursing Homes: Hermeneutic Approach to Narratives

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Abstract: Nurses administer medicines amidst constant interruptions. They must simultaneously perform other tasks, such as direct patient care or addressing system failures. However, there is a lack of research relating to nurses' perspectives on these work interruptions: what they are, and what they are not. The purpose of this chapter is to elucidate nurses' perspectives on and experience of work interruptions, as well as discuss the significance of their perspectives for safe drug management among nursing home residents. The study has a qualitative design. Data consisted of narratives on work interruptions shared by nurses. The narratives were analyzed, and a sample narrative was developed using Gadamer's hermeneutical circle. The narrative stems from several years of experience as a nurse administering medicines in nursing homes, and as a researcher doing field studies, along with testimony developed from narratives nurses shared on how they view work interruptions during medicine rounds. In a sample narrative, a nurse reflects on administering medicines during constant interruptions in a somatic ward in a Norwegian nursing home. The residents' needs define whether a work interruption is a work interruption, or a source of knowledge important for medication treatment and care in nursing homes.

Keywords: work interruption, medicine administration, nursing homes, nurses, narrative, source of knowledge

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In healthcare services worldwide, nurses administer medicines amidst constant interruptions (Alteren et al., 2018; Biron et al., 2009; Cottney & Innes, 2015; Thomson et al., 2009; Trbovich et al., 2010). Work interruptions are caused by breaks in the activities being performed in order to carry out a task: for example, direct patient care or addressing system failures, such as missing medicines (Alteren et al., 2018). In Norway, the health and care services in municipalities have an overall responsibility for ensuring safe drug use among the residents of nursing homes. In terms of daily activities, it is the nurses who have the closest contact with residents and who follow-up their drug use.

The theme chosen for the current chapter was developed from nurses' experiences relating to administering medicines in the healthcare services in Norway. Nurses shared narratives in which they described and reflected on work interruptions while they administered medicines. Their reflections served as documentation of their ideas on work interruptions: what they are, and what they are not. Nurses' perspectives on work interruptions during medicine administration, and their significance for responsible and safe drug handling, must receive greater attention in order to achieve best practices.

Background

Work Interruptions During Medication Administration

Work interruptions (WIs) are common, and frequently cause problems during medication administration rounds (Alteren et al., 2018; Getnet & Bifftu, 2017). Further, WIs generally have negative consequences for patients' safety and outcomes, employees' well-being and performance, as well as a country's resources (Alteren et al., 2018; Getnet & Bifftu, 2017; WHO, 2016). Nurses are rarely able to complete nursing activities without being interrupted (Alteren et al., 2018; Biron et al., 2009). An observational study on work interruptions during medication administration in nursing homes concluded that work interruptions happen four or five times per hour (Lee, et al., 2015). The findings of several studies in

hospitals have described nurses' colleagues, other staff, and nurses themselves performing other activities, as the most common sources of interruptions during medication administration (Alteren et al., 2018; Schroers, 2018; Schutijser, et al., 2018). In nursing homes, the residents are the major source of work interruptions, especially during the administration phase (Lee et al., 2015).

Odberg et al. (2017) describe interruptions during medication administration in nursing homes. Interruptions are prevalent and can be characterized as passive, for example alarm and background noises, or active, such as discussions or technological interruptions, such as use of mobile phone apps. In hospital environments, perceived interruptions from patients, and telephone calls seemed to be the most problematic (Schroers, 2018). However, few interruptions are related to medication tasks, demonstrating a considerable opportunity to reduce unnecessary interruptions (Westbrook, et al., 2017).

Safe Administration of Medicines

Patient safety is defined as freedom from harm and adverse events while receiving healthcare (WHO, 2020). Odberg et al. (2017) have observed factors that contribute to the complexity of medication administration in nursing homes. Factors observed were: the high number of single tasks; varying degree of linearity; the variability of technological solutions; demands regarding documentation; and staff's apparent freedom as to how and where to perform medication-related activities. Five categories are identified as work system factors affecting medication safety in nursing homes (Dilles et al., 2011; Pharm & Doucette, 2017). These are: persons; residents and staff, organization; tools and technology; tasks; and environment; staff distraction and interruptions. While preparing, administering and monitoring medication, being interrupted, not knowing enough about interactions, and barriers to interdisciplinary cooperation, caused the most hindrances (Dilles et al., 2011).

Studies conducted in hospitals have examined the safe administration of medications by nurses to inpatients, despite the challenges in their working environment (Alteren et al., 2018; McLeod et al., 2015). In their

study, Alteren et al. (2018) found that when nurses were interrupted, they left the medicine round, and then subsequently re-entered the procedure. Nonetheless, they managed to re-focus and continue to administer the medication. Interruptions and disturbances made little difference to the behavior and actions of experienced nurses. McLeod et al. (2015) identified three interrelated themes in the work environment, which both facilitated and impeded safe medication administration. The first relates to specific configurations and features of the ward-based medication system, which in turn could influence nurses' behavior in terms of workflow. The second pertains to how nurses manage interruptions and distractions, and the third involves nurses' interaction with patients.

Strategies for Handling Interruptions

Medication administration is typically considered inseparable from other nursing work and embedded in their day-to-day activities (Odberg et al., 2018; Sitterding, 2014). The nurse's role is compensating, flexible and adaptable (Odberg et al., 2018). Nurses individualized their coping strategies and techniques, either by multi-tasking, engaging with the task (Alteren et al., 2021; Jennings et al., 2011; Sitterding, 2014; Sitterding et al., 2014), or focusing solely on patient interactions (McLeod et al., 2015), depending on the complexity of the task and their nursing experience (Colligan & Bass, 2012). Some nurses use the medicine round as an opportunity to interact with their patients, in addition to the administration of medicines (McLeod et al., 2015). McLeod et al. (2015) observed that nurses appeared to have a general inherent tendency either to be primarily "task-focused", where the main goal was to administer medicines as efficiently as possible, or "patient-interaction focused", where the medicine round was an opportunity to interact with their patients in addition to the administration of medicines. Colligan and Bass (2012) found that nurses prioritized task execution based on both risk and workflow efficiency assessments. Handling interruptions depended on both task and experience.

To handle these interruptions and the ward organization in hospitals, nurses developed their own personal strategies to overcome

inherent problems with their working conditions, the absence of effective management, and colleagues' reluctance to assume responsibility for minimizing interruptions (Alteren et al., 2021). Odeberg et al. (2018) describe a dynamic interaction between several contributory factors in nursing homes: shifting responsibility; need of competence; invisible leadership; varying available competence; staff stability; and vulnerable shifts.

Nurses can divide their attention efficiently across several resource-demanding tasks (Alteren et al., 2018; Sitterding, 2014; Sitterding et al., 2014). For example, they can simultaneously walk and make patient-related decisions, administer medicine whilst answering the phone, notice another patient's physician and decide to engage with them while administering intravenous medicine (Alteren et al., 2018; Sitterding, 2014; Sitterding et al., 2014). In another study, managing time was the dominant strategy for handling interruptions (Jennings et al., 2011). In addition to their own strategies, nurses must adhere to the organization's expectations of how interruptions were to be handled (Sitterding et al., 2014). Maximizing patients' satisfaction could weigh against patient safety. For example, nurses judged when it was more important to stop to answer a call light, than to administer medicines on time.

Previous research sheds light on interruptions and how the nurses deal with them during the distribution of medicines, as well as errors as a result of interruptions, and the consequences these errors may have for the patient's safety, mainly in a hospital setting. However, how the nurses experience their own work situation, and the importance of interruptions to patient safety is, only to a small extent, present in previous research. The ongoing discussion regarding the importance of nurses' perspectives for patient safety requires an elaboration of their perspective, within the municipal setting. Drug management is the nurses' responsibility, and knowledge regarding their perspective provides essential information on how to increase patient safety in nursing homes and reduce severe avoidable medication-related harm by 50% globally by 2022, a figure set by WHO (World Health Organization, 2016; 2020). The purpose of this chapter is to elucidate nurses' perspectives on and experiences of work interruptions: what they are, and what they are not, as well as discuss

the importance of their perspectives for safe drug management among nursing home residents.

Research Methodology

Data Collection

The narrative "Losing Concentration on the Medicine Round" is a sample narrative representing the nurse's perspective when administering medicines in a nursing home. This narrative stems from several years of experience as a nurse administering medicines in nursing homes and as a researcher doing field studies, along with testimony developed through several field studies. During the field studies, I collected narratives of how nurses experience work interruptions during medication administration.

The nurses represented in this study, were purposely selected to participate in the different field studies relating to different perspectives on administering medicines. In the field studies, I followed the nurses through their shifts, where administering medicines was one of their areas of responsibility. The nurses shared narratives on their views of work interruptions during medicine rounds. The narratives were recorded and transcribed by me. After a day in the field, I wrote field notes regarding our reflections on the theme and personal notes regarding my reflections and thoughts related to interruptions during medicine rounds.

The Context of the Study

In this chapter, the field of action was a somatic ward in a Norwegian nursing home. The nursing home consisted of four wards, 20 residents living in each ward. Three of the wards are somatic wards, while one ward is for the demented. The representative nurse in the narrative has been given a fictitious name, Bente. She has worked as a nurse for 12 years, seven of them in nursing homes. Bente works in a somatic ward where she has the responsibility to administer medicine to 15 women and five men. The residents live alone in one-bed rooms. The age of the residents is between 68 and 92. They have multiple diagnoses and to varying degrees need help with basic nursing.

In the daytime, there are often two nurses at work, but in the evening and night shifts, there is only one nurse. In daytime, there are all together five healthcare personnel at work, including Bente. In addition, there is a ward nurse, who has the overall professional and administrative responsibility for the staff and care in the ward. Bente administers medicines twice during the day shift, during breakfast from 8.30 a.m., and dinner from 1.30 pm. She administers medicines from a drug trolley.

Research Approach

The narratives were analyzed using the hermeneutic circle described by Gadamer (2003). The hermeneutic circle is a philosophy of interpretation involving a dialectic transition between the whole and the parts – between the phenomenon being interpreted and the environment, as well as the phenomenon and one's personal prejudices that influence this interpretation. The narratives relating to interruptions during the administration of medicines were brought together interpretively by constructing a narrative that was grounded in their actual experiences, and was representative of the participants. In the interpretation the analysis moved towards understanding the essence of the narratives and of the nurses' working situation.

I read the narratives without trying to attain an overall impression of the content. When I read them again, I tried to form a picture of the central idea in the narratives. Starting with my first experience and understanding of the narratives, I read the narratives again. In the next round, I interpreted these descriptions in relation to my first understanding of the content of the single narrative, as well as a holistic perspective of the narratives. In this process, I combined my own narrative with the nurses' narratives in order to develop a narrative representing our common experiences. This draft, the narrative, was constantly edited considering what emerged as I explored the theme further. This process resulted in the constant composition of a new draft narrative, describing the nurse administering medicines during constant interruptions in a somatic ward in a nursing home.

The result of the analysis was the sample narrative: "Losing Concentration on the Medicine Round", which is presented below. In the analysis,

I extensively explored Bente's reflections on administering medicines in the situation in which she found herself. By providing a further analysis and reflection on this narrative, I seek to amplify the nurse's perspective on work interruptions during medicine rounds, as well as their significance for patient safety.

Ethical Considerations

The research projects were approved by the Norwegian Centre for Research Data, NSD. The researcher requested participation, verbally and in writing, from the nurses participating in the field studies. The nurse leader explained the study and asked the nurses if they wanted to participate, and they gave verbal and written informed consent. They received the assurance that participation was voluntary, and they could withdraw from the studies whenever they wanted to without consequence or having to explain why. No one withdrew from participation during the studies.

Losing Concentration on the Medicine Round: A Sample Narrative

The situation I am going to tell you about is typical for distributing medicines in the ward. This is when the residents have their breakfast. The residents need their medicines in the morning. Administering medicines during breakfast requires time and concentration. When I administer medicines, I follow my own and the ward's routines, and I follow a specific route. Before I start the medicine round, I check the medicine in the dose distribution system according to the medicine journal. I find the medicine that is not in the dose distribution system in the medicine room or the refrigerator. I prepare the drug trolley and bring with me the medicine journal, glasses, and a jug of water.

Normally, I begin distribution of medicines in the living room, where most of the residents have their breakfast. Sometimes residents ask me

for help getting to the living room, either by using the alarm clock or asking me for help. Then, I interrupt the medicine round: close, and lock the drug trolley and help the resident. Other times, residents may ask for painkillers. I check which medicine they can get in the medicine journal, and if the painkillers are in the dose distribution system. If not, I interrupt the medicine round and return to the medicine room for the resident's painkillers. When I return to the living room, there are often colleagues requesting medicines on behalf of other residents. In the living room, I distribute the medicines based on where the residents are placed. While I hand out, colleagues can ask for medicine for the residents eating their breakfast. Other nurses who help residents with care can ask for painkillers. Again, I check the medicine journal, find painkillers, and sign the medicine journal before I give the medicine to the resident.

Interruptions from colleagues happen many times every day, and mostly I find them disturbing. When I prepare the medicine round, I am very concentrated. When I am disturbed, I lose concentration. I must work my way into the procedure again, and that takes time. There are situations where I am not interrupted, when I administer medicines the way I find appropriate. I do not experience it as an interruption when communicating with residents, serving coffee, or bringing the residents water. But sometimes there are too many tasks like this. Then I experience them as interruptions, and I lose concentration.

Many interruptions like this, not only in the living room, residents' rooms, and corridors, but also in the medicine room, delay distribution and increase time pressure. The consequence might be that the residents do not receive their medicine at the right time. Other disturbances where I lose concentration are when I must interrupt distribution and answer the phone or an alarm clock. There is a doctor's visit every Wednesday. Sometimes the doctor comes earlier than the predicted routine, and other times I am so late that I am not done with the medicine round. The interruptions delay and shift the work I am responsible for in the ward. This applies not only to administering medicines. Patients do not receive their medication on time, which has consequences for treatment, care, and patient safety.

The Narrative: Interruptions as a Source of Knowledge

In the narrative, a nurse administers medicines to residents amidst constant interruptions. Through the narrative, she reflects on being interrupted, and how she defines and handles the interruptions. In the narrative, the interruptions are caused by breaks in the activities being performed in order to carry out a task: for example, helping residents to the living room for breakfast and serving coffee. The nurse states that she is concentrated and focused. When she is disturbed, she loses concentration. At the same time, the nurse feels that the interruptions are not experienced as interruptions when she finds them appropriate. It depends on the situation and to what extent the nurse needs information about the patient, relevant to the patient's use of medication.

Discussion: Work Interruptions as a Source of Knowledge

There are many sources of interruptions in the nursing home ward (Lee et al., 2015; Odberg et al., 2017). Odberg et al. (2017) characterized interruptions in nursing homes as passive, active, and technological. The major source of work interruptions was the residents, especially during the administration phase (Lee et al., 2015). This chapter highlights in particular, residents, nurses, head nurses, relatives, the nurses themselves, and the ward's daily routines as sources of interruptions. The ward's daily routines are planned to be carried out in time periods. An example is breakfast, which is served between 8.30 and 9.30 am. During this period, many of the residents are gathered in the living room where breakfast is served. It creates a limited area for the interruptions, which both hinders and contributes to interruptions. It hinders interruptions, as many of the residents are gathered in a limited area. The nurses have an overview of the situation and can distribute medicines in a concentrated manner. At the same time, many people in a room creates more activity, as well as inquiries from residents and other healthcare professionals, which can also contribute to interruptions. This two-sidedness places demands on

the nurses when it comes to staying concentrated on the task they are to perform. Three interrelated themes are identified in the work environment in hospitals, which both facilitated and impeded safe medication administration (McLeod et al., 2015). They are: the wards medication system; how nurses manage interruptions and distractions; and nurses' interactions with patients. The findings in this chapter show that when Bente administers medicine during constant interruptions, she moves between holding onto and losing concentration regarding the medication and the resident concerned.

Bente said that she must interrupt the distribution of medicines and perform other tasks not relevant to the distribution of medicines. Findings indicate that performing nursing tasks is more of a normal condition than an exception, which is supported by other research (Alteren et al., 2018). The consequences of WIs are generally negative for patients' safety and outcomes, employees' well-being and performance, as well as a country's resources (Alteren et al., 2018; Getnet & Bifftu, 2017; WHO, 2016). When Bente must interrupt distribution, close and lock the medicine trolley, she loses her concentration and her plan for distributing medicines. Alteren et al. (2018) found that nurses subsequently re-entered the procedure and managed to re-focus and continue to administer the medication. Further, research showed that interruptions and disturbances made little difference to the behavior and actions of experienced nurses. Nevertheless, these interruptions can create a domino effect, in which the rhythm of the ward is disturbed, and the nurses fall behind in other nursing tasks for which they are responsible, such as follow-ups of the dying and their relatives, or more specific tasks, such as wound care. The consequence is missed nursing care in the form of delays in order to complete necessary patient care (Abdelhadi et al., 2021).

At the same time, Bente states that whether she experiences the task as an interruption depends on what tasks she has to do, and whether the tasks are relevant to the resident's medical treatment. Research in hospitals show that some nurses used the medicine round as an opportunity to interact with their patients in addition to administering medicines, defined as patient-interaction focused (McLeod, et al., 2015). This chapter shows that it is the patient's needs that define whether an interruption is

an interruption. Bente did not experience the situation where she helped a resident from their room to the living room as an interruption. The situation became an opportunity to observe the resident's physical and mental condition, and the effect of the medication. The knowledge she obtains is, for example, whether the painkiller the resident received at six o'clock has had an effect or not.

Drug handling involves more than the technical, such as physically taking the tablets out of the glass and giving them to the resident. Competence in drug management is complex (Sulosaari et al., 2010) and involves knowing which drug the resident receives, the effect, side effect, and why the resident is receiving that particular drug. Competence in drug management involves 11 areas of knowledge (Sulosaari et al., 2010). These areas of knowledge are described as: anatomy and physiology; pharmacology; communication; interdisciplinary collaboration; information retrieval; mathematical and drug calculations; drug administration; drug management; summary and evaluation; documentation; and establishing drug management as part of the resident's safety. The areas of knowledge are connected through handling medicines, and the knowledge the nurses must master to be able to handle medicines safely.

A theory of knowledge developed by Aristotle, among other things, distinguishes between different forms of knowledge (2006). These are: episteme, theoretical-scientific, techne, skill knowledge, and phronesis, practical knowledge. Knowledge about the diagnosis of rheumatism and how the disease is expressed is defined as episteme. Bente is aware that a resident diagnosed with rheumatism has pain, and may be stiff in their joints and muscles in the morning, which can lead to unsteady walking. Knowledge of how to help the resident from their room to the living room is defined as techne. In addition to using theoretical knowledge about the patient's illness, Bente uses her thinking to find out how she should concretely perform the action, so that the walk to the living room is as comfortable as possible for the resident. Through conversation and the resident's body language, Bente experiences and observes the resident's pain and gait. Phronesis is to act wisely based on the specialness and uniqueness of the situation. When Bente helps the resident, these three forms of knowledge are integrated and her overall knowledge about the

resident's state of health is developed. This knowledge becomes important for the nurse's assessment and decisions on new measures.

For Bente, these tasks do not constitute interruptions, but a situation where she acquires knowledge about the resident, which is relevant and related to medication management, and the responsibility she has for medication management in the ward. Conversations with other healthcare professionals are also examples of situations where knowledge is obtained about the resident's condition. Healthcare personnel who, for example, have helped a resident and ask for painkillers can convey to Bente the resident's degree of pain, and how the resident is functioning today. This knowledge is important in order to be able to follow up their treatment. This knowledge can also mean that Bente should have a conversation with the patient later, as well as convey the observation to the doctor for further medical treatment.

Interruptions that are not relevant nor can be linked to medication management and responsibility for the resident are experienced by Bente as interruptions. Helping a resident who is stable onto the toilet, or situations where there are no reasons for extra observation are examples of interruptions. Serving coffee and food to the residents during breakfast when there are other healthcare personnel responsible for the task, is another example. Focus is removed from medication management and the nurses lose concentration. There will be a break in the train of thought in which the nurses make observations, on the medication and how the resident works in context, integrating the knowledge that is relevant to the patient (Aristotle, 2006). An interruption creates a break in this cognitive thought, and the nurses lose concentration.

Conclusions

The resident's needs define whether a work interruption is a work interruption or a source of knowledge important for medication treatment in nursing homes. When nurses administer medicines, they simultaneously give medicines and acquire knowledge about the resident's health. Interruptions as a source of knowledge should therefore receive greater attention in the organization of medication administration, especially

aimed at interruptions related to caring and medical treatment. Greater attention to interruptions as a source of knowledge also contributes to increased knowledge about the patient, safeguarding patient safety. This knowledge forms the basis for the nurse's assessments and decisions about further treatment and care, as well as aiding the development of evidence-based practice in nursing homes. A change in focus requires management, and an organization in which tasks that are not related to medication treatment and care are handled by other professionals than nurses.

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Part Four:

Systems and Practices of Medication

CHAPTER 14

Facilitators and Barriers to Safe Medication Administration in Nursing Homes

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Abstract: Medication administration in nursing homes is a complex and dynamic process, in which the characteristics of the socio-technological work system interact and adapt according to shifting circumstances. Therefore, safe medication administration entails a broad set of tasks and interactions conducted by healthcare professionals, and the process is influenced by a complex web of facilitators and barriers. In our study of two Norwegian nursing home wards, we identified a total of 60 facilitators and barriers to safe medication administration. Several facilitators and barriers were intertwined, meaning that they could act as both facilitators and barriers depending on situational factors in the nursing home's work system.

Keywords: Nursing home, patient safety, medication administration, facilitators and barriers

The majority of the approximately 40,000 nursing home patients in Norway are long-term residents aged 80 or older. They are cared for by approximately 140,000 full-time registered nurses, nursing assistants and other healthcare personnel (Ministry of Health and Care Services, 2015; Statistics Norway, 2019). Although there are few systematic efforts to map

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and describe adverse medication events in Norwegian nursing homes, the assumption is that a significant number of adverse events related to medication administration occur here.

Therefore, the objective of this chapter is to describe the facilitators and barriers to safe medication administration in nursing homes using a human factors approach.

Traditionally barriers are viewed as factors that may hinder or impede actions that may result in adverse events. This chapter considers barriers as factors that may hinder safe care, and cause adverse medication administration events. Facilitators are regarded as factors that facilitate or improve the medication administration process.

The chapter is based on the results from a PhD thesis entitled, "A Human Factors Approach to Medication Administration in Nursing Homes" (Odberg, 2020), in which a re-analysis using narrative synthesis has been conducted, offering new insights into the medication administration process in nursing homes.

Medication Administration Events

Older patients are vulnerable to adverse drug events due to individual factors, such as frailty, disability, comorbidity, drug interactions and a high prevalence of polypharmacy. Also, high potency drugs such as opioids, antipsychotics, antidepressants, antiepileptics and anti-infectives increase the risk of cognitive impairment and falls (Al-Jumaili & Doucette, 2017; Field et al., 2001; Herr et al., 2017; Violan et al., 2014).

Patient safety literature describes the following system-level factors affecting the risk of adverse drug events (Al-Jumaili & Doucette, 2017):

- staff competence
- indistinct procedures
- inadequate staffing
- high workload
- time pressure
- interruptions
- ineffective interprofessional collaboration

These factors are supported by findings from audits by the Norwegian Board of Health Supervision (2010). They found deviations from standards in medication management in 51 out of 67 (76%) of the nursing homes audited. The deviations included: unclear lines of responsibility; time pressure; lack of competence; poor interprofessional collaboration; variations in observing and documenting the effects of medications; poor availability of vital patient information due to multiple documentation systems; and separate documentation systems for the medical doctor.

International literature indicates that 13%-31% of all nursing home patients experience some form of medication administration error. Simultaneously, the incidence of severe adverse drug events is low (Al-Jumaili & Doucette, 2017; Ferrah et al., 2017). In Norway, there is no available information on medication administration events in nursing homes or in primary healthcare in general.

The Medication Administration Process

The medication administration process is well documented to be complex and dynamic across healthcare domains, and this also holds true in the nursing home context (Carayon, et al., 2014). Traditionally, nurses are taught to practice the six "rights" of medication administration: 1) right patient; 2) right medication; 3) right dosage; 4) right route; 5) right time; and 6) right documentation (Yoost et al., 2015). The nurse plays a central role throughout the medication administration process (Jennings et al., 2011; Odberg et al., 2019). Specific tasks related to medication administration are often difficult to separate from work processes of daily care. To structure and describe the medication administration process, it may be deconstructed into six consecutive stages:

1) **Ordering** is when the physician decides what medicines to prescribe, with details such as dosages and timing. This is often done in collaboration with the registered nurse.
2) **Transcribing** is the formalizing of the orders into forms or an electronic medication administration system.

3) **Dispensing** is when the registered nurse checks the medication list against the electronic medication administration system and dispenses the medicines into pill boxes.
4) **Preparing** is when the registered nurse readies the medication for ingestion and performs a double-check before administration.
5) **Administering** is the actual delivery of medications to patients.
6) **Observing** entails monitoring the patients for effects after they take the medicines, and the subsequent documentation.

The following flowchart (Figure 1), is based on observations of the medication administration process in two Norwegian nursing homes, visualizing the dynamic flow and intrinsic complexity of delivering medications to nursing home patients (Odberg et al., 2017). The stages of the medication administration process are vertically listed on the left side in Figure 1, while on the right side are corresponding elements detailing tasks and interactions.

Human Factors and Patient Safety

To gain further knowledge of the complexity of the medication administration process in nursing homes, including the facilitators and barriers to safe medication administration, a socio-technical systems approach is useful. *Human factors* embodies a systems approach concerned with designing safe and effective systems with human beings at the core (Dul et al., 2012). Carayon et al. (2006) describe a human factors system engineering model promoting patient safety, the System Engineering Initiative for Patient Safety (SEIPS model). The basis of the model lies in the interacting elements of the work system, as shown in Figure 2. The five elements of the work system: persons, physical environment, tasks, tools and technology, and organization, do not exist as isolated cells. Still, they interact in often subtle ways and must, therefore, be seen as a whole. These elements interact when humans engage in healthcare processes, such as medication administration in nursing homes, to produce specific outcomes. Outcomes may be positive or negative consequences of different processes in the work system. An example of a negative outcome is

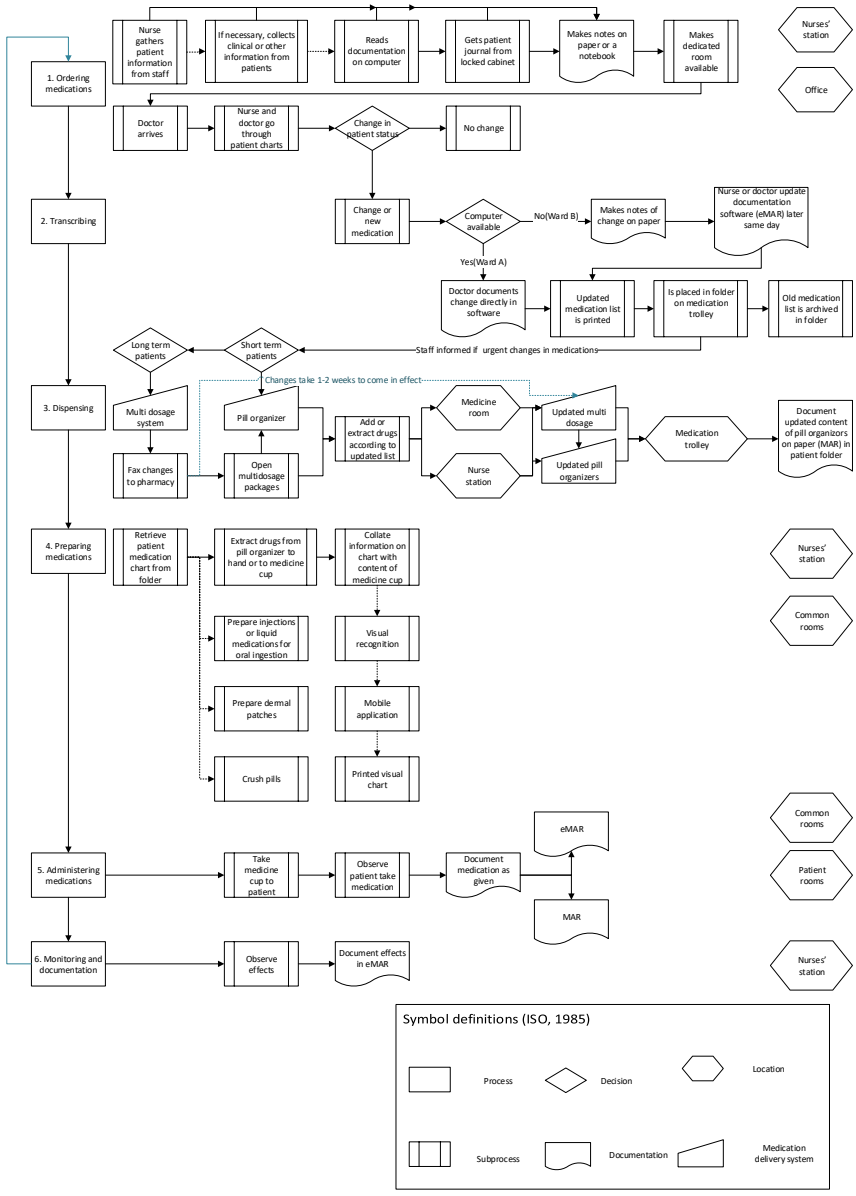

Figure 1. Flowchart of the Medication Administration Process in Nursing Homes (Odberg et al,. 2017)

an adverse drug event, while a positive outcome can be safe and effective medication administration.

The five elements of the work system can be described as follows (Carayon et al., 2006; Dul et al., 2012; Holden et al., 2013):

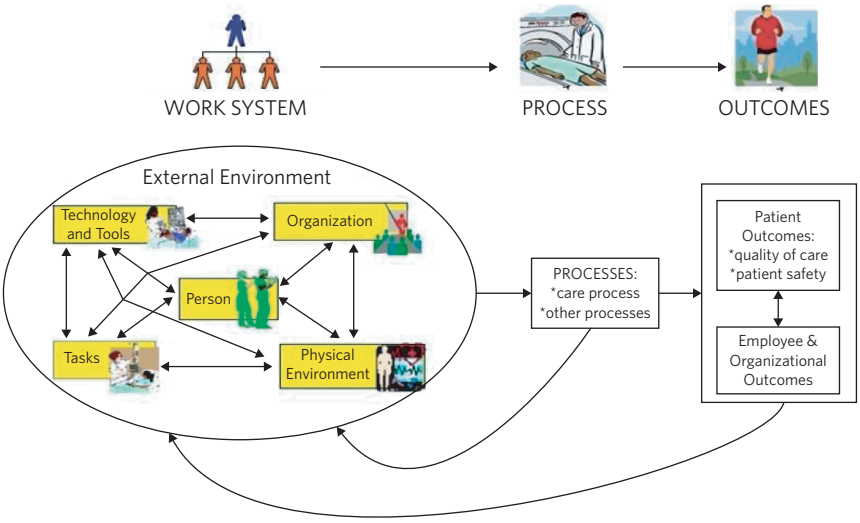

Figure 2. The SEIPS Model (Carayon et al., 2006)

Persons are at the center of the work system and represent the stakeholders involved in a given process: patients, next of kin, registered nurses, physicians or other healthcare professionals. These individuals exhibit cognitive, physical, and psychosocial characteristics, such as age, experience, competence, knowledge, training or education.

The physical environment represents the characteristics of the facilities in which healthcare workers provide care, including: noise, temperature, lighting layout, distances and air quality.

Tasks are the specific activities within different work processes, such as medication administration, and are characterized by attributes describing difficulty, complexity and variety.

Tools and technology specify how healthcare workers utilize equipment and medical devices, such as medical electronic administration records, blood glucose meters or tools to mobilize patients. Typical features relate to the usability, familiarity, functionality and portability of various equipment.

Organization indicates the collective structures that guide and organize activities, resources, time and space. Typical examples are work schedules, management type, policies or patient safety culture.

Human factors provides insights into healthcare processes by offering distinct, descriptive opportunities to simplify and visualize complex systems and processes. Using the work system of the SEIPS model as descriptive categories facilitates structuring the medication administration process.

Methodology

The PhD thesis on which this chapter is based used a QUAL-qual mixed methods study design (Morse, 2016). The main component (QUAL) was 140 hours of observations, while the supplemental component (qual) consisted of 16 individual interviews (Odberg, 2020).

By conducting a re-analysis of data using a narrative synthesis (Thomas & Harden, 2008), this chapter offers new insights into the medication administration process by further reflecting on the work system complexity of nursing homes, and how this influences the safety of medication administration. New data is presented in the form of quotations throughout the results section below.

Two different nursing home wards in different municipalities were recruited to capture some of the variability in Norwegian nursing homes. They were one urban palliative care nursing home ward (A), and one rural nursing home ward (B) catering to persons with dementia. The inclusion criteria for participating in the interviews were that staff members had a role in the medication administration process and were employed in at least a 50% position. In all, sixteen participants agreed to be interviewed, including special care nurses, registered nurses, nurse managers, medical doctors, physical therapists, and nursing assistants.

Data was collected through 140 hours, distributed between participant field observations spread evenly across wards A and B (QUAL), and semi-structured individual interviews (n = 16) (qual) with healthcare professionals dispersed across wards A and B. An interview guide and an observation guide based on the work system of the SEIPS model were used. Inductive and deductive qualitative content analyses inspired by Elo and Kyngäs (2008) were performed.

Ethics

All participants were informed about confidentiality and of the right to withdraw at any time. The study adhered to ethical guidelines and was approved by NSD (NO: XX).

Results

The study confirmed the picture of medication administration in nursing homes as a complex and dynamic process, in which the characteristics of the socio-technological work system interact and adapt according to shifting circumstances. The medication administration process according to the six stages (Figure 1) was found to contain 60 facilitators and barriers to safe medication practice. Throughout the process, the nurse plays a central role, compensating for variations in the work system, while demonstrating great flexibility in meeting the demands of the patients.

A nurse described how the workplace had transformed with increasing complexity during the past few years:

> Our patients have more complex illnesses than was the case earlier. A few years ago, this was a place for persons with dementia, and they were quite healthy. However, now we receive patients with more diverse and complex illnesses. Everything from heart and lung diseases, atrial fibrillation and all the medications that follow. It has become a lot more taxing to follow up, medically speaking.

While another nurse reflects on the increased workload associated with medication administration:

> The complexity of medication administration varies a lot. We have oral, subcutaneous, and transcutaneous patches. Some patients have tablets, mixtures, patches, and a pump as well … Then it becomes an issue, and you have to sit down and take stock.

Figure 3 is an adapted SEIPS model documenting how the 60 facilitators and barriers to safe medication administration have been condensed into 17 groups, and systematized across the five work-system elements. A +

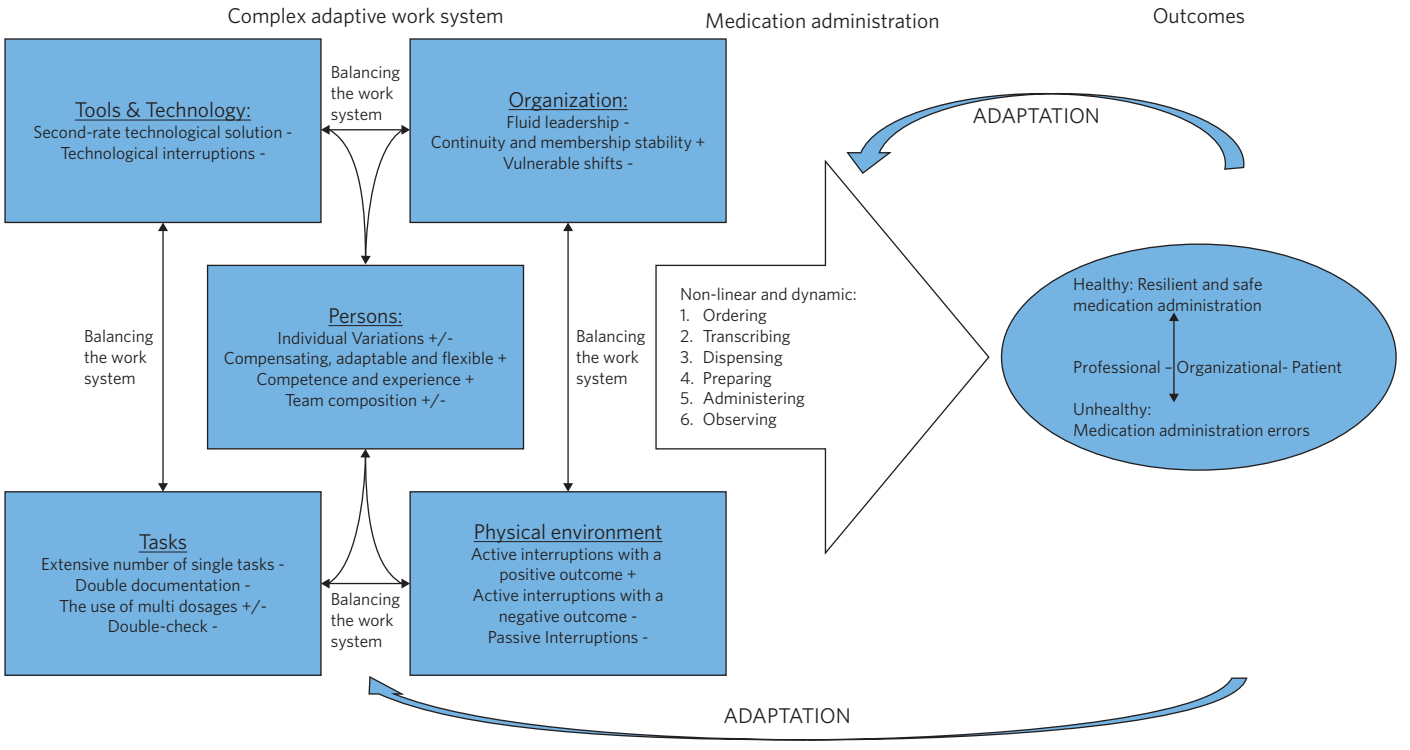

Figure 3. An Adapted SEIPS Model With Key Facilitators and Barriers to Safe Medication Administration

indicates a facilitator, while a – indicates a barrier. Some groups exhibit both, +/-, and thus indicate dual traits that may perform as both facilitators and barriers, depending on the circumstances. Dual traits are a novel element and tied to how individual staff members embody different knowledge and competence, which in turn will influence how they perform their tasks in different situations. For example, the electronic Medication Administration Record (eMAR) is in itself complex, multilayered software, and effective workflow depends on IT skills and knowing specific codes and shortcuts by heart.

Persons

This work-system element focuses on the nurse's role, and how individual variations and differences in competence and experience can function as facilitators or barriers in how staff use their flexibility to modulate team composition, navigate everyday care, and perform medication administration.

In the context of the two nursing homes, different stakeholders were involved at different times of the medication administration process. The main ones included the patients and their informal carers, and professional stakeholders such as registered nurses (RN), nursing assistants, physicians and physiotherapists. The RN's unique role, being involved in all the stages of the medication administration process, was reflected in how RNs took on responsibilities beyond their given assignments to ensure patient care. The RNs expended massive resources navigating everyday tasks in order to perform medication administration of a very high standard. Time pressure, singular responsibility, high activity, and demands for documentation required strict prioritizing. In many instances, the nurse felt constrained by administrative tasks and delegated direct patient care to colleagues. These decisions also impacted the team composition during a shift. A nursing assistant described this collaboration:

> We use each other's strengths and qualities and trust each other, assign tasks and cooperate. Sometimes I have shortcomings, and a nurse is needed; other

> times I can assist them (the nurses) when things are bustling. We cannot relieve the nurses for everything, but I do what I can for them, and that seems to work.

A vital facilitator was identified by three specific characteristics of the RNs: compensatory, flexible and adaptable.

The RNs compensated for the different individual skill sets and competencies of the surrounding staff on a given shift. This dynamic and continuous evaluation led to shifting responsibilities, where the RNs often took on tasks beyond their work description to fulfill all medication-related tasks.

On a given shift, the RN had to be flexible regarding structuring the workday and delegating medication-related tasks. As team members differed from day to day, a particular regard for individual skill-sets and competencies always informed the RN's role. Sometimes lack of skill redundancy on a shift led to vulnerabilities as the single RN prioritized administrative tasks.

The RN constantly adapted to changing workloads and a shifting environment, working with different staff members. Staff stability and good leadership were therefore underscored as essential to minimize stress and ensure good collaboration.

These characteristics were crucial to enable safe medication administration, and showed how tenacious and vulnerable this balancing act of the RN was.

Organization

Three distinct features of the facilitators and barriers stood out under the work-system element of organization (Figure 3): leadership was fluid; membership stability was important; and vulnerable shifts could be critical.

Scattered and fluid leadership was a barrier affecting the day-to-day handling of medications. This was reflected clearly on a team level, where the role of team leader was interchangeable, depending on shifting conditions in the ward. If circumstances arose where the team leader

had to shift priorities, another team leader was appointed ad hoc with a minimal transfer of information. Consequently, the responsibilities of the different team members often appeared unclear, and, in addition, guidelines and procedures to supplement decision-making when needed were inadequate. A nurse manager described how task delegation ideally took place:

> As a leader, I get an overview and assign patients and tasks, and help them structure their workday. The staff is organized into groups with primary care nursing, and I assign them their tasks to the best of my ability. Even though they get assigned to a group of patients, they should be flexible and help each other.

Another example of fluid leadership arose during pre-visitations when an RN as team leader prepared for the ward round with the resident physician. The RNs may have more familiarity with the patients, and sometimes they were more experienced than the physician. Consequently, in some cases, the RNs took on tasks and responsibilities beyond their training and expectations, as they saw it necessary to safeguard the medication administration process.

Membership stability was found to facilitate safe medication management during periods of high activity in the wards. Several staff members reported that working together during extreme conditions led to more effective communication and better task distribution. One may assume that heavy workloads over more extended periods might lead to resignations and higher turnover, but it was also found to be an incentive that induced the staff to find creative solutions and creative workarounds. Membership stability within work groups thus seemed to counter adverse conditions and have a stabilizing effect:

> When you work with someone you do not know or assistants you do not fully trust, you spend much energy caring about their tasks as well. You feel the responsibility of having an overview, since you are unsure whether all tasks will get done the way you would like them to. (Interview with an RN)

Meanwhile, periods of high activity also led to vulnerabilities, as there were few extra resources to handle unforeseen situations. Extreme

situations led to the staff needing to prioritize medications for those patients most in need, while stable and self-sufficient patients received less attention. Sometimes this resulted in missing or delayed medications, and less time to observe, document, and perform generic administrative tasks. Vulnerable shifts as barriers were typically night shifts, weekends, and major vacations that coincided with heavy workloads and unforeseen activities, increasing the perceived risk of medication administration errors. Shortcuts, workarounds, and an acceptance of these inferior working conditions became accepted and normalized by the staff, while they also described such shifts as highly challenging and debilitating. To counter vulnerable shifts, the staff always tried to plan ahead:

> I think they (the nurses) are good at preparing for the night shifts in a way that ensures that all the patients will receive the best possible care. Somehow they get ready if they identify increasing unrest or something else in the ward. If patients are ill, they prepare for the night. They may contact the doctor and arrange a prescription for morphine, and even prepare the medicine itself in advance. (Interview with a nursing assistant)

Over time an acceptance of inferior working conditions and behavior that may deviate from standards and norms seemed to grow.

Tools and Technology

Two key barriers are presented in Figure 3: inferior technological solutions and technological interruptions.

Nursing homes use many different tools and technologies to perform daily activities. Many medication-related tasks are tied directly to documentation and the use of electronic medication administration records (eMAR). Other municipalities may apply different types of software to fulfill the same role, replacing paper records of journal entries, patient records, medical records, and nursing reports. This, however, poses challenges for the staff due to poor design choices, lengthy login procedures, separate closed modules within the same software, and challenges when communicating with external networks and devices.

Together, it leads to an inferior technological solution for supporting administrative tasks in general, and documenting medication administration in particular.

> The eMAR is not very user friendly. It is all about how it is put together, searching for specifics is nearly impossible … you just have to read and read until you find it … some information just seems to disappear and you have to retrieve it manually. (Interview with an RN)

An example of this is how on-demand medication documentation exists within separate modules in the eMAR, which do not connect to the primary medical records. In turn, this leads to double documentation and creative workarounds, and in some instances also delays or omissions of documentation.

Another key barrier in this work-system element is technological interruptions. They are typically caused by inferior technology, such as a lack of Wi-Fi or bugs and glitches in the documentation software forcing the user to alter, delay or omit tasks. An example of a technological interruption was during pre-visitation, when the physician depended on an application on a mobile device to access the Norwegian Medicines Manual for Health Personnel. However, this meeting took place in the basement and lacked Wi-Fi or cellular signals. This led to significant delays and disrupted the medication review.

Physical Environment

In the physical environment, active and passive interruptions were prominent, as shown in Figure 3.

The physical environment of the nursing home plays a distinct role in how and where the staff perform medication-related tasks. The medicine rooms were far from the nursing station and adjoining patient rooms in both of the observed nursing homes. To compensate, the staff used mobile medication trolleys extensively, which often led to medication administration occurring in busy environments characterized by interruptions and a cluttered workspace.

> I believe the nursing station is unfit, there is so much noise. There are always people coming and going … It makes it hard to concentrate and be focused on our task … Also the computers are there and you never get the peace and quiet you should … so it is not the best. (Interview with an RN)

Two additional types of interruptions were identified that affected the medication administration process. Firstly, there were passive interruptions, such as background noise and activities that may lower cognitive functions and proceed to become active interruptions.

Secondly, active interruptions occur when a primary work task is disrupted due to nearby activities, conversations, incoming calls or spontaneous engaging in conversations. Breaks in a primary task often led to extended breaks before resuming, or that the staff member took on a secondary task even though the primary task did not always resume. Active interruptions often took place in busy environments, such as the nursing station or common rooms. Most active interruptions had negative outcomes, but sometimes they could also lead to positive ones. Examples of positive outcomes were informal conversations about patient issues that led to discoveries or revelations resulting in changes in medications or treatment plans.

Tasks

In this work-system element, the extensive number of tasks, double documentation, double-check, and multi-dosage medications were vital facilitators and barriers.

Within the medication administration process, we identified 29 distinct tasks throughout the six stages from ordering to observing and documentation (Figure 1). These tasks were perceived differently among the professional stakeholders, sometimes with a feeling of being overwhelmed by all the daily activities:

> And then we have so many different tasks. You are supposed to take part in the social patient-related activities in the ward. You have medication administration, mapping of patients, follow-up of the annual controls, medication reviews, blood sampling and such. Then comes the doctor's visitation, for which you are responsible. Moreover, there are many practicalities to handle. (Interview with an RN)

The RN often regarded medication-related tasks as complex and challenging, while nursing assistants tended to view the process as more linear and rule-bound. The mapping of the medication administration process within the work system of the nursing homes revealed that most barriers occurred during the first two stages: ordering and transcribing. These barriers are often related to unclear communication and inferior documentation systems. Therefore, ordering and transcribing seem to be especially vulnerable to medication administration errors, potentially cascading, thus causing sequential errors and adverse events at a later stage.

Double-check is often marked as a critical step in delivering medications to the patients, but practical challenges often interfere. A lack of qualified health care personnel or busy schedules sometimes do not permit double-control, and creative workarounds often replace this safety measure. An example arose when an RN prepared intravenous morphine for a patient, but there was no qualified personnel nearby to perform the obligatory double-check. The RN documented the process by taking pictures with a private cellular device and sending them to an off-duty colleague for confirmation. Night shifts present a particular challenge:

> To be honest, double-checking medications on a night shift … That just does not work. (Interview with an RN)

Double documentation was detectable, since the RNs kept separate notes in a "black book" to keep track of daily activities and medication-related tasks. This was partly due to challenges maintaining an effective workflow in the eMAR. To ease the transition between modules in the eMAR, medical charts were sometimes printed and put in a patient folder and stored physically.

Many patients use multi-dose medications. These are prescribed two weeks at a time and then dispensed and delivered to the wards from the pharmacy. The RN would then manually alter all previous multi-dose medicines and physically transfer them to new dispensers. This often proved challenging, as visitations took place once or twice a week and often led to prescription changes. In addition to being time-consuming, it was also a perceived safety risk.

Human Factors and Steps to Minimize Adverse Drug Events

As medication administration is ingrained in the daily activities of healthcare professionals' work in nursing homes, identifying single measures to improve medication management or reduce medication administration events is challenging. Using human factors to categorize facilitators and barriers across the various work-system elements may aid such efforts. Since prior interventions, such as guidelines or checklists, aiming to safeguard medication administration in nursing homes only partly address all the challenges, systematically mapping facilitators and barriers may inform future improvement efforts (Keers et al., 2013; Odberg et al., 2020). This study shows how facilitators and barriers across the five elements of the work system may impact the medication administration process. Yet, it is essential to keep in mind that they interact dynamically. This means that changes in one work-system element may have consequences in one or several interconnected elements. For example, the physical distance between the medicine room and the ward (physical) affects social interactions (persons) and how the staff manages medications (task), making the medication administration process more susceptible to interruptions. At the same time, social congregation around the medication trolley may also serve as a safety net, where potential medication events are intercepted before reaching the patient. Therefore, being surrounded by colleagues is often perceived as an added safety measure by the staff, and may reflect a need for vigilant communication and coordination to promote safe practices (Odberg et al., 2017; Raban & Westbrook, 2014). In consequence, moving the medicine room closer to the ward or altering the medication trolley routines may have unforeseen consequences.

Working together in limited physical spaces also increases the risk of being interrupted. At the same time, the literature describes several interventions to minimize interruptions, but the evidence is scarce that such interventions reduce medication events, since the complexity of the work system often entails unforeseen consequences. Examples of interventions to reduce interruptions are: dedicated medication rooms; the use

of yellow vests or tabards; no-interrupt zones; safety checklists; and various technological solutions (Lapkin et al., 2016; Westbrook et al., 2017). Since humans are at the center of the work system, interventions that improve the cognitive skills needed to cope with interruptions may have a more effective impact. Nursing students training to handle interruptions in a simulated environment report heightened awareness and positive learning experiences in relation to how they perceive the medication administration process. The nursing students also learned techniques for managing interruptions by using enhanced clinical reasoning and judgement (Hayes et al. 2015). Training nursing home staff on how to handle interruptions may therefore be a useful measure.

Double-checking as a procedure involving independent, simultaneous medication checking by two competent persons was a critical factor identified in the two nursing homes in our study. Several barriers across the work-system elements seem to play a role in how the staff manages the practice of double-checking. Vulnerable shifts (organization), varying competence (persons), unclear guidelines (organization), team composition (persons), under par technological solutions (technology), and task complexity (tasks) all contribute to the challenging nature of mandatory double-checks. The study showed that problems most often arose when there was only one RN on a shift. This often resulted in workarounds and delays, or altogether skipping the double-check. Nevertheless, adverse medication events still appear to occur during double-checking, and RNs have mixed perceptions of the procedure. It is a way of feeling safe for some, while others perceive it as redundant (Alsulami et al., 2012). At the same time, there is little evidence for the effectiveness of double-checking in reducing medication errors (Lapkin et al., 2016). More research is needed to explore the efficacy of double-checking in nursing homes.

Double documentation often introduces the risk of adverse events. This study showed how the first two stages of the medication administration process (ordering and transcribing) were especially vulnerable to many associated barriers across several work-system elements. Most visible was how a lack of computers with eMAR functionality, or separate modules within the eMAR, led to analogue solutions and double documentation.

Such practices may lead to subsequent problems retrieving vital information quickly or losing information, leading to sequential issues (Carayon et al., 2014). An example from the observations showed how the staff had documented the weight of a patient in a separate folder that had gone missing. The patients' weight was essential to dose a specific drug, resulting in dosing and prescribing having to be postponed to the next week. Electronic medication administration record systems may reduce the perceived risk of committing medication errors (Alenius & Graf, 2016), but it seems that only well-integrated electronic barcoding effectively reduces medication events. Electronic barcoding entails measures to check correct medicines, dosages and patient identity (Shah et al., 2016).

Nursing Homes as Complex Adaptive Work Systems

Most of the identified facilitators and barriers in the two nursing homes indicate how the staff change behavior and reasoning to overcome challenges and perform safe medication administration. From a human factors perspective, the wards' functionality reflects how different adjustments across each of the work-system elements interact during medication administration to balance the work system as a whole.

Nursing homes can, therefore, be labelled as complex adaptive work systems. They may be described as nonlinear, in which diverse agents capable of spontaneous self-organization interact. These dynamic work systems evolve and adapt to meet foreseen and unforeseen events (Matlow et al., 2006; Rouse, 2008). Individuals make adaptations according to psychological, physical, and social rules, and they adapt to each other. In addition, persons learn from past events. This may result in self-organization, through which patterns of behavior emerge. Such patterns may have healthy or unhealthy consequences for an organization (Rouse, 2008). Examples are when individuals adopt workarounds or shortcuts, such as omitting double-checks or utilizing double documentation. Over time, these practices may spread to the remaining staff and become normalized. The normalization of deviance may be necessary to maintain effective care, but may also create vulnerabilities in the work system enabling

adverse events. In most cases though, normalization of deviance centers on adapting to a changing work system, and minimizing the gap between work as imagined and work as done (Hollnagel, 2012; May & Finch, 2009). This is reflected in how staff members utilize their competence, experience and cognitive faculties to provide safe medication management.

Conclusion

The study of two Norwegian nursing home wards identified a total of 60 facilitators and barriers to safe medication administration. Several facilitators and barriers were intertwined, meaning that they could act as both facilitators and barriers depending on situational factors in the nursing home's work system. Taking the complexity of the medication administration work system into account, it seems prudent that future interventions that address medication safety in nursing homes should be multifaceted, involving all personnel, including leaders. The SEIPS model may facilitate a systems approach that can assist staff and management in nursing homes in identifying relevant critical issues in this area. More specifically, the work-system elements can serve as a practical guide to inform any improvement measures.

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CHAPTER 15

Multidose Drug Dispensing in Primary Care: A Review of the Literature

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Abstract: Multidose drug dispensing (MDD) is an adherence aid that provides patients with machine-dispensed medicines in disposable unit bags, usually for a 14-day period. The system has been implemented in primary care in some European countries. This review aims to summarize the current evidence on the MDD system's effect on patient safety in home-dwelling patients. We found 60 peer-reviewed articles from five different countries. The studies indicate that MDD has both positive and negative effects on patient safety, and can affect all steps in the medication-use process: prescribing, dispensing, administration and monitoring. Specifically, MDD can increase medication adherence and reduce discrepancies in medication records for patients in primary care. However, it also seems to result in more inappropriate prescribing and more medication errors during discharge from hospitals. In order to improve the MDD system, it is necessary to involve all actors in the medication-use process and define their responsibilities. Specifically, we see that there is a need for better systems to identify patients during care transitions, and increased involvement of the patients themselves.

Keywords: Multidose drug dispensing, primary care, patient safety, review, dose administration aid, home care services

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Multidose drug dispensing (MDD) is a dispensing system in which solid medicines (tablets and capsules) are removed from their original packaging and machine packed in disposable plastic pouches (Figure 1). The pouches are labelled with the patient's name and date of birth, the name and strength of the medicines, and the time the medicines should be taken. MDD is common in hospitals around the world, but is also used in primary care in Australia, Finland, Norway, Denmark, Sweden and the Netherlands (Rechel, 2018).

Figure 1. Multidose Drug Dispensing Pouches Reproduced with permission from Apotek 1 Gruppen AS, Norway

When utilized in primary care, MDD has been promoted as an adherence aid to ensure better medical treatment for patients with medication management problems and polypharmacy. The system was expected to reduce medication costs by reducing medicine waste, saving nurses' working time, improving medication adherence, and reducing medication errors (Association of Finnish Pharmacies, 2003; Price Waterhouse Coopers, 2007; Riksförsäkringsverket, 2001). However, the effects of the MDD system on patient safety in primary care has been mostly experience-based rather than evidence-based (Søndergaard et al., 2005, p. 74)

Systematic reviews on patient safety by Sinnemäki et al. (2013), and on MDD in the Scandinavian countries by Halvorsen and Granas (2012) found only seven and 18 studies, respectively. Both groups of reviews

conclude that the expected benefits of the MDD system have been only partly achieved, and that the system can have negative effects, such as increasing polypharmacy and the use of potentially inappropriate drugs. Despite the limited evidence of the MDD system's effects on patient safety, health authorities continue to encourage MDD in primary care, and its use is increasing (Foundation for Pharmaceutical Statistics, 2015; Norwegian Pharmacy Association, 2010; Rechel, 2018).

The review underlying this chapter aims to describe the pros and cons of the MDD system for home-dwelling patients, and summarize the current evidence in order to provide evidence-based knowledge for optimising the MDD system for these patients.

Methods

A scoping review was conducted to gain knowledge on the use of MDD in primary care (Arksey & O'Malley, 2005). Our aim was to produce a broad overview of the existing peer-reviewed literature addressing MDD and patient safety. We searched the databases Pubmed, Embase, Cochrane and SweMed+, using the keywords "apodos", "automated medication/drug dispensing", "automated dose dispensing", "dosisdispensering", "multidose", "multidose dispensing", "multidose drug dispensing", and "unit-dose dispensing". The literature search was broad, semi-systematic (Snyder, 2016), conducted several times, and did not have a time limit. The first search was conducted in 2016 and the last in August 2021. We also contacted authors from Denmark, Finland and the Netherlands (one from each country) asking for more detailed information about their MDD systems.

Titles and abstracts were screened and all articles that included information about MDD were included. Full-text articles were then retrieved and read by two researchers. We also manually searched the reference lists of the included articles to identify papers missed in the search. We included peer-reviewed articles in English or one of the Scandinavian languages.

The inclusion criteria for this literature review were: all qualitative and quantitative studies conducted in a primary care setting or during care

transitions for home-dwelling patients using MDD. Studies on hospital in-patients and nursing home residents were excluded. We did not assess the quality of the included studies, but we have highlighted the longitudinal studies and articles that compare MDD to ordinary prescribing.

The main focus of this review was to describe the impact of MDD on patient safety for home-dwelling patients. We categorized the articles by combining, integrating, and summarizing the main outcomes of the papers according to the main objectives in the included studies (Perestelo-Pérez, 2013). The following categories emerged: medication safety, prescribing quality, and patient perspectives. We have also summarized how the MDD system is organized in the different countries and highlighted differences that might affect patient safety.

Results

Description of the Studies

We found 60 peer-reviewed articles on the MDD system in primary care from five different countries: 22 studies from Sweden, 21 from Norway, nine from the Netherlands, four from Denmark, and four from Finland. Thirty-three studies related to medication use for home-dwelling patients, six were about medication use during care transitions, and 21 studies were about patients' or health care personnel's experiences in various settings.

Organization and Differences Between the Countries

The MDD system varies between the countries. In Sweden, Finland and Norway most MDD users are home care clients (Bardage et al., 2014; Josendal et al., 2020; Sinnemäki et al., 2014). In the Netherlands, however, the largest group of MDD users are home-dwelling patients who get MDD directly from the community pharmacy (Cheung et al., 2014).

In both Sweden and in Norway the prescribing procedure for MDD differs from that of ordinary prescribing. In Sweden, MDD requires a separate log-in procedure which cannot be performed directly from the medical record (Sjoberg et al., 2012). In Norway, ordinary prescriptions

are electronic, while the MDD system is still mostly paper-based (Josendal et al., 2020). In Finland and the Netherlands, the prescribing procedure is the same for patients with ordinary dispensing and MDD (Mertens, personal communication, 22 September; Sinnemäki, personal communication 30 September).

In Finland, the MDD packaging fee is partly reimbursed for home care patients 75 years and older, who use six or more reimbursable prescription medicines suitable for MDD (Sinnemäki et al., 2013). In addition, a medication review should be performed before patients start MDD (Sinnemäki et al., 2014). In Norway and Sweden, the MDD packaging fee is reimbursed for all patients in home care, regardless of age (Bardage et al., 2014; Helfo, 2018). In the Netherlands and Denmark, the MDD service is also reimbursable for patients without home care services if a prescriber authorizes its use (Mertens et al., 2018a; Reuther et al., 2011).

Medication Safety

Health Care Personnel's Views on Patient Safety

We found 12 studies that reported the experiences of health care personnel regarding prescribing, dispensing and administering medicines. Most health care personnel felt that the MDD system improved patient safety, but there were also concerns about unclear routines and responsibilities.

According to health care personnel the benefits of MDD were: the patients got medicines as prescribed; there were fewer errors; and medication management was improved (Bardage et al., 2014; Herborg et al., 2008; Johnsen et al., 2018; Josendal & Bergmo, 2021; Nilsen & Sagmo, 2012; Wekre et al., 2012; Wekre et al., 2011).

Several studies also indicated that the MDD system resulted in a better overview of patients' medication for GPs and nurses (Bardage et al., 2014; Bell et al., 2015; Bergmo et al., 2019; Frøyland, 2012; Wekre et al., 2012). However, some nurses were concerned that a reduction in manual dispensing would reduce their knowledge about drugs (Nilsen & Sagmo, 2012; Wekre et al., 2011), and some felt that the prescribing procedure was so complicated that it might pose a risk to patient safety (Bardage

et al., 2014). Three studies also pointed out that MDD was less flexible when it came to changes in medications/dosages. (Frøyland, 2012; Herborg et al., 2008; Wekre et al., 2011).

The MDD system has its limitations. A reoccurring topic in many of the studies was an unclear division of responsibilities in the MDD system (Heier et al., 2007a; Herborg et al., 2008; Johnsen et al., 2018; Josendal et al., 2021). Some expressed uncertainty as to who can access and update the medication lists for MDD patients, and thus who should be notified about changes (Heier et al., 2007a; Johnsen et al., 2018; Josendal et al., 2021). GPs have also noted that it can be difficult to take over responsibility for medication started by other doctors, and some think that only the GP should be allowed to make changes (Frøyland, 2012; Wekre et al., 2012). In a survey by Nilsen and Sagmo (2012), nurses and nursing assistants stated that MDD reduced their responsibility for errors in the medication management process.

Discrepancies in Medication Records

In eight studies, discrepancies between medication records in primary care were investigated. Discrepancies are common, but MDD might reduce their occurrence.

We found four Norwegian studies investigating discrepancies between medication records from the GP, the home care service and/or the MDD pharmacy. These showed discrepancies in 51–88% of patients' records (Bakken & Straand, 2003; Heier et al., 2007b; Josendal & Bergmo, 2019; Mamen, 2016). In the interview study from Josendal and Bergmo (2019) the GPs, home care nurses and community pharmacists described how discrepancies could lead to unintended changes in the patients' medication regime, when changing from an MDD system based on paper prescriptions to one based on electronic prescriptions.

Sinnemäki et al. (2014) examined how medication lists were reconciled when patients started MDD in Finland. They found that over half of the medication lists were incomplete at initiation, and that 43% of the patients got treatment-related changes and 96% technical changes in their medication lists during initiation. Tiihonen et al. (2016) compared

the medication list in the electronic medical record and actual drug use among home care clients and found that MDD was not associated with having discrepancies.

A cross-sectional study by Josendal and Bergmo (2018) found that the number of patients with discrepancies was reduced from 60% to 29% when comparing medication lists in the initiation of the electronic MDD system in Norway, to lists 2 years after initiation.

We found only one controlled before/after study on discrepancies. In this study, from Wekre et al. (2010), discrepancies in medication records between the home care service and GP were reduced by 34% after implementation of MDD. After implementation, 31% of the patients' records still had discrepancies.

Transitions Between Care Levels

We found nine studies indicating that MDD patients are at an increased risk of medication errors upon hospital discharge.

A case study by Lysen et al. (2011) described two patients whose use of MDD was not noted in the medication records at admission. This resulted in patients continuing their old medications when transferred back to primary care. Another Danish study also found that 14% of changes in MDD patients' medication treatment during hospital stays were not reported to the GP or MDD pharmacy (Reuther et al., 2011).

In a survey and a focus group study of GPs in primary care units in Sweden, participants noted difficulties with managing MDD patients after discharge (Caleres, Bondesson, et al., 2018; Caleres, Strandberg, et al., 2018). Similarly, nurses and nursing assistants reported that there is a need for improved cooperation to minimize medical errors in the transition from hospital to primary care (Bardage et al., 2014). In a study by Alassaad et al. (2013) it was found that 25% of MDD users had discrepancies in their medication records during hospital discharge, and 3% were considered serious.

Three Swedish studies compared patients with MDD to patients with ordinary prescribing during care transitions and found that MDD patients have between three and 18 times increased risk for errors during

discharge from hospitals (Bergkvist et al., 2009; Caleres et al., 2020; Midlöv et al., 2005), but not on admission (Midlöv et al., 2005).

Prescribing Quality

Inappropriate or suboptimal prescribing was the area that was studied the most in the studies included here. Most of the 21 studies found that prescribing quality for MDD patients is poor, and seems to be worse for patients with MDD compared to patients with ordinary prescribing.

Prescribing Quality in MDD Patients

From the cross-sectional studies, we find that MDD users are prescribed more medicines than patients with ordinary prescribing and are more exposed to chronic polypharmacy (Belfrage et al., 2014; Johnell & Fastbom, 2008; Morin et al., 2018; Wastesson et al., 2019).

Several different quality indicators have been used to measure the degree of potentially inappropriate prescribing (PIMs): the Norwegian General Practice Criteria (NORGEP); quality indicators from the Swedish National Board of Health and Welfare; START/STOPP criteria; and the European Union EU(7)-PIM list. Depending on the indicators, the exposure to PIMs varied from 20% to 97% of patients (Belfrage et al., 2014; Halvorsen et al., 2012; Hammar et al., 2014; Josendal et al., 2020; Lesen et al., 2011; Lönnbro & Wallerstedt, 2017; Söderberg et al., 2013). Three studies found that the majority of problematic prescriptions were considered clinically relevant (Belfrage et al., 2014; Hammar et al., 2015; Lönnbro & Wallerstedt, 2017). A Dutch study examining the effect of a pharmacist-led medication review on drug-related problems (DRPs) in older patients found that MDD patients had, on average, 8.5 DRPs (Kwint et al., 2011). In addition, a study from Milos et al. (2014) found that elderly MDD users were using a high number of drugs, which could increase fall risk and cause/worsen orthostatic symptoms.

In the five studies that compared patients using MDD with patients using ordinary prescribing it was found that PIMs and DRPs were up to eight times more common in MDD patients (Belfrage et al., 2014; Johnell

& Fastbom, 2008; Lea et al., 2019; Lönnbro & Wallerstedt, 2017; Sjoberg et al., 2011). However, one study found that MDD was associated with a lower probability of statin use, and one found that MDD users were less exposed to drug-drug interactions and long-acting benzodiazepines than patients with ordinary prescribing (Johnell & Fastbom, 2008; Sundvall et al., 2019)

Changes in Prescribing Patterns After Enrollment in the MDD System

Some studies have also examined data after the enrollment of patients in the MDD system looking at changes in prescribing patterns.

A Swedish longitudinal study of more than 30,000 patients found that initiation of MDD was associated with an increased number of drugs prescribed per patient, and an increased number of PIMs, but fewer drug changes (Wallerstedt et al., 2013). Sjoberg et al. (2012) looked at hip fracture patients at discharge from the hospital and after 6 months. Of these, 107 patients used MDD and 47 patients used ordinary prescribing. They found that MDD patients had fewer drug changes (dosage adjustments, withdrawn or newly prescribed) compared to patients with ordinary prescribing.

Two Finnish studies have looked at patients as they started using MDD. Bobrova et al. (2019) used the European Union EU(7)-PIM list and found that the proportion of patients exposed to clinically significant PIMs increased 6 months after enrollment (59% vs. 64%). The proportion of patients with clinically significant drug-drug interactions was the same at follow-up. The number of medications increased for 61% of the patients. Sinnemäki et al. (2017) found that drug consumption was reduced for 11 of the 20 most used active substances 1 year after initiation of MDD. There were also more starts and discontinuations in the MDD group compared to the control group.

A Norwegian study from Hindhammer et al. (2012) included 1,060 new MDD users, and found that drugs with a potential for abuse was reduced by 11% after initiation of MDD. They also found a normalization of the retrieval of these drugs (i.e., patients with unusually high retrieved

amounts decreased and unusually low amounts increased). The total amount of drugs increased by approximately 10% 1 year after enrollment. However, this was also the case for the control group without MDD.

Changes in Prescribing, Dispensing and Administering Procedures

Three studies described differences in medication-use processes for MDD patients and patients with ordinary prescribing, and an additional three studies described changes in time use for the two systems.

Cheung et al. (2014) used data from the Dutch Central Medication Incidents Registration system to describe medication incidents related to MDD. Of 3,685 reported incidents from community pharmacies, 227 (6.2%) were related to MDD. Most reported incidents occurred while entering the prescription into the pharmacy information system and during filling the MDD bag (e.g., broken tablets). MDD also introduced four new phases within the medication process not present with ordinary prescribing: processing the MDD module; sending the MDD file to the supplier; filling the MDD bag; and adjustment of the MDD bag.

Mertens et al. (2018b) evaluated the MDD process in community pharmacies. Over a 3-week period, 261 MDD adjustments involving 364 drug changes were documented. Of these, 52% were effectuated immediately, and about half of these were effectuated manually. The pharmacists felt that about one quarter of the adjustments could have been deferred. Immediate adjustments took significantly longer than deferred adjustments.

In Josendal et al. (2021) pharmacists identified problems with 11% of the 4,121 MDD prescriptions dispensed. The most common issues were expired prescriptions (29%), drug shortages (19%), missing prescriber signatures (10%), and unclear/missing medication names or strengths (10%). They also discovered that responsibilities and work practice for community pharmacists differed when dispensing MDD prescriptions compared to ordinary prescriptions: they took on more responsibility to get prescriptions renewed, and they did less patient counselling.

In terms of time use, Heier et al. (2007a) and Wekre et al. (2012) reported that GPs found MDD more time consuming than ordinary prescribing. While Frøyland (2012) found that only one third of GPs found MDD more time consuming, while one third found it less time consuming than ordinary prescribing. In Bardage et al. (2014) about one third of GPs reported that MDD limited their time with patients.

Nurses and nursing assistants reported that MDD was less time consuming than ordinary prescribing (Heier et al., 2007a), and that the system did not limit their time with patients (Bardage et al., 2014). Meanwhile, a study from Josendal and Bergmo (2021) reports that both home care nurses and community pharmacists experienced an increased workload with the electronic prescribing system compared to the paper-based system, due to an increased need for clarifications.

Patient Perspectives

Inclusion of Patients in the MDD System

In a questionnaire conducted among GPs, nurses and nursing assistants in Sweden the majority reported that MDD was suitable for patients with memory deficiencies, patients whose medicines are not changed often, patients with many medications, and patients with poor adherence. Most nurses and assistants also responded that MDD is suitable for patients with difficulties opening medicine packages (Bardage et al., 2014). The Danish study by Reuther et al. (2011) concluded that MDD can be suitable for persons who use several drugs long-term, and whose medication is not changed frequently. The pharmacists interviewed in the study by Koster et al. (2016) suggested that the use of aids such as MDD could be a strategy to improve medication use in patients with limited health literacy.

In two studies it has been suggested that MDD is mostly used for the convenience of healthcare staff (Bardage et al., 2014; Wekre et al., 2011), but in a study by Mertens et al. (2018a) it was found that for most home-dwelling patients MDD was initiated after shared decision making. Mertens et al. (2018a) also found that potential medication management problems (functional, organizational, adherence, and medication

knowledge) were more prevalent among MDD users compared to non-MDD users. MDD users were also older, used more medications, and were more often cognitively impaired and frail.

Adherence and Medication Knowledge

Health care personnel generally seem to think that MDD improves medication adherence (Bardage et al., 2014; Frøyland, 2012). However, some are concerned that MDD may reduce patient involvement (Bardage et al., 2014).

In interviews with patients, Larsen and Haugbølle (2007) and Holbø et al. (2019) found that most patients reported incidents where they were non-compliant: taking out tablets, changing the time of the day they took the tablets, or forgetting to take medicines, whether or not they were the medicines in MDD or those they took from their original package. However, the former study reported that MDD did not seem to change the users' understanding of medications, while the latter concluded that MDD patients lack adequate information and adaptations enabling users to get the full benefit of the system.

Mertens et al. (2019) surveyed 62 patients where most felt that MDD had supported them in their medication use and improved their medication management. In a questionnaire study of 1,645 MDD users, Bardage and Ring (2016) reported that the majority of users felt that MDD made it easier for them to remember to take their medication. It helped them take the correct dosage and they felt secure with it. About half of these patients also stated that MDD allowed them to become more involved in decisions about their treatment. However, 12% said they failed to take their medicines, and 25% called for better information from prescribers about the purpose of treatment and on changes in drugs.

Kwint et al. (2013) compared self-reported medication adherence and knowledge in 127 MDD users and 96 non-MDD users. They found that MDD users had higher adherence than non-MDD users (81% vs. 58%), while knowledge about medicines was lower (40% vs. 79%). However, the MDD users reported more knowledge of their manually dispensed drugs compared to their MDD drugs.

Two Dutch studies have measured the time in therapeutic range for vitamin K antagonists in relation to patients using MDD. Van Rein et al. (2018) found that MDD was associated with better adherence in the first month compared to instructing patients, but they found no difference after 4 months. Mertens et al. (2020) found that MDD patients had an increased time in therapeutic range compared to the control group, and thus improved the quality of anticoagulation. There was no reduction in the number of bleedings or thromboembolic events between the intervention and control group.

Discussion

This review, consisting of 60 articles, indicates that MDD increases medication adherence and reduces discrepancies in medication records for patients in primary care. In addition, the MDD system may make it easier to identify medication-related problems and reduce drug-drug interactions. However, MDD also seems to result in more inappropriate prescribing, more medication errors during discharge from hospitals, and may potentially increase the number of drugs prescribed.

Even though MDD is often referred to as a dispensing system and an adherence aid, this review shows that MDD affects more than just dispensing errors and medication adherence. We argue that MDD can affect all steps in the medication-use process: prescribing, dispensing, administration and monitoring. In order to optimise the MDD system and reduce potential negative effects, it is thus necessary to look at the entire medication-use process and all the actors involved.

Administration and Monitoring of MDD Medicines

It is estimated that 50% of patients with chronic illnesses are non-adherent, resulting in poorer health outcomes and increased medical costs (Brown & Bussell, 2011, p. 304). The three quantitative studies on medication adherence in our review all show that MDD users have a higher adherence than non-MDD users (Kwint et al., 2013; Mertens et al.,

2020; van Rein et al., 2018). However, in the interviews and surveys, most patients still said that they sometimes had been non-adherent (Bardage & Ring, 2016; Holbø et al., 2019; Larsen & Haugbølle, 2007). Non-adherence is, however, not always inappropriate. Adjusting medication dosages might be valid as a form of intelligent non-adherence, such as skipping diuretics before going shopping. Other adjustments might be the result of having too little information about or understanding of their medicines or diseases. These adjustments, especially when based on too little knowledge, might increase the risk of errors, such as taking out the wrong tablet from the MDD pouches.

We did not find any studies investigating administration errors in home-dwelling MDD patients. However, a Dutch nursing home study showed that despite MDD reducing the frequency of errors, they still occurred in one fifth of medication administrations. The most common types of errors were the wrong administration technique, and medicines given at the wrong time (van den Bemt et al., 2009). Similarly, the Danish Patient Ombudsman found 4,000 incidents relating to MDD during a one-year period. Half of these incidents were related to the administration of medicines, most commonly that the medicines were not given to the patients, they were given at the wrong times, or the patients did not take the medicine (Pasientombuddet, 2013). So even if MDD ensures that the patient gets the right medications, errors can still occur when the medicines are administered, or the patient might not take the medicine at all.

Interestingly, Kwint et al. (2013) found that medication knowledge was lower in MDD users than non-MDD users, and that MDD users had more knowledge of their manually dispensed medicines compared to those in the MDD bags. It would thus seem that the MDD system reduces the patient's knowledge about medicines. This is similar to findings from studies on other dosing aids. When filled by a third party, dosing aids might reduce the patient's autonomy and knowledge about medicines, and as such be disempowering (Elliott, 2014).

We also find similar results for the health care personnel who administer MDD to patients. Several had concerns that the MDD system reduced their knowledge of medicines (Nilsen & Sagmo, 2012; Wekre et al., 2011).

After introduction of MDD some health care personnel also felt reduced responsibility for medication administration (Nilsen & Sagmo, 2012). If both the nurses and the patient identify symptoms as potential side effects of medications to a lesser degree, this might result in them contacting their GP to a lesser degree as well, which again might result in more inappropriate prescribing for these patients.

Recommendations

- To ensure that the MDD system does not disempower patients, patient involvement in the initiation phase is necessary. There should be clear guidelines as to which target groups should be offered MDD. Included patients should be instructed to report to health care personnel if they experience side effects or other problems with their medications.
- To avoid increased costs for patients and errors when patients adjust their medications, there must be good routines for communicating which medicines should be dispensed as MDD, and which should be dispensed in their original packaging.
- To be able to observe and report effects of the patient's medications, home care nurses need to keep updated on medicines and their side effects.

Dispensing MDD

Some of the rationale behind implementing MDD has been to reduce dispensing errors. We did not find any studies on the accuracy of MDD dispensing in home-dwelling patients, but studies from other settings have shown that dispensing error rates are very low with MDD, and lower compared to manually filled dosing aids (Gerber et al., 2008; Klein et al., 1994; Palttala et al., 2013; Søndergaard et al., 2005).

Even though MDD seems to increase the chance of giving the right medication at the right time, errors can still occur at a later stage. When a physician changes a patient's medication, this may wait until the next MDD delivery, the medicine may be administered on the side until the

next delivery, or the bags may be manually adjusted. Both of the latter options increase the risk of errors, but for certain medications it might be too long to wait until the next delivery. Manual adjustments are also time consuming (Mertens et al., 2018b).

One of the benefits of the MDD system is that it gives the pharmacist a better overview of medication use, including prescriptions from both GPs and hospital physicians. Increased access to medication history also seems to result in pharmacists detecting more errors and inappropriate prescribing of these prescriptions (Josendal et al., 2021). This increased overview has also been suggested as an explanation as to why these patients seem to have fewer serious drug-drug interactions in their medication lists, and use fewer psychotropic medicines (Johnell & Fastbom, 2008).

However, because the MDD system works as a subscription, and many patients get medicines via their home care service, there is limited contact between the patient and the pharmacist during the dispensing process. It would seem that pharmacists do little patient counselling of home care patients with MDD (Josendal et al., 2021). MDD patients have also reported that they would like more information about the medicines they are taking, the reason for use, information about changes in their treatment, and pictures of the tablets that are dispensed in MDD (Bardage & Ring, 2016). Less contact with the pharmacist might be a contributing factor as to why MDD patients have less knowledge about their medicines.

Recommendations

- To avoid dispensing errors, medication changes in MDD should be deferred until the next delivery whenever possible. There should also be a clear agreement with the GP on how to assess whether a change can be deferred.
- To assure that patients get essential information about their medicines, the pharmacist has to provide adequate information about medicine use, either directly to patients or via the home care service. For home care patients, the responsibility for patient counselling should be clearly placed between the pharmacist and the home care service.

- To reduce errors in manual adjustments to MDD bags, the pharmacist needs to supply information on how to identify the MDD tablets.
- To improve quality in prescribing, the pharmacist should use all available information about the patient's medication history in order to assess the medication regime for MDD patients as a whole.

Prescribing for MDD Patients

Several of the included studies reveal that MDD changes doctors' prescribing procedures and prescribing patterns. The majority of studies on this topic are, however, from Norway and Sweden, where there are different procedures for prescribing MDD than for ordinary prescriptions. This in itself can increase the risk of errors. GPs might have to document medication changes in several systems, which might increase the risk of duplicate prescriptions and perhaps result in prescriptions not being sent to the correct system, so the patient never gets the intended changes to their MDD.

However, studies from both Finland and the Netherlands, where the prescribing procedures are the same for MDD patients and patients with ordinary prescribing, also find that MDD patients are frequently exposed to PIMs, DDIs and DRPs (Bobrova et al., 2019; Kwint et al., 2011). Though PIMs are common for elderly patients in general (Nyborg et al., 2012), it seems that they are more common in MDD patients than for patients with ordinary prescribing (Johnell & Fastbom, 2008; Sjoberg et al., 2011). It is, however, difficult to assess whether this is due to the MDD system, or whether this is because the patients with the most complex medication regimes use MDD (see also methodological considerations).

The included articles present possible explanations for why MDD patients have more inappropriate prescribing than patients with ordinary prescribing. One explanation might be that the procedures for renewing prescriptions are too automated and the lists might be reviewed less frequently (Sjoberg et al., 2011; Sjoberg et al., 2012; Wallerstedt et al., 2013). This is supported by two Swedish studies showing that MDD patients have fewer changes in their mediation regimen than patients with ordinary

prescribing (Sjoberg et al., 2012; Wallerstedt et al., 2013). However, the Finnish study from Sinnemäki et al. (2017) found an increased number of starts and discontinuations in the MDD group compared to patients with ordinary prescribing, which might indicate that this is specific to the Swedish prescribing system.

Regardless of whether MDD is the direct reason for poor prescribing quality, we can see that PIMs and DDIs are very common in MDD patients, and action should be taken to improve the prescribing quality for these patients. A possible way to improve quality would be to do medication reviews. Kwint et al. (2011) found that medication reviews can increase the quality of pharmacotherapy for MDD patients, and other studies have also suggested that MDD medication lists can be used to identify patients with PIMs, who can then be selected for medication reviews (Halvorsen & Granas, 2012; Josendal et al., 2020). However, none of the included articles described regular medication reviews as current practice for these patients.

Even though discrepancies between medication lists in primary care are reduced with MDD, the included studies indicate that discrepancies may increase for patients transitioning from secondary to primary care. Errors during care transitions and discrepancies in the medication lists between the hospital and the GP are very common (Foss et al., 2004; Michaelsen et al., 2015; Redmond et al., 2018; Tam et al., 2005); however, the use of MDD increased the risk of these errors occurring (Bergkvist et al., 2009; Caleres et al., 2020; Midlöv et al., 2005). The included articles found that there was an unclear division of responsibility regarding MDD patients at discharge, which might have led to the errors. In particular, it was unclear who had access to and was allowed to change the medications of MDD patients. Unclear responsibility might also explain why an increased number of prescribers increased the risk of inappropriate prescribing (Söderberg et al., 2013).

Recommendations

- To reduce errors and discrepancies in medication lists, there should be uniform procedures for ordinary prescribing and MDD prescribing.

Existing systems should be integrated to reduce the need for double documentation and parallel prescribing procedures.

- To improve quality in prescribing, GPs, in collaboration with other health care personnel, should regularly review the medication lists of MDD patients.
- To avoid errors during care transitions there is a need for clear routines to identify patients with MDD on hospital admission. MDD should be paused during the hospital stay, and the medication list updated after hospital discharge. The hospital's and the GP's responsibility for prescribing and updating the medication list must be clearly defined.

Methodological Considerations

The main purpose of this review was to describe and summarize peer-reviewed studies on safety in MDD patients. We found that the procedures for prescribing MDD, the patients offered MDD, and routines among health professionals handling MDD differed between countries. Furthermore, the studies had different approaches, settings and designs. It is therefore difficult to draw definite conclusions about MDD and patient safety. However, this work gives an overview of the literature and highlights some trends that can be used to improve safety for MDD users.

When interpreting the results, it is important to look at the study designs used. Most of the studies did not have a control group. Even for those with a control group, it was difficult to conclude whether the differences we see in prescribing between the two groups are due to the MDD system or other factors related to the patients offered MDD. Patients using MDD generally use more medicines, have more complex drug regimens, and have trouble managing their own medication. Thus they might not be comparable to patients who do not use MDD. The same is true for the longitudinal studies. We can see that the number of PIMs and total number of drugs increase after initiation. However, we cannot conclude whether this is due to the MDD system, or if there was an increase in medications or medication complexity that resulted in the patients starting MDD.

We also acknowledge that the term "multidose" is not easily defined. Some studies may have used other terms and definitions to describe the prepacking of medicine in pouches.

Conclusions

To summarize, the MDD system has both positive and negative effects on patient safety. MDD has the potential to improve some aspects of medication use, in particular by increasing adherence and decreasing the number of discrepancies between home care services and GPs. However, the MDD system does not solve the problems of potentially inappropriate prescribing, medication errors, and the risk of adverse drug events. On the contrary, the MDD system might increase the risk of such events.

In many of the included studies, unclear routines and division of responsibility were suggested as the causes of the negative effects of MDD. This is not surprising as the MDD system has been implemented with the idea that it would primarily relieve the burden of dispensing tablets from many containers, and ease the administration process of handing over the medicines to the patients. However, as this review shows, the MDD system can affect all phases in the medicine-use process. In order to improve the MDD system, it is thus necessary to involve all actors in the process and define their responsibilities. Specifically, we see that there is a need for better systems to identify patients during care transitions, and a need for increased involvement of the patients themselves.

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CHAPTER 16

The Role of Medication Management in Hospital Readmissions in Norwegian Primary Healthcare Services: A Secondary Analysis

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Abstract: Medication management and the transmission of medication information between healthcare services have proven to be essential factors in hospital readmissions. The patients primary healthcare services are caring for at present have complex medical conditions, leading to even greater challenges in transferring correct information across different healthcare services. This chapter describes how healthcare personnel perceive medication management as an influencing factor in hospital readmissions, and explores which elements may lead to medication-related hospital readmissions from the primary healthcare service.

Keywords: Medication management, hospital readmissions, primary healthcare services, patient safety

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Background

Transitions in healthcare are well-documented sources of preventable harm. One of the key influencing factors relates to medications and medication management, which often lead to hospital readmissions as a consequence (Dautzenberg et al., 2021; van der Does et al., 2020). More specifically, research has shown that a large percentage of medication errors connected to hospital readmissions (30%) were transition errors, and that 40% of all medication-related readmissions were preventable (Uitvlugt et al., 2021). When a patient is transferred from one healthcare service to another, the risk of adverse events increases (Kapoor et al., 2019). In particular, this relates to coordination, communication and information exchange between the different healthcare actors during this process (Kripalani et al., 2007; Laugaland et al., 2014; Storm et al., 2014). As the world population grows older, and more people receive complex medical care at home and in primary healthcare services, more complex information must be exchanged between healthcare actors (Glans et al., 2020; Schoonover et al., 2014). This implies that the problem of medication-related hospital readmissions is likely to continue to increase.

A hospital readmission is, according to the Norwegian national quality indicator, "an acute admission, regardless of the cause or hospital of the readmission, which occurs between eight hours and 30 days after discharge from a prior hospital stay (primary admission)" (Kristoffersen et al., 2017, p. 5). In addition, the literature often distinquishes between necessary and unnecessary hospital readmissions. Patients are readmitted necessarily if the readmission is due to acute illness, worsening of a chronic illness, complications after surgery, or if they are in need of other kinds of hospital care. An unnecessary hospital readmission is a readmission that could potentially be avoided, but still occurs due to, for example, organizational difficulties, such as lack of patient information, lack of competence or staffing or poor communication between different healthcare actors (Australian Commision on Safety and Quality in Health care, 2019; Kent et al., 2011).

Hospital readmissions related to medications are defined in different ways. The most common definition is, "admissions due to adverse drug reaction (ADR)", where a drug reaction is an unintended response to a medication, for example a side effect. Another definition is, "admission

due to an adverse drug event (ADE)", which includes any unfortunate occurrence related to the use of a drug. And lastly, a hospital readmission related to medications may be defined as "admission due to drug-related problems", which includes events involving a patient's medication, which may inhibit achieving an optimal outcome (Linkens et al., 2020). This chapter includes all types of drug-related hospital readmissions using the term "medication-related readmissions".

Aim and Research Question

This chapter aims to describe how healthcare personnel perceive medication management as an influence in hospital readmissions from primary healthcare services, and further, what factors within medication management may lead to hospital readmissions.

The research question was as follows: How do healthcare personnel perceive medication management as an influencing factor in hospital readmissions? The results will be discussed in light of previous research and human factors theory.

Context

The Norwegian healthcare service is managed and financed through two separate decision pathways, that is, the specialist healthcare services are subordinate to the state, and the primary healthcare services are subordinate to the municipalities (Grimsmo et al., 2015; Ministry of Local Government and Modernisation, 2019). The specialist healthcare services include somatic and psychiatric hospitals, while the primary healthcare services include general practitioners (GP), nursing homes, home care services, health centers, emergency rooms and rehabilitation services. In Norway, there are 356 different municipalities, and each one provides healthcare services at their own discretion, within comprehensive national regulations (The Health and Care Services Act, 2011). This means that there is considerable variation in how the different primary healthcare services are organized and delivered, including differences in areas of expertise, differences in skill mix, and differences in task allocation (Sperre et al., 2020).

Coordination, cooperation and holistic patient pathways between the hospitals and the primary healthcare services have been on the agenda for decades (Veggeland & Berg, 2013). This did, however, gain even more attention when the coordination reform (an overarching health reform) was introduced to the Norwegian healthcare services in 2012 (Bruvik et al., 2017). This reform encouraged earlier hospital discharges, and subsequently increased the responsibilities of primary healthcare services, particularly in terms of caring for a larger number of patients with complex medical needs (Abelsen, 2014).

Method

This chapter was based on a secondary analysis (Ruggiano & Perry, 2019) of data from a previously conducted case study on hospital readmissions (Glette, 2020; Glette et al., 2019; Glette, Kringeland, et al., 2018; Glette, Røise, et al., 2018). Two municipalities with four affiliated nursing homes (one short-term home and one long-term home in each) were included in the primary study, in addition to a common hospital for both municipalities. Data collection consisted of interviews with general practitioners (GPs) (n = 8), nursing home physicians (n = 2), hospital physicians (n = 15) nursing home leaders (n = 7), nursing home nurses (focus groups) (n = 17), and nursing home observations (ca. 40 hours). In the secondary analysis, Braun and Clarke's (2006) analysis method was applied (as opposed to Graneheim and Lundman's approach, which was used in the primary analysis). Braun and Clarke's (2006) approach enabled the identification of focused features of the dataset, which in this case were medication management and hospital readmissions. The aim of the secondary analysis was to view the dataset in a new way, with the new research question as the backdrop. A distinctive view of the dataset was ensured by using clean uncoded transcripts, and applying a different analysis approach than was used in the parent study (Ruggiano & Perry, 2019). However, some of the results identified in the secondary analysis overlapped with the primary analysis, due a similarity of focus in the two studies. The analysis resulted in three themes, with seven subthemes, describing how medication management may influence hospital readmissions (Table 1 demonstrates the analysis process in Theme 1).

Table 1. Example of Analysis: Theme 1

Themes	Sub-Themes	Codes
T1: Inadequate coordination and communication of the patients' medical treatment	Lack of Access to the patients' medication lists	Lack of knowledge of the patient and their medication list
		Lack of medication information in the ER
		Needing the medication lists to make medical assessments of the patients
	Changes in medication are poorly communicated	Challenge in relation to dissemination of medication changes
		Poor medication information when the patient arrives at the nursing home
		Poor coordination when there are changes in the medication
		Lack of updated medication lists after stay at short-term nursing home
		A common documentation system could reduce readmissions
		Hospital stay summaries with updated medication list arrives too late
		The use of outdated medication list in the hospital
	Early discharges: Lack of observations of the effect of medication changes leads to readmissions	Too early discharge after an infection
		Early hospital discharge leads to inadequate observation of the effect of the medication

Ethics

The primary study was approved by The Norwegian Center for Research Data (NSD) (reference number: 49331). All participants signed a written informed consent form before participating in the study. Written approval was retrieved from the participating hospital, and oral approval was received from municipal leaders. Overall, the research complied with the Norwegian National Research Ethics Committee's research guidelines.

Results

Inadequate Coordination and Dissemination of the Patient's Medical Treatment

An overview of the patient's medications was perceived as essential in adequately assessing the patient's medical condition, and further treatment

and care. However, this information was lacking or incomplete in several primary care contexts. In the emergency room (ER) the information they had access to was described as random. They did not have access to patients' medical records, and needed to rely on the information the patients themselves could provide. If the patient had been admitted to the hospital previously, there could be a hospital stay summary available, but this was not always the case. The ER doctor needed to find information by making calls to the hospital, which was considered burdensome when the ER was busy. A too busy ER combined with lack of patient information could lead to a hospital readmission.

The nursing home nurses observed that the patients, in some cases, arrived from the hospital to the nursing home with poor information about medications, medication changes or explanations for medication changes – a problem solved by making calls to the appropriate actors. It was also stated that the hospital sometimes used outdated medication lists during the patient's hospital stay. This meant that when the patient came back to the nursing home, previous changes done by the nursing home physician a long time ago, were reset, and therefore incorrect. This overall coordination issue was described by a nurse in a short-term nursing home:

> I believe that the biggest issue is the medication. We're starting up [medical treatment] here [at the nursing home] and they're [the hospital] starting up [medical treatment] there … there is no coordination between them [the nursing home and the hospital].

It was also explained that there could be poor access to information on medication changes, and the assessments that had been done in relation to these changes, when the patients had been on a short-term stay (in a nursing home), and were transferred to a long-term nursing home.

Hospital physicians found it difficult to communicate changes done in the patient's medication lists. Medication changes were written in the hospital stay summary, but they worried that the changes did not reach the right actor (home care service in this case), since the hospital stay summary was not sent to them directly, but to the patient's general practitioner (GP). It was also said that all patients received a discharge note in

which medication changes were communicated, but there was no guarantee that this note was passed on to the nurses by the patient. Issues described in transferring medication information to the primary healthcare services from the hospital are illustrated in the following quote by a hospital physician:

> Multidose, yes … They don't appear in the e-prescription, so if we add a new prescription, it is not certain that it will be included in that multidose …. There are also medication adjustments that we don't necessarily include in the e-prescription, but which we add to the hospital stay summary, and it's not certain that the home care services see it, because we don't have the possibility to send it to them [the home care service] directly, and we don't have an overview of which home care service [area] each patient belongs to.

Additionally, the primary care physicians stated that the hospital stay summary (with included medication lists) sometimes arrived late. This was also seen during nursing home observations on several occasions. Nursing home physicians made calls to the hospital to have the summaries faxed over. In one nursing home they even went to the hospital physically to get the necessary documents (they were close to the hospital). Another concern mentioned by a hospital physician, was that different medication treatment regimens were started up by different healthcare professionals (nursing home physicians, GPs, hospital physicians) with limited coordination between them. It was suggested by several healthcare professionals that a common documentation system with access to all patient information (including the medication lists) could reduce hospital readmissions, improve coordination, and save time in regard to transferring the medication list back and forth in the different systems.

As also identified in the parent study, there was agreement among primary healthcare professionals that patients were often discharged too early from the hospital after intravenous (IV) antibiotic treatment. In many cases, the patients were discharged from the hospital to the primary healthcare services the same day that they had switched from IV treatment to oral treatment, leading to limited observation of the effect of this change. The patients frequently relapsed and needed to be readmitted to the hospital. This was described as an issue in both nursing

homes and among GPs. Hospital physicians argued that it was difficult to know when and if an infection flared up, and that they could not keep the patients in the hospital indefinitely to avoid relapses. Another said that in light of a readmission related to an infection relapse, it could be thought that the hospital discharge was too early.

Discrepancy Between the Primary Care Service's Treatment Capacity and the Hospital's Expectations

Several hospital physicians had opinions on what medical treatments the primary healthcare service should be able to offer to the patients discharged from the hospital. These options included IV antibiotic treatment, fluid treatment, and blood transfusions. Some patients were even discharged from the hospital while still receiving IV antibiotics, but only in special cases (e.g., a patient suffering from dementia). However, not all nursing homes had the competence nor capacity to provide IV antibiotic treatment for their patients. In one nursing home they did not always have a nurse on call, for example during the night shift. This was not only problematic in relation to antibiotic treatment, but also, for example, in pain management. There were further descriptions of limited knowledge of the effects, and uses, of some of the medications the hospital physicians requested. And in some cases, they did not have the medication the patient needed in place for the patient's arrival, especially if the hospital discharge was abrupt. One nurse said:

> What's a little strange is that sometimes they come out [from the hospital] very quickly. Fast in and fast out. And then there are some notes and stuff, what [medications] they're supposed to have. Because they've started on new medications, and we don't have these medications at the nursing home, and they [the medications] have to be ordered. You can order urgently and receive the medication in a couple of hours, but you can't do that with all of them [all medication types].

Another challenge described by nursing home physicians was that it was difficult to dose medication without having access to appropriate testing

equipment (e.g., increase or decrease diuretics without access to blood-work). Most nursing homes had IV treatments incorporated into their routines, and could provide this service to their patients, but they did not have access to all antibiotic types. That said, there were different opinions on whether the hospital physicians were responsible for familiarizing themselves with the treatment capacity in the different nursing homes or not. Some admitted that they investigated whether the nursing home, to which the patients were being discharged, could continue treatment. Others expected the nursing homes to have this competence in place.

Targeted Work to Avoid Medication-Related Hospital Readmissions

Health personnel worked with the objective of avoiding hospital readmissions. Some patients had an observational stay at a nursing home after a hospital stay, when medication lists and their ability to administer the medications themselves were reviewed. This was perceived as a measure to reduce medication-related hospital readmissions. Primary care physicians often called hospital physicians for advice on how to provide the best treatment for their patients. Some examples are guidance on pain management for patients with back pain or advice on what medications to use for anxiety in patients suffering from dementia. Some hospital physicians tried to figure out where the patient was going after the hospital stay (e.g., what home care area they belonged to) to provide necessary information to the home care service nurses regarding medication changes, for example. This was, however, extremely time consuming, and not possible to do in all cases. In one nursing home they explained that they reorganized their personnel across wards to ensure adequate competence in all wards if there was a lack of personnel. This was to ensure that no nurses were responsible for both administration of medications and their shift at the same time. Lastly, healthcare personnel described working intentionally to keep patients in the nursing homes if they needed antibiotic treatment, when this was the best option for the patient. The following quote from a nursing home physician describes this:

> The patient is better served by having familiar personnel around them, and we have good access to antibiotics and most things here. So, it shouldn't be necessary with [hospital] admissions for elderly patients severely affected by dementia.

It was also observed that a patient, who became acutely ill on the day he was being discharged from the nursing home, was rather moved to a more advanced ward at the nursing home for antibiotic treatment, in order to be spared a hospital admission.

Discussion

The results from this study showed that access to patient information varied, and coordination and communication in relation to medicine changes were poor. These were issues identified in both the hospital and in the primary healthcare service. Moreover, patients were discharged from hospital after medication changes (IV antibiotic to oral antibiotics) without proper observation of the effect of this change, often leading to a relapse and a need for hospital readmission. Most nursing homes had the competence to treat patients with antibiotic IVs, but they did not have access to all antibiotic types. Overall, all healthcare personnel worked to avoid medication-related hospital readmissions.

Treating Patients with Complex Medical Conditions

All Norwegian municipalities are responsible for ensuring access to good quality health and social services, for all their inhabitants, independent of age or diagnosis (Ministry of Health and Care Services, 2021). The scope of this responsibility has, however, increased in recent years, and will continue to increase in primary healthcare services worldwide (World Health Organization, 2018). Patients the primary healthcare services are now caring for, have more complex medical conditions, with more complex medical needs (Loeb et al., 2016; Osborn et al., 2015; Wallace et al., 2015). However, it has been demonstrated in this and similar studies, that there is a lack of suitable equipment, competence, and in some cases, access to correct medication, to care for these patients adequately (Glad et al., 2018; Søreide et al., 2019). For example, as demonstrated in this study, there was a lack of access

to the correct antibiotic type, and competence to provide antibiotic treatment in some nursing homes, despite the large amount of nursing home patients needing antibiotic treatment (5.2% of all Norwegian nursing home residents) (Norwegian Directorate of Health, 2019). Moreover, like Rustad et al. (2017), we found that there were difficulties in providing the correct type of medication at the right time, particularly when hospital discharges were abrupt, or occurred during weekends.

Transfer of Patient Information

This study identified problems relating to the transfer of patient information between healthcare service levels. Particularly, information about changes in medications and treatment regimens have been previously well-documented, and perceived as problematic at both ends of the healthcare service (the hospital and the primary healthcare service) (Laugaland et al., 2014; Pinelli et al., 2017; Rustad et al., 2017; Storm et al., 2014; Vatnøy et al., 2019). Several issues concerning the transfer of patient information tied to medication management directly were found. Some examples were: confusion with the medication list; and subsequent application of outdated lists; medication lists arriving late (along with the hospital stay summary); lack of access to the medication list (particularly among ER doctors); and having to transfer medication lists from one system to another. These issues are not unfamiliar (Breuker et al., 2021; Johnson et al., 2015; Kerstenetzky et al., 2018). In their literature review, Kerstenetzky et al. (2018), for example, found that medication discrepancies were common when patients transitioned between healthcare settings. Their quantitative analysis found that 76% of long-term care facility records had at least one medication discrepancy when compared to the hospital medication list. Similar results were also found in Breuker et al. (2021), where unintended medication discrepancies occurred in 29.4% of admissions or discharges, demonstrating the potential hazard of transferring medication lists from one system to another. Overall, Frydenberg and Brekke (2012) found that inadequate communication about patients' medications across healthcare service levels resulted in numerous and potentially harmful medication errors. In our study, poor information

exchange regarding patients' medications was perceived as a factor potentially leading to hospital readmissions.

Another issue that worried some of the physicians included in this study, was that different medication treatment regimens were started up by different physicians at different healthcare levels, with limited coordination between them. Communication and coordination between hospital physicians and primary care physicians are believed to be essential in providing high-quality, safe medical care (Sankey, 2017), and physicians are mostly well aware of this importance. However, studies supporting our findings say that physicians' ability to accomplish this in their daily work is limited by organizational factors. Jones et al. (2015), for example, found that heavy workloads and subsequent time limitations, lack of proper communication tools, lack of feedback loops to confirm receipt of information, and difficulties in locating the right information about the patients were barriers to adequate coordination.

Overall, efforts to address communication and coordination inadequacies have, in previous research, been shown to reduce errors and hospital readmissions, demonstrating that there is an untapped potential to improve quality of care in this context (Bellon et al., 2019; Henke et al., 2017; Laugaland et al., 2012).

Human Factors Theory

Human factors theory has gained recognition, due to its ability to provide system design methods that address the needs and desires of stakeholders in the healthcare system, in addition to other important sociotechnical aspects of healthcare (e.g., document and establish a shared understanding of different processes to identify improvement areas) (Wooldridge et al., 2017). According to human factors theory, performance (e.g., providing safe patient transfers) results from interactions in the healthcare system, whereas healthcare personnel are considered one of several embedded components. However, healthcare personnel are considered to be central in the work system, meaning that efforts must be taken so that system design (e.g., organization of the healthcare service) supports the healthcare personnel working within it (making sure that the design

fits their capabilities, limitations, and performance needs) (Holden et al., 2013). Through the perspective of medication management and hospital readmissions, several issues perceived as unsupportive of healthcare personnel's needs were identified. These include a lack of communication tools to provide well-coordinated care, poorly established guidelines on how to communicate the upstart of new treatment regimens, and lack of suitable equipment to treat patients in nursing homes. These results, if taken into account and applied by healthcare services policymakers, may facilitate an improvement of the systemic factors that do not support healthcare personnel's performance, and thereby improve healthcare quality (Wooldridge et al., 2017). Moreover, there is a need for more research exploring how medication-related hospital readmissions occur, focusing particularly on healthcare personnel's perspectives, so that a shared understanding of how processes may be improved can follow.

Conclusion

This study demonstrated a need for improved communication and coordination regarding medication management and medication changes, and in addition, a need to increase healthcare personnel's knowledge of each other's activities and treatment capacities. The lack of access to proper communication tools and well-functioning coordination routines were perceived, by the healthcare personnel in this study, as factors increasing medication-related hospital readmissions. Human factor theory can facilitate research exploring healthcare personnel's perspectives on how these issues may be addressed, and thereby enable organizational changes, which can better support healthcare personnel's performance. In doing so, unnecessary medication-related hospital readmissions and errors may be reduced.

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CHAPTER 17

We Are No Better Than the Weakest Link: Nurses' Experiences With Medication Management in Primary Healthcare

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Abstract: Today patients are discharged earlier from hospital, and consequently, an increasing number of seriously ill patients are being followed up by the primary healthcare services, and use various medications. Errors in pharmaceutical treatment, which cause deaths and adverse events, are among the errors most frequently reported. In this study, we explored experience, competence and competence needs related to medication management among nurses in primary healthcare. One hundred and ten nurses working in four municipalities in southeastern Norway were invited to fill in a paper-based questionnaire, and 87 responded (79%). Bivariate and cross-table analyses were performed.

Of these, 84% considered their medication management competence to be good or very good, but 70% of the nurses did not feel confident about drug interaction, and 45% were not confident about the effects and side effects of medication. Further, 55% had administered medication incorrectly or to the wrong patient (35%). The most common adverse event was to administer medication at the wrong time. The most common way to update one's knowledge was by reading the Norwegian Pharmaceutical Product Compendium (95%), and through dialogue with colleagues and doctors (94%). Most of the nurses (75%–85%) expressed a need for more knowledge. There was little difference between nurses working in home nursing care and in nursing homes. Despite reporting a low incidence of errors, few

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nurses have taken part in formal training after qualifying. Our findings indicate a special need for structural measures to increase nurses' competence related to medication and medication management in primary healthcare.

Keywords: Nursing, competency, medication management, medication administration, primary healthcare services

Background

Since the coordination reform (St.meld. nr. 47, 2008–2009), patients are discharged from hospital sooner, and the primary healthcare services are given greater responsibility for health and care services. The increased responsibility for treatment, and the increasing proportion of patients who are seriously ill, place heavy demands on the knowledge and skills of nurses in the primary healthcare services (Bing-Jonsson et al., 2015; Norheim & Thoresen, 2015; Tyrholm et al., 2015). Many elderly patients have comorbidity and use multiple medications. This increases the risk of medication errors, side effects and unfortunate drug interactions (Storli et al., 2016). Focus on safety and proper use of medication is important to the health of elderly people, and has a bearing on their quality of life (Romskaug et al., 2020).

The World Health Organization (2017) has defined medication safety as a global patient safety challenge. Incorrect use of medication can put life, health, and quality of life at risk. Patient safety is about protection against unnecessary injury as a result of the services performed by the healthcare service, or their failure to provide services (World Health Organization, 2017). The Norwegian patient safety program, "In Safe Hands", puts particular emphasis on the importance of safe medication management to avoid harm to patients (Norwegian Directorate of Health, 2019). Medication errors in hospitals is one of the error categories most commonly reported to the Norwegian Board of Health Supervision, and errors in double-checking are often cited as an important factor (Norwegian Directorate of Health, 2018). In Norway, 190 deaths and 160,000 adverse patient events are caused by medication every year (Olsen & Devik, 2016).

Regulations for medication management for healthcare organizations and personnel are intended to ensure appropriate and good medication management, and they stipulate professional responsibility requirements for all who provide healthcare (Helse- og omsorgsdepartementet, 2014). A survey conducted in 2019 by the Norwegian Nurses Organization showed that three out of ten nurses, on a weekly basis, are afraid of making a mistake that could harm a patient, and they link this to heavy workloads and inadequate training, among other factors (Helmers, 2019). A Belgian cross-sectional study found that nurses experience several barriers to safe medication management in nursing homes (Dilles et al., 2011). A recent systematic review that focused on identifying methods for measuring and describing nurses' medication administration skills found that medication management requires complex competence (Luokkamäki et al., 2021). The review highlights the need to address and develop nurses' competence in this field, and safe medication administration was defined as comprising nine areas: (1) safe ordering, handling, storing, and discarding of medications; (2) preparing of medications; (3) the administration of medications to patients; (4) documentation; (5) evaluation and assessment of medication-related issues; (6) drug calculation skills; (7) cooperation with other professionals; and (8) with the patients; and (9) reporting of medication information.

Medication management is one of the key responsibilities of nurses. However, research shows that nurses lack knowledge of how to administer medication (Hagesæter et al., 2016; O'Shea, 1999; Simonsen et al., 2011), and Johansen (2019) points out that nurses' knowledge of generic substitution is also inadequate. Inadequate mathematical knowledge is one of the factors linked to medication errors (O'Shea, 1999; Sulosaari et al., 2010). An integrative review by Kerari and Innab (2021) provides strong evidence that occurrences of medication errors are directly associated with level of education, training courses and extent of experience. In a qualitative systematic review Schroers et al. (2021) found that fatigue and complacency were personal factors described as reasons for medication errors, while knowledge factors related to lack of medication knowledge. Two smaller Norwegian studies also suggest the same thing. Wannebo and Sagmo (2013) found that nurses have a great need for

more knowledge on age-related physiological changes and pharmacology. Måløy et al. (2017) found that, among a sample of 262 nurses, 30% rarely or never read medical literature, and half have never attended a course or taken further education.

A review by Brady et al. (2009) pointed out the importance of management responsibility for systems of reporting and follow-ups of pharmaceutical treatment, in addition to the importance of the nurses' individual mathematical skills. Andreassen et al. (2011) found that there is little focus on drug calculation in practice. Schroers et al. (2021) emphasize the importance of contextual factors in medication administration, which are often underlying personal and knowledge-based factors. Contextual factors involve workload, interruptions, poor communication, lack of support, physical working conditions, and unsafe practice norms. There is little systematic competence building in the field of practice, and according to Storli et al. (2016), medication management training is not taken sufficiently seriously in the Norwegian context.

Nurses working in primary healthcare have a great responsibility for medication management, but we do not know enough about how they characterize their experience, competence, and competence needs relating to medication management. The aim of this chapter was to study nurses' experience of medication management in nursing homes and home nursing care, and how they perceive their own medication management practices. We asked the following research questions:

- How do nurses, working in nursing homes and home nursing care, rate their own knowledge and competence in the field of medication management?
- How do nurses update their own knowledge, and what training do they think they need?
- How well do nurses in nursing homes and home nursing care know the medication management procedures in their own workplace?
- Are there differences in knowledge, knowledge needs and knowledge of medication management procedures, which depend on the nurses' experience and on whether they work in a nursing home or in home-based services?

Method

Questionnaire

We conducted a quantitative questionnaire survey in order to obtain answers to our questions. We could not find a suitable questionnaire, so we developed one with seven background questions (part I), and 16 questions about medication management (part II). The background questions came with pre-defined answer alternatives with variables for place of work, experience, percentage of a full-time position, further education, and gender. Respondents could answer the question on further education in their own words. Part II consisted of questions about the experience of making errors, understanding the doctors' prescription, handling of non-conformities, and medication management procedures. Four questions focused on how confident nurses felt, their knowledge needs, and updating of their own knowledge. Fifteen of the questions had fixed responses, but the question about how nurses update their knowledge was open to answer in their own words. See the enclosed questionnaire for details (Appendix 1).

Recruitment

We approached the heads of eight entities, four in home-based services (home nursing care) and four in nursing homes, in four municipalities in eastern Norway, with information about the study. They all approved our request for participation. The criterion for participating was that the entity employed authorized general nurses in full-time or part-time positions. The entities in question employed a total of 110 nurses who met the inclusion criteria. The questionnaires were distributed to the institutions around the turn of the year 2017–2018. Eighty-seven completed questionnaires were returned (79%).

Ethics

The nurses received an information letter describing the objective of the study, accompanied by the questionnaire and anonymous envelopes to

submit their responses. They were informed that participation was voluntary and that their responses would be anonymous. Since the study was anonymous and did not involve processing personal data, the Norwegian Centre for Research Data (NSD) was not notified. The municipalities and institutions in the study are anonymized. In addition, as very few nurses in the sample and in nursing in general are male, we eliminated gender in the analysis to protect informants' identity. The questionnaire was paper-based, and nurses consented to taking part by completing the questionnaire and submitting it in a sealed envelope in a pigeonhole in the department.

Statistical Analysis

The data were analyzed using SPSS version 24.0. The transfer of data from the completed questionnaire forms to the data matrix was checked by a third party. Univariate analysis was used, and the variables were presented as frequencies and percentages. Bivariate analysis with contingency tables was used to identify relationships between variables. Among other things, we looked at whether self-reported practice, knowledge and skills depended on the nurses' place of work and work experience (practice, knowledge and skills as dependent variables). We made dummy variables for questions one and 14 in part II, where we assigned the value 0 to "Never" and the value 1 to the answers "1–4 times" and "more than 5 times" for question one. For question 14, we assigned the value 0 to "Yes" and 1 to "No" and "Uncertain". All the significance tests are two-sided, and $p \leq 0.05$ was considered significant. We used Pearson's chi-square test to test the significance level. Some cells where we found significant differences had the value 0, and they were checked using Fisher's test. This test produced the same result as the chi-square test, $p < 0.005$.

Results

Of the nurses in our sample, 56.3% were working in nursing homes, 81.6% were working in rotating shifts, and 88.5% were employed in more than 60% of a full-time position (Table 1). The proportion who had less than

4 years' work experience was 35.6% overall, with a somewhat higher percentage in home nursing care than in nursing homes. Of the nurses who worked in nursing homes, 28.6% had taken further education, while the corresponding percentage for those in home nursing care was only 10.5%.

Table 1. The sample with the number (percentage) who responded in different categories and with the given significance level (p value) and calculation of effect size (Cramer's V) for the correlation between the sample's workplace and the relevant variables

		Total (N = 87)	Nursing home N = 49 (56.3%)	Home nursing N = 38 (43.7%)	p values[a]	Cramer's V
Years of work experience	0–4 years	31 (35.6%)	15 (30.6%)	16 (42.1%)	0.420	0.18
	5–10 years	21 (24.1%)	11 (22.5%)	10 (26.3%)		
	11–15 years	17 (19.5%)	10 (20.4%)	7 (18.4%)		
	16 years or more	18 (20.7%)	13 (26.5%)	5 (13.2%)		
Further education		18 (20.7%)	14 (28.6%)	4 (10.5%) (sig. diff.)	0.060[b]	0.22
Percentage of full-time position	21–40%	3 (3.4%)	2 (4.0%)	1 (2.6%)	0.046[c]	0.23
	41–60%	7 (8.0%)	6 (12.3%)	1 (2.6%)		
	61–80%	19 (21.8%)	12 (24.5%)	7 (18.4%)		
	81–100%	58 (66.7%)	29 (59.2%)	29 (76.4%)		
Rotating shifts	No rotating shifts	16 (18.4%)	11 (22.4%)	5 (13.2%)	0.010	0.32
	Two-shift system	63 (72.4%)	30 (61.3%)	33 (86.8%)		
	Three-shift system	8 (9.2%)	8 (16.3%)	–		

[a]The two-sided chi-square test is used unless otherwise specified.
[b]Fisher's exact test is used.
[c]The chi-square test was performed on the binary outcome 100% or not 100% of a full-time position. This was done because the high number of cells with few answers posed a problem.

We found a significant correlation between place of work (nursing home or home nursing) and percentage of a full-time position ($p = 0.046$) and rotating shifts ($p = 0.010$), respectively, and the power of both these correlations was moderate with Cramer's V of 0.23 and 0.32, respectively. The correlation between place of work and further education was almost significant ($p = 0.060$), and the power of the correlation was moderate

(Cramer's V = 0.23). We found no statistically significant relationship between place of work and years of work experience (p = 0.420).

Table 2. How Informants Update Their Knowledge of Medication

	Place of work		Experience	
	Nursing home (N = 49)	**Home nursing (N = 38)**	**0–4 years' experience (N = 31)**	**More than 5 years' experience (N = 56)**
Norwegian Pharmaceutical Product Compendium	47 (95.9%)	36 (94.7%)	29 (93.5%)	54 (96.4%)
Conversations with colleagues	46 (93.9%)	36 (94.7%)	28 (90.3%)	54 (96.4%)
Contact with doctors	36 (73.5%)	28 (73.7%)	21 (67.7%)	43 (76.8%)
Specialist literature	26 (53.1%)	21 (55.3%)	17 (54.8%)	30 (53.6%)
Professional meetings	8 (16.3%)	9 (23.7%)	4 (12.9%)	13 (23.2%)
In-house courses	12 (24.5%)	12 (31.6%)	5 (16.1%)	19 (33.9%)
External courses	12 (24.5%)	7 (18.4%)	5 (16.1%)	14 (25%)
Further education	4 (8.2%)	3 (7.9%)	2 (6.5%)	5 (8.9%)

Furthermore, 96% of nurses updated their knowledge of medication by reading the Norwegian Pharmaceutical Product Compendium, and 94% did so through conversations with colleagues (Table 2). Contact with doctors was mentioned by 73.5%, and 53% read specialist literature to keep up to date. Experienced nurses and those employed in home nursing care cited professional meetings as a source of knowledge update to a greater extent than nurses working in nursing homes.

When asked how they rated their own medication management skills, 46% of the nurses responded that they were good, 38% that they were very good, and only 3% that they were fair. The nurses' practice and knowledge of medication management procedures are shown in Table 3. This shows that 34% have given medication to the wrong patient, and 34.7% of nurses in nursing homes and 39.5% of nurses in home nursing care have administered an incorrect dose. Only one nurse reported having administered medication that caused harm to a patient, while 30.6% in nursing homes and 28.9% in home nursing care stated that they have administered medication that had unexpected side effects. As many as 79.6% of nurses working in nursing homes and 76.3% of nurses in home nursing

Table 3. Self-reported practice and knowledge of medication management procedures by place of work

Background variable	Nursing home N = 49			Home nursing N = 38			Pearson's chi square
	Yes (%)	No (%)	Don't know (%)	Yes (%)	No (%)	Don't know (%)	Significance
Self-reported practice							
Have you at any time in your career:							
Administered an incorrect dose of medication	17 (34.7)	32 (65.3)	–	15 (39.5)	23 (60.5)	–	0.498
Administered medication incorrectly	29 (59.2)	20 (40.8)	–	19 (50)	19 (50)	–	0.694
Administered medication to the wrong patient	17 (34.7)	32 (65.3)	–	13 (34.2)	25 (65.8)	–	0.962
Administered medication at the wrong time	39 (79.6)	10 (20.4)	–	29 (76.3)	9 (23.7)	–	0.714
Administered medication that had an unexpected effect/side effect	15 (30.6)	24 (69.4)	–	11 (28.9)	27 (71.1)	–	0.933
Made a mistake that caused harm to a patient	0 (0)	49 (98.0)	1 (2)	1 (2.6)	33 (86.8)	4 (10.5)	0.119
Administered medication without the patient's consent	29 (59.2)	29 (49.8)	0	13 (34.2)	23 (60.5)	2 (5.3)	0.030*
Disagreed with the doctor's prescription and contacted another doctor	20 (40.8)	29 (59.2)	0	19 (50)	19 (50)	0	0.393
Are pill organizers double-checked?	47 (95.9)	1 (2)	1 (2)	37 (97.4)	1 (2.6)	0	0.666
Knowledge of medication management procedures							
Are procedures for reporting non-conformities in place in your workplace?	43 (87.8)	5 (10.2)	1 (2)	33 (86.8)	3 (7.9)	2 (5.3)	0.680
Have you ever reported a medication-related non-conformity?	42 (85.7)	7 (14.3)	0	35 (92.1)	3 (7.9)	0	0.254
Are you familiar with your place of work's medication management guidelines?	47 (95.9)	2 (4.1)	0	36 (94.8)	1 (2.6)	1 (2.6)	0.491
Do you know who is responsible for medication management at your place of work?	36 (73.5)	8 (16.3)	5 (10.2)	34 (89.5)	0	4 (10.4)	0.032*
Are you aware of the narcotic drugs inventory frequency?	49 (100)	0	0	27 (71.1)	7 (18.4)	4 (10.5)	0.000*
Do you know who the advisory pharmacist is?	16 (32.7)	31 (63.2)	2 (4.1)	22 (57.9)	14 (36.8)	2 (2.3)	0.048*

care had administered medication at the wrong time. In addition, 87% of nurses stated that they were familiar with non-conformity procedures and division of responsibility, while 85.7% of nurses in nursing homes and 92.1% of nurses in home nursing care had reported non-conformities. There were no significant differences associated with place of work in these areas. Of the nurses working in nursing homes, 59.2% had administered medication without the patient's consent, a significantly higher percentage than in home nursing care (34.2%)

In nursing homes, 33% of nurses knew who the advisory pharmacist was, compared to 58% in home nursing care (Table 3). Corresponding figures for whether they knew who was responsible for medication management were 73.5% and 89.5%, respectively. In both these areas, nurses working in home nursing care knew significantly more than those working in nursing homes. The opposite was true of knowledge of the narcotic drugs inventory frequency. Significantly more nurses in nursing homes (100%) possess this knowledge compared to those working in home nursing care (71%).

Table 4 shows how nurses regard their knowledge and skills, when asked about how confident they were about their different skills, and what they needed more knowledge about. When asked whether they were confident about their own skills, 89.8% of nurses in nursing homes and 84.2% of nurses in home nursing care responded that they felt confident about the use of generic medications. There were similarly high figures for the question on whether the nurses were confident about the rules and procedures relating to expiry dates and documentation. As regards drug calculation, 83.7% of nurses in nursing homes and 78.9% of nurses in home nursing care stated that they were confident. However, 45% and 42% replied that they were not confident when it came to the effects and side effects of medication, and about 70% of nurses in both nursing homes and home nursing care stated that they were not confident about drug interactions. There was a significant difference for place of work in the responses to the question about procedures for changing the form of medication, as 83.7% of nurses in nursing homes felt confident, while the same was true of only 60.5% in home nursing care.

Table 4. Self-reporting and knowledge and skills by place of work

	Nursing home (N = 49) (n = %)		Home nursing care (N = 38) (n = %)		Pearson's chi square
	Yes (%)	No/Don't know (%)	Yes (%)	No/Don't know (%)	Significance
Knowledge					
Are you confident when it comes to ...?					
Using the Norwegian Pharmaceutical Product Compendium	46 (93.9)	3 (6.1)	37 (97.4)	1 (1.1)	0.441
Drug calculation	41 (83.7)	8 (16.3)	30 (78.9)	8 (9.2)	0.573
The effects and side effects of different medications	27 (55.1)	22 (44.9)	22 (57.9)	16 (42.1)	0.794
Medication dosage	45 (91.8)	4 (8.2)	36 (94.7)	2 (5.3)	0.596
Drug interactions	14 (28.6)	35 (71.4)	12 (31.6)	26 (68.4)	0.761
Administering generic medications	44 (89.8)	5 (10.2)	32 (84.2)	6 (15.8)	0.437
Procedures for changing the form of medication	41 (83.7)	8 (16.3)	23 (60.5)	15 (39.5)	0.015*
Rules for storage of medication	44 (89.8)	5 (10.2)	32 (84.2)	6 (15.8)	0.437
Rules and procedures relating to expiry dates	44 (89.8)	5 (5.7)	35 (92.1)	3 (7.9)	0.712
Rules and procedures relating to documentation	45 (91.8)	4 (8.2)	33 (86.8)	5 (13.2)	0.448
Need for knowledge	**Nursing home (N = 49) (n = %)**			**Home nursing care (N = 38) (n = %)**	
I need more knowledge about:	**Yes (%)**	**No (%)**	**Don't know (%)**	**Yes (%)**	**No (%)**	**Don't know (%)**	**Significance**
Age-related physiological changes and pharmaceutical treatment	41 (83.7%)	6 (12.2%)	2 (4.1%)	33 (86.8%)	4 (10.5%)	1 (1.1%)	0.900
General pharmacology	36 (73.5%)	11 (22.4%)	2 (4.1%)	29 (76.3%)	7 (18.4%)	1 (2.3%)	0.880
Medication's side effects and mechanisms of action	39 (79%)	9 (18.4%)	1 (2%)	30 (78.9%)	7 (18.4%)	1 (2.6%)	0.983
Different forms of medication	21 (42.9%)	25 (51%)	3 (6.1%)	18 (47.4%)	19 (50%)	1 (2.6%)	0.716
Routes of administration	18 (36.7%)	29 (59.2%)	2 (4.1%)	15 (39.5%)	21 55.3%)	2 (2.3%)	0.921
Drug calculation	19 (38.8%)	28 (57.1%)	2 (4.1%)	16 (42.1%)	19 (50%)	3 (7.9%)	0.669
The Norwegian Pharmaceutical Product Compendium	6 (12.3%)	42 (85.7%)	1 (2%)	10 (26.3%)	26 68.4%)	2 (5.3%)	0.152

When asked about their need for more knowledge, 83.7% in nursing homes and 86.8% in home nursing care stated that they needed more knowledge about age-related physiological changes and medication. More knowledge about general pharmacology was needed by 73.5% of nurses in nursing homes and 76.3% in home nursing care, while 79% in both groups needed more knowledge about medication side effects and mechanisms of action. More knowledge about different forms of medication was needed by 42.9% of nurses in nursing homes and 47.4% in home nursing care, while 36.9% and 39.5%, respectively, needed more knowledge about their routes of administration. The need for more knowledge about the Norwegian Pharmaceutical Product Compendium was reported by 12.3% of nurses in nursing homes and 26.3% of nurses in home nursing care. There was no difference between nursing homes and home nursing care in the nurses' need for knowledge.

Discussion

The findings of this study show that the vast majority of nurses in primary healthcare services deem their own medicine management competence to be good or very good. Nearly half of them state that they are not confident about the effects and side effects of medication, and two out of three state that they do not feel confident about drug interactions. The most important sources of knowledge are use of the Norwegian Pharmaceutical Product Compendium (*Felleskatalogen*) and dialogue with colleagues and doctors. The percentage of nurses who have attended formalized training courses appears to be somewhat higher among nurses who have been working for more than five years. However, the differences were not statistically significant. Few nurses have made serious medication errors that have harmed a patient. Generally speaking, the most commonly reported error relates to the time of administration. Half of the nurses had administered medication incorrectly or to the wrong patient. As regards competence-raising needs, a majority state that they need more knowledge, particularly about age-related physiological changes and pharmaceutical treatment, general pharmacology, side effects, and mechanisms of action. Half of the nurses call for more

knowledge about different forms of medication, routes of administration and drug calculation.

There is little difference between nurses working in home nursing care and in nursing homes, but a significantly higher percentage of nurses in nursing homes have further education and longer work experience. When it comes to medication procedures, nurses in nursing homes are more familiar with the advisory pharmacist scheme and narcotic drugs records. However, nurses in home nursing care know more about the division of responsibility for medication management. The majority of nurses who took part in the study were familiar with the non-conformity reporting system and have reported non-conformities.

The differences in medication practices between nursing homes and home nursing care could be related to differences between their respective fields of practice. Nurses in nursing homes work within a single institution, and probably have more routine work practices and a common system for all patients. In home-based services, the patients live at home, and many use the multi-dose packaging system and are more involved in organizing their own medication. Nurses are further away and have less opportunity to observe their patients than in nursing homes, for example when it comes to effects and side effects of medication. This could explain why nurses in home nursing care have not administered medication without the patient's consent. The community nurses have to address any questions to the individual patient's regular GP in the municipality, and this can be assumed to raise their awareness of responsibility. This could be one explanation for why the study showed that community nurses were more aware of the division of responsibility.

Otherwise, the differences between nurses working in home-based services and nursing homes were minor, but both groups express a need for more competence when it comes to drug interactions. It also appeared that a majority of nurses in home nursing care felt less confident about changing forms of medication. This can be interpreted in line with Johansen (2019), a study on the use of substitution lists among nurses working in hospitals, where the nurses were found to have inadequate knowledge of generic substitution. The vast majority of nurses in our study rank their overall medication management skills as good or very

good, while they also want to raise their competence. This finding agrees with Norheim and Thoresen (2015), who interviewed nurses working in home nursing care, in relation to competence in more general terms. They found that the nurses felt that they had the competence they needed to deal with the challenges that arose, while nevertheless describing their competence as inadequate and expressing a wish to improve it. The fact that nurses generally feel competent, but still wish for increased knowledge and competency may be understood as an indication of the nurses' professional responsibility.

Based on Johansen's (2019) study on generic substitution and nurses' lack of insight into their own inadequate competence, it is important to question whether the knowledge and competence reported by the nurses themselves are representative of their actual medication management competence. It is common for nurses to work alone, both in nursing homes and in home nursing care. This offers few opportunities for discussion, guidance and feedback from colleagues if needed, because the nurses do not see each other in relevant work situations, which is also described by Schroers et al. (2021). Bjørk (1999) demonstrated how weak professional practices become routine for newly qualified nurses precisely because they perform the procedures alone, with no one to discuss them with. If nurses are unaware that they lack competence or do things incorrectly, this could contribute to incorrect practices continuing if they remain undetected.

In our study, nurses reported that they feel confident performing most tasks relating to medication management, at the same time as they need more knowledge in major areas such as general pharmacology and age-related changes. Nurses have a responsibility as healthcare personnel to keep up to date professionally, and it is reassuring that the nurses state that they need more competence. At the same time, only half of them report reading medical literature to keep up to date. This is slightly higher than in the study by Måløy et al. (2017), in which the figure was only one in three.

Few of the nurses who have worked for a short time have taken part in professional meetings and further education to update their knowledge, and they keep up to date professionally through dialogue with colleagues

and doctors. This means that medication information is communicated, and training provided, in less formalized forms. Despite this, the nurses responded that their place of work facilitates safe and secure medication management. Sadeghi (2020) describes challenges associated with informal and unstructured training in the workplace. She points out that in the absence of targeted training, tacit knowledge is produced that could lead to inexpedient or even incorrect practices. Informal learning is not suited to keeping abreast of rapid developments and changes, for example in the field of medication. Formal training (in the form of courses) should form a basis and a condition for informal training. Adapted training in the workplace is therefore deemed to be important in ensuring good and correct learning, and thereby also good practice (Sadeghi, 2020). The findings in our study indicate that nurses have limited access to formal training and courses. This is cause for concern and indicates shortcomings at the system level. There is reason to emphasize the importance of training and competence-raising measures in the workplace as structural measures to maintain sound professional practice (Schroers et al., 2021). Sound medication practices involve a complex chain of skills (Luokkamäki et al., 2021), and weak links in this chain can lead to errors and adverse events that cause harm to patients.

It is particularly worrying that our results show that employees with short work experience state that they have received little training. Sulosaari et al. (2010) point out that there is an attitude that newly graduated nurses are expected to have learnt everything they need to know. This is cause for concern, both in relation to workloads in primary healthcare and rapid developments in the pharmaceutical industry. This supports Wannebo and Sagmo (2013), who conclude in their study that repeated in-house courses, with concrete learning objectives and subject matter related to the needs of the employees, are important in the field of medication and medication management. They point out that medication management skills require continuous updates, and that all employees with medication management responsibility should be offered competence-raising measures. Based on the fact that nurses often find medication errors to be multifactorial and interconnected, Schroers et al. (2021) argue for an emphasis on changing the system.

The introduction of the coordination reform brought changes to the tasks and complexity of the primary healthcare services, as well as new and greater demands in terms of the knowledge required to meet patients' needs. Heads of entities, and in some cases pharmacists, have been delegated the responsibility for medication management by doctors. Greater importance should be attached to this area of responsibility in order to improve the knowledge culture and attitudes towards developing and updating knowledge among nurses. Systematic training and reporting of non-conformities are important factors that can help to prevent errors from being repeated, ensure that knowledge is updated, and that nurses are reassured and procedures changed. The regulations for management and quality improvement in the health and care services (2017) instruct enterprises to facilitate safe and secure medication management. Considering that medication management errors make up the biggest group of errors reported to the Norwegian Board of Health Supervision, the findings from this study provide grounds for questioning whether enough has been done at the structural level to ensure safe medication practices in primary healthcare.

Methodology discussion

The high response rate (79%) and the fact that the study included nurses working in four different municipalities are the clear strengths of this study. Nevertheless, 87 informants is a relatively small sample, and this makes it difficult to demonstrate significant relationships and differences.

We developed the questionnaire that was used ourselves, and it has not been validated. One may question whether self-reporting of competence produced reliable answers, and whether the participants gave honest answers. The reliability of self-reporting of experience that, for some of the participants, goes back as far as 20 years, can also be questioned. Despite these weaknesses, we consider the material to be satisfactory overall, and find that it provides important indicators and answers to the study's research questions. We also consider the study to be an important recommendation for interesting issues relating to medication management in primary healthcare.

Conclusion

The results of this study show that the majority of nurses in primary healthcare services deem their own medicine management competence to be good or very good, and that few have made serious medication errors. At the same time, only half of them state that they are confident about the effects and side effects of medication, and two out of three state that they do not feel confident about drug interactions. The most important ways in which they update their professional knowledge is by using the Norwegian Pharmaceutical Product Compendium and through dialogue with colleagues and doctors, while only half of them use specialist literature for this purpose. Few have attended formal medication management training. A vast majority of the nurses state that they need more knowledge, particularly about age-related physiological changes and pharmaceutical treatment, general pharmacology, side effects, and mechanisms of action. Half of them also want more knowledge about different forms of medication, their routes of administration, and drug calculation. The vast majority of nurses are familiar with the non-conformity reporting system and have reported non-conformities, but nurses in nursing homes are less aware of the division of responsibility for medication management than those working in home nursing.

These findings are consistent with findings from other studies, and support the need to raise competence and strengthen medication management practices in primary healthcare. The absence of formal training in the form of in-house and external courses reveals a particular need for structural competence-raising measures relating to medication and medication management. There is reason to believe that strengthened and structured training can help to reduce the proportion of adverse events, and even deaths, reported as a result of errors relating to the use of medication outside a hospital setting.

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Appendix 1: Questionnaire

I. Background questions

1. I work in:

A nursing home ☐ Home-care services ☐

2. Years of work experience as a nurse

0-4 years ☐ 11-15 years ☐

5-10 years ☐ 16 years or more ☐

3. Do you have further education?

Yes ☐ No ☐

If yes, please elaborate:_____

4. For how long have you been working in the workplace where you work today?

0-4 years ☐ 11-15 years ☐

5-10 years ☐ 16 years or more ☐

5. What is the percentage of full-time equivalent today?_____

6. What rotation shifts do you work?

Two-shift system ☐ Three-shift system ☐

Not working shift ☐

7. Gender

Male ☐ Female ☐

II.

1. Have you at any time in your career as a nurse:
(if you don't remember exactly, you can estimate)

		Never	1- 4 times	5 times or more
a	- administered an incorrect dose of medication	☐	☐	☐
b	- administered medication incorrectly	☐	☐	☐
c	- administered medication to the wrong patient	☐	☐	☐
e	- administered medication at the wrong time	☐	☐	☐
f	- administered medication that had an unexpected effect/side effect	☐	☐	☐

		Yes	No	Do not know
2	Have you at any time in your career made a mistake that caused harm to a patient	☐	☐	☐
3	Have you at any time in your career administered medication without the patient's consent	☐	☐	☐
4	Have you at any time in your career disagreed with the doctor's prescription and contacted another doctor	☐	☐	☐
5	Are procedures for reporting non-conformities in place in your workplace?	☐	☐	☐
6	Have you ever reported a medication-related non-conformity?	☐	☐	☐
7	Are you familiar with your place of work's medication management guidelines?	☐	☐	☐
8	Do you know who is responsible for medication management at your place of work?	☐	☐	☐
9	Are you aware of the narcotic drugs inventory frequency?	☐	☐	☐
10	Are pill organizers double-checked in your workplace?	☐	☐	☐
11	Do you know who the advisory pharmacist is?	☐	☐	☐

		Very good	Good	Poor	Very poor
12	In your experience, how do you describe the state of your work-place as regards safe medication management:	☐	☐	☐	☐
13	How would you describe your own ability in medication management:	☐	☐	☐	☐

14. Are you confident when it comes to …?

		Yes	No	Uncertain
a	- using the Norwegian Pharmaceutical Product Compendium	☐	☐	☐
b	- drug calculation	☐	☐	☐
c	- the effects and side effects of different medications	☐	☐	☐
d	- medication dosage	☐	☐	☐
e	- drug interactions	☐	☐	☐
f	- administering generic medications	☐	☐	☐
g	- procedures for changing the form of medication	☐	☐	☐
h	- rules for storage of medication	☐	☐	☐
i	- rules and procedures relating to expiry dates	☐	☐	☐
j	- rules and procedures relating to documentation	☐	☐	☐

15	I need more knowledge about:	Yes	No	Do not know
a	- age-related physiological changes and pharmaceutical treatment	☐	☐	☐
b	- general pharmacology	☐	☐	☐
c	- medication's side effects and mechanisms of action	☐	☐	☐
d	- different forms of medication	☐	☐	☐
e	- routes of administration	☐	☐	☐
f	- drug calculation	☐	☐	☐
g	The Norwegian Pharmaceutical Product Compendium	☐	☐	☐

16 How do you update your knowledge of medication?

Norwegian Pharmaceutical Product Compendium	☐
Conversations with colleagues	☐
Contact with doctors	☐
Specialist literature	☐
Professional meetings	☐
In-house courses	☐
External courses	☐
Further education	☐

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Medicines constitute an essential part of healthcare delivery and help to prevent or treat illness, influence quality of life, and generally increase life expectancy. However, medications can also cause harm if prescribed irrationally, dispensed or used incorrectly, and monitored or followed up insufficiently.

In this anthology, we showcase the challenges of medication management and the rational use of medicines in municipal health and care services, and present various strategies and measures related to medication safety. The contributors are researchers representing a wide range of disciplines, with experience from different levels of healthcare services and different areas within the research and education sectors. We hope to raise awareness, engage and enable discussion of initiatives and strategies to improve patient safety related to medications in municipal health and care services, and create a basis for further research to promote safe medication management and rational use of medicines.

This anthology will be of interest to anyone involved in or concerned with medication safety, primarily healthcare professionals, academic staff, researchers, policymakers, and managers in healthcare services.

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