

# Multidose drug dispensing in home care services

Impact of a shared medication list on medication safety

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Thesis submitted for the degree of Philosophiae Doctor

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2022

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*Series of dissertations submitted to the  
Faculty of Mathematics and Natural Sciences, University of Oslo  
No. 2568*

ISSN 1501-7710

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Print production: Graphics Center, University of Oslo.

## Acknowledgements

First and foremost, I would like to thank my supervisors Anne Gerd Granås and Trine Strand Bergmo. With your different scientific and personal skills, you have formed a great supervising team. Anne Gerd, I have greatly appreciated your broad scientific competence, your ability to challenge me and help me put my research into a broader context. Trine, thank you for the brainstorming, the quick feedback and for always being available, not to mention the many phone calls when I was less motivated.

I am very grateful to my employer, the Norwegian Centre for E-health Research (NSE) and Monika Johansen for giving me the opportunity to do this PhD project, including the Digital Health Services department, where I have always felt included despite us being physically located at opposite sides of the country. I would also like to thank Alma and my other colleagues at the PharmaSafe research group at the University of Oslo, for including me in this great scientific and social environment.

Thank you Kaitlyn and Iselin for the many, many, many hours of *shut up & write* these last two years. These sessions have always been my most efficient writing time, but the 15-minute breaks between the sessions have been just as important to me. I hope we get to meet in person soon.

I would also like to thank Apotek 1 AS for providing data for Paper I and for letting me do the other studies in your pharmacies. Thank you to Almira Ticevic and Maria Simmack for helping me collect data for Paper III and to the nurses, GPs and pharmacy employees who participated in Paper II, III and IV.

To my dad, thank you for all the discussions and brainstorming, for the many hours you have listened to me talking about my research and helped me sort my chaotic ideas. You have also helped me keep a community pharmacist's perspective on my research.

Fosser, May 2022

Anette Vik Jøsendal





## Summary

Multidose drug dispensing (MDD) is machine dispensed medicines into unit bags for each administration time. About 100,000 patients use MDD in Norway, primarily patients receiving home care services. MDD can improve medication adherence and cooperation between health care personnel in primary care, but may also increase potentially inappropriate prescribing and the risk of discrepancies in medication records during care transitions.

The Directorate of e-health is currently developing a nationwide electronically Shared Medication List (eSML), whereby a list of all the medications of a patient is shared across care providers. The goal of the eSML is to increase medication safety by generating a complete and updated overview of the patient's current medication treatment accessible to all health care personnel. The eSML is expected to improve the quality of medication treatment and reduce the time health care personnel spend on medication reconciliation. Because MDD patients already have a complete medication list, though this is presently paper-based, these patients are the first to pilot the eSML system. When implemented, the paper-based list will be replaced by an eSML and accompanying e-prescriptions. The aim of this thesis is to examine medication safety in the MDD system and how this is affected by the eSML system, with a focus on the pharmacist's responsibilities.

The first paper in this thesis is a cross-sectional study investigating the quality of medication treatment in MDD patients, using the Norwegian General Practice Criteria. The results show that the current paper-based MDD prescription lists gives a good overview of the patient's total medication use, including dietary supplements and *when needed* medications. As one-third of the 45,593 patients included in this study used 10 or more medicines regularly, we found that overall medication consumption is higher in MDD patients than the general elderly population. In addition, we found that one-fourth are prescribed potentially inappropriate medications and half are exposed to drug-drug interactions.

In the second paper, pharmacists from eleven community pharmacies used self-completion forms to register prescription problems they encountered whilst dispensing MDD. They identified and resolved problems with 11% of the 4121 MDD prescriptions dispensed, the most common were expired prescriptions (29%), drug shortages (19%) and missing prescriber signatures (10%). The high intervention rate might be explained by the pharmacists actively

using the medication dispensing history and having increased access to information about the medication use, such as discharge notes from the hospital. In terms of responsibilities, we find that the pharmacists provided limited patient counselling while dispensing. However, they took on additional responsibility for renewing MDD prescriptions compared to ordinary prescribing, and frequently dispensed emergency refills due to void prescriptions.

In the third paper, we compared the medication lists at the GP, home care service and pharmacy for 189 patients (100 intervention; 89 control) 3 months before and 18 months after the implementation of the eSML. Medications present in all three lists increased from 77% to 94% in the intervention group, thus improving the overview of the patient's total medication use compared to the paper-based list. The increase in the control group was not statistically significant. After the implementation, 56% of patients still had discrepancies and the eSML system does not eliminate the need for medication reconciliations.

In the fourth paper, we interviewed in total 36 nurses and pharmacists about their experiences with the eSML system. They described how changes in the medication treatment was initiated faster in the MDD bags, less manual transcribing of prescriptions, and increased access to information about the patient's medication use. However, increased access to information and more actors who could prescribe for the patients increased the need to clarify what is the current and correct treatment for the patients, resulting in an increased overall workload. Renewing void prescriptions remained among the most frequent reasons for the pharmacist to contact the prescriber.

It seems the eSML system increases access to information and reduce discrepancies in medication records, thus further improving the overview of the patient's total medication use that is one of the benefits of today's MDD system. However, there is an unfulfilled potential for health care personnel to cooperate and utilize this increased overview to improve the quality of medication treatment in this vulnerable patient group. The current guidelines for MDD do not reflect what pharmacists actually do, and as more actors can influence prescribing in the upcoming eSML system, this makes it even more important to define each actor's role and responsibilities. For the eSML to fully achieve its goals of increasing medication safety there is a need to define the responsibilities of all the actors in the medication use process, along with the responsibility of assessing the entire medication treatment of a patients, including those medications prescribed by other physicians.

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- Paper I Josendal, A. V., Bergmo, T. S., & Granas, A. G. (2020). Potentially inappropriate prescribing to older patients receiving multidose drug dispensing. *BMC geriatrics*, 20(1), 272. <https://doi.org/10.1186/s12877-020-01665-x>
- Paper II Josendal, A. V., Bergmo, T. S., & Granas, A. G. (2021). The Practice Guidelines for Multidose Drug Dispensing Need Revision-An Investigation of Prescription Problems and Interventions. *Pharmacy*, 9(1), 13. <https://doi.org/10.3390/pharmacy9010013>
- Paper III Josendal, A. V., Bergmo, T. S., & Granas, A. G. (2021). Implementation of a shared medication list in primary care - a controlled pre-post study of medication discrepancies. *BMC health services research*, 21(1), 1335. <https://doi.org/10.1186/s12913-021-07346-8>
- Paper IV Josendal, A. V., & Bergmo, T. S. (2021). From Paper to E-Prescribing of Multidose Drug Dispensing: A Qualitative Study of Workflow in a Community Care Setting. *Pharmacy*, 9(1), 41. <https://doi.org/10.3390/pharmacy9010041>



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## Abbreviations

ADE – adverse drug event

ADR – adverse drug reaction

DID – drug-drug interactions

DRP – drug-related problems

EHR – electronic health record

eSML – electronically shared medication list

MDD – multidose drug dispensing

NORGEF criteria – Norwegian general practice criteria

PIM – potentially inappropriate medications



## BACKGROUND

Multidose drug dispensing (MDD) is a system where medications are machine dispensed into unit bags for each administration time. The system is commonly used for patients receiving home care services instead of manually-filled dosettes. When electronic prescriptions were implemented in Norway in 2011–2013, this did not include prescriptions for MDD. MDD prescriptions are thus still paper-based, usually printouts from the GP medication record, which are sent by fax from the GPs to an MDD pharmacy. This thesis is a part of a larger project that evaluates the effects of the electronic prescribing system that is currently being piloted in Norway (Bergmo, 2022). The focus of this thesis is on medication safety in the MDD system.

### **Personal background and motivation**

MDD has been an important part of my entire career and I have worked with this system in different settings over the years. I have hands-on experience with the system from pharmacies serving MDD patients, I have worked at the MDD manufacturer assessing the suitability and stability of medicines for dose dispensing, and as a product owner of an MDD dispensing program I have defined how this system should support pharmacies' work processes. Throughout these various positions, I have been interested in how to work efficiently while also prioritizing medication safety — particularly how technology can assist in this process. My attitude towards MDD is that the system is safer than manual dispensing of dosettes and therefore it is important to make it as efficient and safe as possible for all actors involved.

Figure 1a and 1b shows two pictures from my current workplace. No less than four fax machines are needed to process all the incoming paper prescriptions related to MDD, and Figure 1b illustrates just how many paper sheets pass through this pharmacy in one day. Having worked with this system for years, I know from personal experience how much time is spent on sorting faxes and clarifying issues regarding these prescriptions. So, when I heard that the Directorate of e-health was working on an electronic prescribing system for these patients, I had high expectations for how this would replace the need for sorting and transcribing heaps of paper prescriptions, in addition to eliminating time spent on clarifications due to prescriptions being faxed with the wrong side up, prescriptions with unclear handwritten notes and prescriptions without the prescriber's signature.

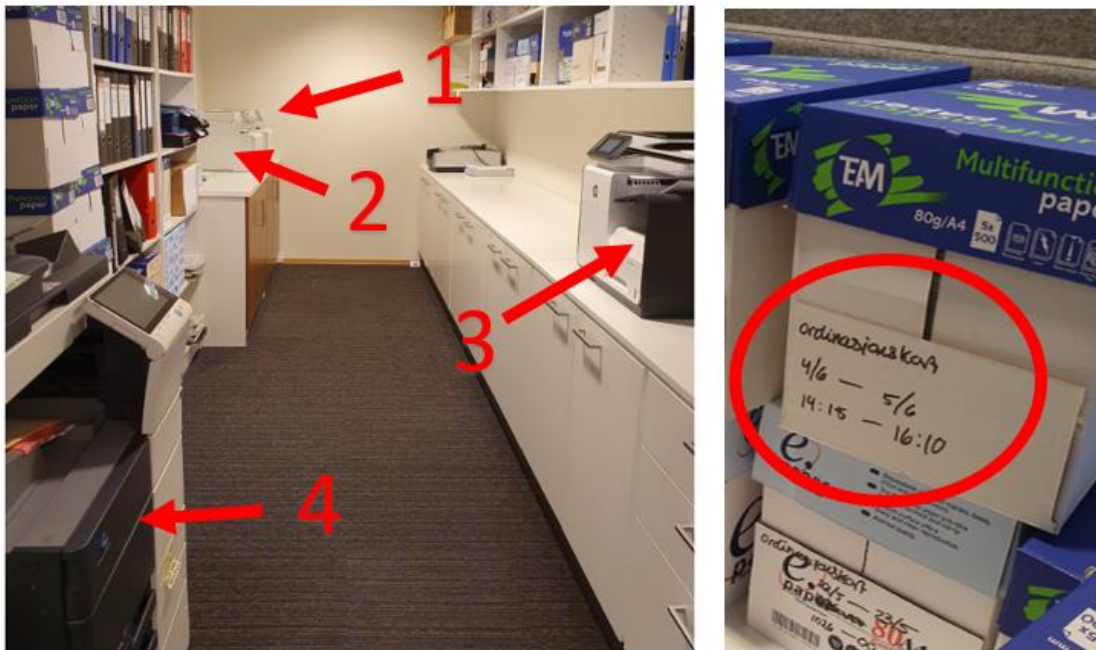


Figure 1: The faxes at Apotek 1 Skårersletta. Left side: A picture of the 4 fax machines. Right side: An archive box for MDD prescriptions with the print "4.June 14:15 - 5.June 16:10" - illustrating the amount of paper sheets generated during one day.

However, my expectations changed when the actual pilot of the system started in 2014. I had been involved in adapting the MDD dispensing program for electronic prescriptions, and I was responsible for the technical/practical support of the first pharmacies testing this system. We quickly noticed that this system did not save as much time for the pharmacy as I had hoped for. Despite continuing to correct errors and adapt our systems and routines to improve workflow, the pharmacies continued to express that the electronic prescription system for MDD patients was more time consuming than the paper-based one.

In 2017, I accepted a PhD position to evaluate the electronic MDD system, while still holding a 25% position at the pharmacy chain throughout my PhD. Though I was worried the pharmacy position might lead to mixing of roles, both positions have had the same aim: to optimize the electronic MDD system. Combining research and practice has helped me to focus the research on the areas most affected by the electronic MDD system, as well as making the research more rewarding as I could see immediate effects of the four research papers as we adapted the routines for implementation and systems based on these findings.

## INTRODUCTION

### The medication use process and medication safety

The medication use process describes the process that goes from a physician evaluating the patient's need for medicine to the effect of that medicine being reported and documented. This complex process involves communication and information sharing across different settings and among different actors, including the patients themselves (Aspden et al., 2007, pp. 50-104; Avery et al., 2002; Classen & Metzger, 2003; Ferner & Aronson, 2006; Thomsen et al., 2007; Topinková et al., 2012). The process is usually divided into five different phases: prescribing, transcribing, dispensing, administration and monitoring of medication use (Aspden et al., 2007, p. 67; Clyne et al., 2012; Ferner & Aronson, 2006; Gandhi et al., 2000; United States Pharmacopeia, 2004). Figure 2 shows the medication use process and how the steps are defined in this thesis.

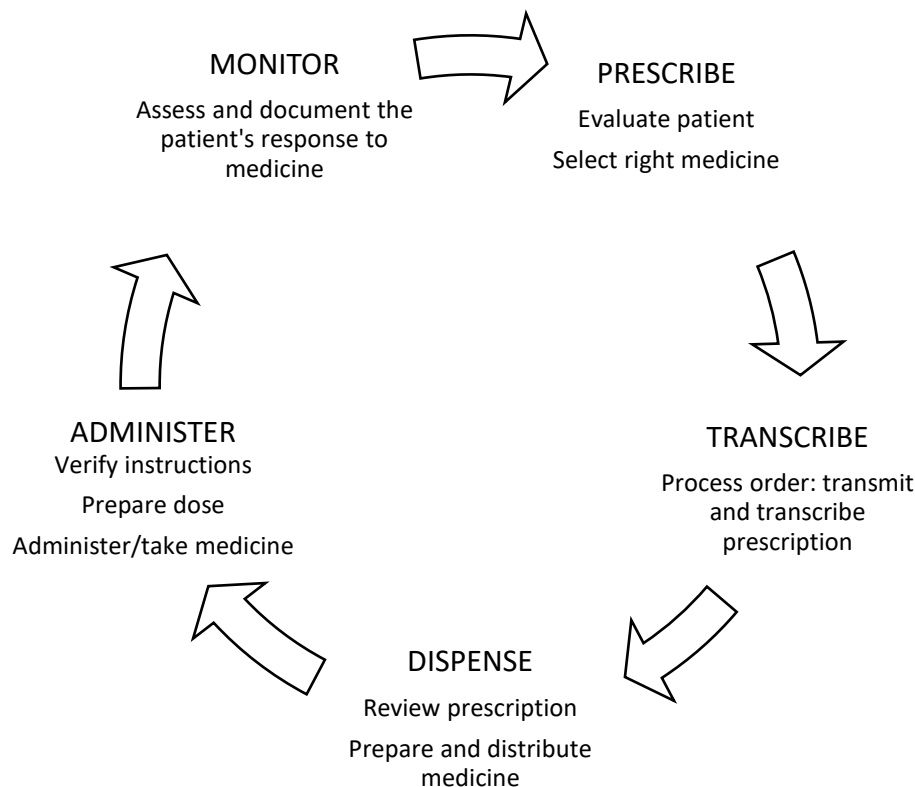


Figure 2: The medication use process.

Errors can happen at any stage in the medication use process. Most commonly reported are errors in the prescribing and administration phase (Bates et al., 1995; Rachel Ann Elliott et al., 2021; Leape et al., 1995; Panesar et al., 2016). Though many medication errors have little or no potential for harm (Bates et al., 1995; Classen & Metzger, 2003; Rachel Ann Elliott et al., 2021), some also cause adverse drug events (ADE) that can lead to hospitalizations, prolonged hospital stays or death (Al Hamid et al., 2014; Bates et al., 1995; El Morabet et al., 2018; Rachel Ann Elliott et al., 2021). The World Health Organisation has estimated that medication errors are associated with a cost of over €40 billion per year globally (World Health Organization, 2017). A recent study from Rachel Ann Elliott et al. (2021) estimated that 237 million medication errors occur in England annually, which contributed to 1700 deaths and had a total cost of €117 million. In Norway, a recent Norwegian study showed that one in five emergency department visits were medication-related (Nymoene et al., 2022).

There are numerous different definitions of medication errors and other terms used to describe safety of medication use (Lisby et al., 2010; Pintor-Mármol et al., 2012). This thesis mostly uses the term drug-related problem (DRP). A DRP is defined as “an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes” (Pharmaceutical Care Network Europe Association, 2020), and includes medication errors and ADE, as well as other circumstances that might interfere with desired health outcome such as potentially inappropriate medications (PIMs), drug-drug interactions (DDI), underuse of medication and medication non-adherence (Pharmaceutical Care Network Europe Association, 2020; van den Bemt et al., 2000; Westerlund & Marklund, 2009).

In this thesis, medication safety will be discussed in the context of DRPs in the different stages of the medication use process.

### **Medication safety in home care services**

A patient group particularly at risk for DRPs are older adults and other patients taking multiple medications (Panesar et al., 2016; World Health Organization, 2017). This is partly due to the characteristics of aging, such as altered fat and water distribution, decreased renal function and potential mental impairment (Rognstad et al., 2009; Romskaug & Bakken, 2020). In



addition, this group often has polypharmacy (the use of 5 or more medications (Masnoon et al., 2017)), which is associated with poor adherence (Barat et al., 2001).

Because the focus of care for older patients has shifted from institutional care towards a model of home care that enables patients to live at home for longer (Holm et al., 2017; World Health Organization, 2008), more patients with a high risk of DRPs receive home care services. There is, however, very limited research on medication safety in this setting, as most research has focused on secondary care (Panesar et al., 2016; World Health Organization, 2008). However, the medication use process differs between primary and secondary care and so does the likelihood of DRPs in the different steps (Olaniyan et al., 2015).

A particular challenge in primary care is that practices are separated like in home care services and GPs, which makes collaboration more difficult (Kaelber & Bates, 2007; Mangoni, 2012; St.meld.nr.47 (2008-2009)). Insufficient interdisciplinary collaboration has also been reported as a key risk factor for DRPs in the systematic review by Meyer-Masseti et al. (2018). In this review, which specifically looked at DRPs in a home care setting, they found 44 studies, with over half (n=23) originating in the US. Overall, they found that up to 50% of home care patients have DRPs, a higher frequency than reported for inpatients (Meyer-Masseti et al., 2018). The most frequently reported DRPs were PIMs and medication errors in the form of discrepancies in medication records. Documentation discrepancies and difficulties obtaining accurate information about the patient's current medications for home care patients have also been highlighted in two recent Norwegian studies (Devik et al., 2018; Manskow & Kristiansen, 2021).

In Norway, all residents have a legal right to home care services, irrespective of age, gender or socioeconomic status (Health and Care Services Act, 2011). These services are organized and primarily financed by the municipalities. They offer both practical assistance, such as cleaning, food delivery and laundry, and home nursing, such as wound care and help with administering medicine (Holm et al., 2017). In 2021, there were about 171,000 patients receiving home nursing services in Norway (Statistics Norway, 2021). Of these, about one-third got help administering their medicines through multidose drug dispensing (Norwegian Pharmacy Association, 2022).

## The multidose drug dispensing system

Multidose drug dispensing (MDD) is a dispensing system where medicines are machine packed in disposable plastic pouches (See Figure 3). The pouches are labelled with patient information, the medicines' content information and the time they should be taken. Only solid medicines such as tablets and capsules can be dispensed in MDD. MDD systems are common in many hospitals across the world, but are also used in primary care in Australia, Denmark, Finland, the Netherlands, Norway and Sweden as an alternative to manually filled dosettes (Rechel, 2018).



Figure 3: Multidose drug dispensing pouches. Reproduced with permission from Apotek 1 Gruppen AS, Norway.

When introduced in primary care, the aim of MDD systems has mostly been to ensure safer medication use, especially for patients with polypharmacy and those who have difficulties handling and administering these medicines. Furthermore, MDD has been expected to save time for nurses who no longer have to manually fill dosettes, reduce medication errors in the dispensing and administration phase and reduce waste of unused medicines. The scientific evidence to support these claims is, however, limited. To the best of my knowledge there have been four previous literature reviews on the MDD system. A systematic review from Sinnemäki et al. (2013) and an updated review in their theses (2020) on the patient safety of MDD systems in primary care, one from the Danish College of Pharmacy Practice on the dose dispensing system as a health technology (Søndergaard et al., 2005), and one from Halvorsen and Granas (2012) on the MDD system in the Scandinavian countries. These reviews conclude

that the expected benefits of the MDD systems are only partly met and, in fact, that the systems might have negative effects on medication safety such as increasing the use of PIMs and increased polypharmacy. The MDD system can thus not just affect the dispensing and administration stages of the medication use process, but also prescribing, transcribing and monitoring.

### **Prescribing in the MDD system**

Inappropriate and suboptimal prescribing are the areas that have been studied most extensively in MDD patients. Studies from Norway, the Netherlands, Finland and Sweden all show that MDD patients are frequently exposed to PIMs, DDIs and DRPs (Belfrage et al., 2014; Bobrova et al., 2019; Halvorsen et al., 2012; Hammar et al., 2014; Hammar et al., 2015; Kwint et al., 2011; Lesen et al., 2011; Lönnbro & Wallerstedt, 2017; Milos et al., 2014; Söderberg et al., 2013). When comparing patients with MDD to patients with ordinary prescribing, PIMs and DPRs have been found to be up to 8 times more common in MDD patients (Belfrage et al., 2014; Johnell & Fastbom, 2008; Lea et al., 2019; Lönnbro & Wallerstedt, 2017; Sjoberg et al., 2011). A proposed explanation for why MDD patients have more PIMs is that the procedure for renewing prescriptions is too automatic, resulting in the the lists being reviewed less frequently (Sjoberg et al., 2011; Sjoberg et al., 2012; Wallerstedt et al., 2013). Other studies also show other differences in prescribing patterns, such as MDD patients being less likely to use statins and long-acting benzodiazepines, and less exposed to serious DDIs (Johnell & Fastbom, 2008; Sundvall et al., 2019). Even in studies that have compared patients with MDD to patients with ordinary prescribing, it is difficult to conclude whether the differences in prescribing quality between these groups is due to the MDD system or other factors related to the patients who are offered MDD. MDD patients generally use more medications, they have more complex medication regimens and have problems managing their medications. They might thus not be comparable to patients who are not offered MDD. Studies that have investigated the initiation of MDD, and looking at effects before and after the initiation, also show conflicting evidence. Most studies show that PIMs increase after initiation of MDD, and that there are fewer changes in the patient's medication regimen (dosage adjustments, withdrawn or newly prescribed medications) (Bobrova et al., 2019; Mertens, 2019; Sjoberg et al., 2012; Vallius et al., 2022; Wallerstedt et al., 2013). However, many of these studies do not have a control group, and therefore one cannot conclude

whether this reduction in prescribing quality is due to the MDD system or whether it is a result of time and aging. A few studies also find the opposite: medication use does not increase more in the MDD group than in a control group, there are more starts and discontinuations in the MDD group, and PIMs may be reduced after the initiation of MDD (Hindhammer et al., 2012; Sinnemäki, 2020; Sinnemäki et al., 2017). An unpublished longitudinal study by Mertens (2019) also showed that the number of medicines and PIMs increased after initiation, but these changes started before MDD was initiated, indicating that a change in the patient's health status causes the patient to start MDD, rather than the MDD system causing increased medication use.

In interviews and surveys, GPs described differences when prescribing for MDD patients and patients with ordinary prescriptions. Some GPs feel that MDD prescribing is more time consuming than ordinary prescribing and might limit their time with patients (Bardage et al., 2014; Frøyland, 2012; Heier et al., 2007a; Wekre et al., 2012), though some also find the MDD system less time consuming (Frøyland, 2012). In one study the GPs described complicated prescribing procedures that might pose a risk to patient safety (Bardage et al., 2014). A reoccurring topic in many studies has been the unclear division of responsibilities between different health care personnel in the MDD system (Heier et al., 2007a; Herborg et al., 2008; Johnsen et al., 2018). Some expressed uncertainty about who has access to and can update the medication lists for MDD patients, and thus who should be notified about changes in the medication treatment (Heier et al., 2007a; Johnsen et al., 2018). GPs have also expressed that taking over responsibility for medication started by other doctors can be difficult and some think that only the GP should be allowed to make changes (Frøyland, 2012; Wekre et al., 2012). However, as for the positive aspects of the MDD system, several studies have described how the MDD system results in a better overview of patients' medication use for GPs and nurses (Bardage et al., 2014; Bell et al., 2015; Frøyland, 2012; Wekre et al., 2012).

To summarize, it is difficult to conclude whether the differences in prescribing quality seen are due to the MDD system per se or due to differences between the patients who get MDD and those who do not. Regardless of whether MDD is the cause, we can see that suboptimal prescribing is very common in MDD patients. In addition, studies consistently show that MDD users are prescribed more medications than patients with ordinary prescribing and are more exposed to polypharmacy (Belfrage et al., 2014; Johnell & Fastbom, 2008; Morin et al., 2018;

Wallerstedt et al., 2013; Wastesson et al., 2019). The last study on MDD patients' exposure to PIMs and DDIs in Norway was done in 2009 (Halvorsen et al., 2012).

### **Transcribing in the MDD system**

Once a medicine has been prescribed, the prescription is sent to the pharmacy and entered into the pharmacy dispensing information system (hereafter referred to as the dispensing program). Though there are few studies investigating the errors at the transcribing stage specifically, several highlight errors during transmitting and transcribing prescriptions in terms of discrepancies in medication records.

Five Norwegian studies have investigated discrepancies between the medication lists of the GP and the home care service/MDD pharmacy, and found discrepancies in 51 – 88 % of the patients' records (Bakken & Straand, 2003; Heier et al., 2007b; Josendal & Bergmo, 2019; Mamen AV, 2016; Wekre et al., 2010). A Finnish study from Sinnemäki et al. (2014) also shows that 43% of patients got treatment-related changes in their medication lists when starting MDD, indicating that many patients have incomplete medication lists before starting MDD. There is, however, one study indicating that discrepancies are reduced after starting MDD (Wekre et al., 2010).

Many of the discrepancies seem to arise during care transitions because the systems for transferring prescriptions are not optimal. Health care personnel have expressed difficulties with managing MDD after the patient has been discharged from the hospital (Bardage et al., 2014; Caleres, Bondesson, et al., 2018; Caleres, Strandberg, et al., 2018), and several studies have found that medication records are not transferred correctly to primary care after a hospital stay (Alassaad et al., 2013; Lysen et al., 2011; Reuther et al., 2011). Though this is a common problem (Redmond et al., 2018), MDD patients seem to be more exposed to errors than patients with ordinary prescribing during care transitions (Bergkvist et al., 2009; Caleres et al., 2020; Midlöv et al., 2005).

There are also some small but distinct differences in the actual transcribing of MDD prescriptions and ordinary prescriptions. In Norway, MDD prescriptions are paper-based and need to be manually transcribed into the MDD dispensing program. In the Netherlands, where the prescriptions are electronic, Cheung et al. (2014) identified two additional sub-steps in the transcribing process: processing the MDD module of the pharmacy dispensing

program (filling in the number of medicines and times of intake) and sending the MDD file to the MDD supplier. Using data from the National Medication Incidents Registration system they found that the majority of reported incidents related to MDD (109 of 268) occurred in the phase of entering the prescription into the pharmacy program.

The Finnish study by Sinnemäki et al. (2014) also describes how almost all patients (93%) have technical changes to their medication lists when starting MDD. Most common was adding or discontinuing medicines to avoid halving a tablet dispensed as MDD, which are changes that would not typically be made with ordinary prescriptions. Except for this study, no others have investigated the pharmacist's responsibilities in the MDD system and the modifications they make to prescriptions.

### **Dispensing in the MDD system**

MDD generally replaces manually filled dosing aids such as dosettes, and the automated process of dispensing MDD is expected to reduce dispensing errors. There are, however, few studies investigating the dispensing error rate while filling MDD or other dosing aids.

The largest MDD supplier in Norway reports dispensing errors in about 1 out of every 13,000 MDD rolls produced (M. Lange, personal communication 13.01.2022). In comparison, errors have been reported in up to one of every 14 manually filled dosing aid (Gerber et al., 2008; Gilmartin-Thomas et al., 2013; Gilmartin-Thomas et al., 2017; Hageler, 2015; Klein et al., 1994). Though the overall error rate is lower, some errors such as broken tablets seem to be more common in MDD than manually filled dosing aids (Cheung et al., 2014; Gilmartin-Thomas et al., 2013; Palttala et al., 2013).

Even if the error rate in the initial dispensing step is low, errors can still occur later in the process. One of the disadvantages of MDD is that MDD bags are less flexible in terms of adjustments in medications and dosages (Frøyland, 2012; Herborg et al., 2008; Wekre et al., 2011). If a physician changes the treatment of an MDD patient, this must either wait until the next delivery, something that is not possible for all medications, or the bags have to be adjusted and/or medicines administered separately from a dosette or the original package until the next delivery. Manual adjustments are both time consuming and can increase the risk of new errors (Cheung et al., 2014; Mertens et al., 2018b; Nyen et al., 2009). Though the overall dispensing error rate of MDD seems lower than for manually filled dosing aids

(Søndergaard et al., 2005), there are concerns that having parallel systems with both MDD and dosettes for the same patient can cause problems with adherence (Bardage et al., 2014; Heier et al., 2007b; Holbø et al., 2019).

### **Administration in the MDD system**

When MDD has been introduced in home dwelling patients, it has been mostly thought of as an adherence aid. MDD users have more potential problems with handling and administering their medicines compared to non-MDD users, are older, use more medication and are more often cognitively impaired and frail (Mertens et al., 2018a). These patients thus have a high risk of non-adherence. The few studies on adherence in the MDD system indicate that MDD users have better adherence than non-MDD users. Two Dutch studies have measured the time in therapeutic range for vitamin K antagonists for patients using MDD. Both showed an increased time in therapeutic range compared to the control group, indicating an increased adherence (Mertens et al., 2020; van Rein et al., 2018). In addition, a survey by Kwint et al. (2013) found higher self-reported medication adherence in MDD users than non-MDD users. Patients generally report being satisfied with the system and feel that the system is safe (Bardage & Ring, 2016; Mertens et al., 2019). However, in interviews with MDD patients there have still been reports of both intentional and unintentional non-adherence. The patients take out tablets, change the time of the day to take tablets or forget to take medicines, either those in MDD or the medicines they take from original packaging (Bardage & Ring, 2016; Holbø et al., 2019; Larsen & Haugbølle, 2007).

In addition to non-adherence, errors can also occur after the tablets are removed from the pouches. In a report from the Danish Patient Ombudsman in 2013, 4000 incidents concerning MDD over a one-year period were reported. Half of these incidents were related to the administration of medicines. The most common errors were that the medicines were not given to the patients, the patients did not take the medicines, or the medicines were given at the wrong time (Pasientombuddet, 2013). A study in Dutch nursing homes showed errors in one in five medication administrations, mainly due to inappropriate crushing of tablets (van den Bemt et al., 2009). Similarly, a recent Norwegian study found that nurses modified the contents of the MDD bags (mostly crushing of tablets) in about one-fourth of dispensing episodes (Solberg et al., 2021). These studies illustrates that even though administration errors seem to be reduced with MDD systems, they still frequently occur.

### **Monitoring of medication use in the MDD system**

The last step of the medication use process is monitoring the effects of the medication. This is mainly the prescriber's responsibility, but both the patient and the home care service should also monitor the risks and benefits of medication use and report relevant DRPs (Britten, 2009; Ellenbecker et al., 2008).

In the study by Kwint et al. (2013) they found that MDD users had lower medication knowledge than non-MDD users. In addition, the MDD users had a poorer knowledge of their MDD-dispensed medicines compared to those that were manually dispensed, indicating that MDD can reduce the patient's knowledge about medicines. The study from Modig et al. (2009) also shows that MDD users have less knowledge of their medicines than patients with ordinary prescribing, and the interview study from Holbø et al. (2019) also concludes that MDD users lack sufficient information to get the full benefit from the system.

Studies on health care personnel who administer MDD to patients have found similar findings. Many nurses have concerns that the MDD system may reduce their knowledge of medicines, and some feel that their responsibility for medication administration is reduced with MDD (Nilsen & Sagmo, 2012; Wekre et al., 2011).

If the patient or the carer administering the medicines has insufficient knowledge about the medicines this might reduce their ability to monitor the effects of these medicines and ability to identify symptoms as a potential side effect of medications. If the effects of medication use are not sufficiently monitored this can again affect the prescribing step, and result in e.g. more potentially inappropriate prescribing.

### **The MDD system in Norway**

MDD has replaced manually filled dosettes in many Norwegian municipalities. The use of MDD has increased in recent years, from 15,700 patients in 2006 to 96,750 in 2021 (Norwegian Pharmacy Association, 2010, 2022). The majority, about 75%, receive home care services, about 20% live in nursing homes and the remaining 5% are home dwelling patients who order MDD at their local pharmacy (Norwegian Pharmacy Association, 2010). This thesis focuses on patients in home care services.

MDD is a service offered by community pharmacies across the country. However, the production of MDD requires specialized equipment and the community pharmacy buys MDD



from a supplier. There are currently two main MDD suppliers in Norway. In addition, hospital pharmacies have the equipment to produce MDD, but they usually only supply MDD for the hospital. The pharmacist has the same responsibility of checking the prescriptions and of patient counselling on MDD prescriptions as for ordinary prescriptions. This check includes assessing the appropriateness of the medication and dosage, checking for DDIs, confirming validity of prescriptions and evaluating whether the patient needs any additional information regarding their medications (Norwegian Pharmacy Association, 2017; Rule on Requisition and Distribution of Medicines from Pharmacies, 2019, §6-8). Once the prescription is checked, an MDD order is electronically sent to the MDD supplier. The MDD supplier dispenses the MDD and sends them either to the pharmacy or directly to the home care services.

The agreement to dispense MDD is between a municipality/home care service and a pharmacy. The home care service pays the packaging fee (tender prices that can vary from municipality to municipality), but they can be reimbursed 500 NOK per patient per year (Helfo, 2018). It is mainly up to the home care services to select the patients in need of MDD, however, it is recommended that both the patient and GP are involved in this decision (Hjelle, 2015). Once a patient starts MDD, the pharmacist makes a “prescription card” – a list of the patient’s complete medication use, containing all regular medication, *when needed* medications, medical devices and dietary supplements. This differs from ordinary, electronic prescriptions in Norway that only contains one medication at a time. The prescription card is based on printouts from the medication list in the GP’s electronic health record, which are sent to the pharmacy by fax or post. The home care services can also add dietary supplements and certain over-the-counter medicines to the prescription card. Once the prescription card is signed by a physician, it is valid for one year supply of all the items on the list. This prescription card is therefore more comprehensive than electronic prescriptions.

As long as the MDD prescription is paper-based, the pharmacist will not get notifications if the patients get electronic prescriptions. As most prescribing in Norway is electronic, this means that the pharmacist will not automatically be notified if doctors other than the GP prescribe medicines. If the pharmacist gets prescriptions from other doctors they can legally dispense these prescriptions, but it is common practice that the GP should approve these changes before they are dispensed in MDD (The Norwegian Directorate of Health, 2019b).

Despite the practical differences between an MDD prescription and an ordinary electronic prescription, the only legal difference between the two prescription types is the timing of the pharmacist's check (Rule on Requisition and Distribution of Medicines from Pharmacies, 2019, §7). For ordinary prescriptions, the pharmacist checks the prescription at each dispensing, usually every three months for repeat prescriptions. For MDD patients, the prescription is checked the first time a medicine is dispensed in MDD and thereafter only if there are changes in the patient's medication treatment. If there are no changes to the medications, it can be up to a year between each check by a pharmacist.

Having paper prescriptions for MDD patients while over 90% of ordinary prescriptions are electronic (Norwegian Healthnet - Public Enterprise, 2021a) has raised several concerns about patient safety (Hjelle, 2015). Some Norwegian GPs have therefore refused to prescribe MDD to their patients until an electronic solution is in place (Helmets, 2019).

The Norwegian Directorate of e-health has since 2014 been piloting an electronic MDD prescribing system. With this system, MDD patients will get electronic prescriptions transferred via the same national database currently used for ordinary prescriptions, and the prescribing procedure will be the same regardless of prescription type. In addition, the system introduces a national electronically Shared Medication List (eSML) where the complete medication list of a patient is shared across organizations and levels of care.

### **Electronically shared medication lists to improve medication safety**

To support more seamless care, several countries are developing systems for sharing medication lists across care levels (Claeys et al., 2013; Manskow et al., 2019). Such systems have the potential to reduce the amount of manual data entry, increase legibility and completeness of medicine information and reduce stress among health care personnel related to lack of information (Bassi et al., 2010; Manskow & Kristiansen, 2021; Mekonnen et al., 2016; Remen & Grimsmo, 2011). However, the research on such systems is limited. The narrative review by Manskow et al. (2019) found only nine studies on the effects of and experiences with digital solutions for a shared medication list. The architecture of such systems also varies between countries. Some countries, e.g. Ireland and the Netherlands, have medication lists that automatically calculate the patient's medication lists based on dispensing databases (Grimes et al., 2013; Uitvlugt et al., 2019), while others, e.g. Denmark and Switzerland, have a separate

medication list that has to be regularly updated by health care personnel (Bugnon et al., 2021; Bülow et al., 2021). The Norwegian system is an example of the latter.

The aim of the eSML is to increase medication safety by generating one structured and complete medication list, to increase access to medicine information for all health care professionals involved in patient care and to reduce the time used on medication reconciliation (The Directorate of e-health, 2021). When an eSML is generated, this is transferred through the national database that is currently used for e-prescriptions, which is accessible from all pharmacies and prescribers in the country. This eSML contains, like the paper-based “prescription card” for MDD patients, a complete list of the patient’s medication use, both regular medication, *when needed* medications, medical devices and dietary supplements. However, unlike the “prescription card”, the current version of the eSML is not legally a prescription that can be used to dispense medicines. This means that there have to be individual e-prescriptions for each item on the eSML in order to dispense medicines. The eSML is therefore just an overview of the current treatment of a patient that comes in addition to the existing e-prescriptions. Both the eSML and the e-prescriptions are valid for 1 year, however the e-prescriptions also contain information about the quantity that can be dispensed on the prescription. This means that the e-prescriptions can be emptied before one year has passed.

The first pilot test of e-prescribing and eSML for MDD began in 2014, the second in 2018 (The Directorate of e-health, 2021). Both of these testing periods have been studied in this thesis. In April 2022, there were about 200 GPs in 19 municipalities who used the electronic prescribing system for MDD, and the implementation is still ongoing. In addition, eSML is now, in 2022, being tested on patients who do not use MDD. The plan is that national implementation of eSML should start for all patients in 2024 (The Directorate of e-health, 2022).



## AIM

The overall aim of this thesis is to examine medication safety in the MDD system used in home care service and how this is affected by the eSML system, with a focus on the pharmacists' roles and responsibilities.

Specifically, the objectives of the four papers were to:

- Examine the quality of prescribing among elderly patients receiving MDD in Norway.
- Document the prescription problems that pharmacists detect, and the responsibilities they adopt when dispensing MDD.
- Investigate whether the eSML system decreases the number of discrepancies between the medication lists of the GP, home care service and the community pharmacy.
- Explore how the e-prescribing system affects the home care nurses' and pharmacists' work regarding MDD patients.



## METHODS

This thesis consists of four studies: two studies on the paper-based MDD system, one pre-post study, and one after the implementation of the eSML for MDD patients.

In the first paper, we collect updated information about the MDD patients, their prescribed medicines and their exposure to PIMs. This gives an overview of the patients who receive MDD and highlights medication safety issues in the prescribing within the current paper-based MDD system. In the second paper, we have looked at the interventions pharmacists make and the responsibilities they adopt while dispensing MDD prescriptions. Documenting errors at this stage of the medication use process is necessary to assess whether the eSML affects prescribing and transcribing errors. Because reduction in discrepancies between medication records is one of the main goals of implementing the eSML, this was the focus of the third paper. Lastly, we investigated the pharmacists' and nurses' experiences with the eSML, specifically how they perceived the medication safety in the eSML system, and how the system affected their work.

All four studies evaluate medication safety in the MDD system, in addition Papers II and IV investigate the pharmacist's role in the MDD system and Papers III and IV the effects of the eSML on medication safety. Figure 4 gives an overview of the four studies and how these are related to the objectives of this thesis.

### **The implementation of eSML**

The Directorate of e-health is responsible for the implementation of the eSML system. The geographical areas piloting the e-prescribing system were selected based on what software provider of the Electronic Health Record (EHR) the GPs used. When the studies in this thesis were performed, only two EHRs could generate eSMLs.

The eSML is a function in the two existing EHR systems that can be turned on manually by each prescriber. Once the function is turned on, the GP can define individual patients as using an eSML. When a patient is defined, the system will automatically send an eSML along with e-prescriptions every time the GP makes changes to a patient's prescribed medication.

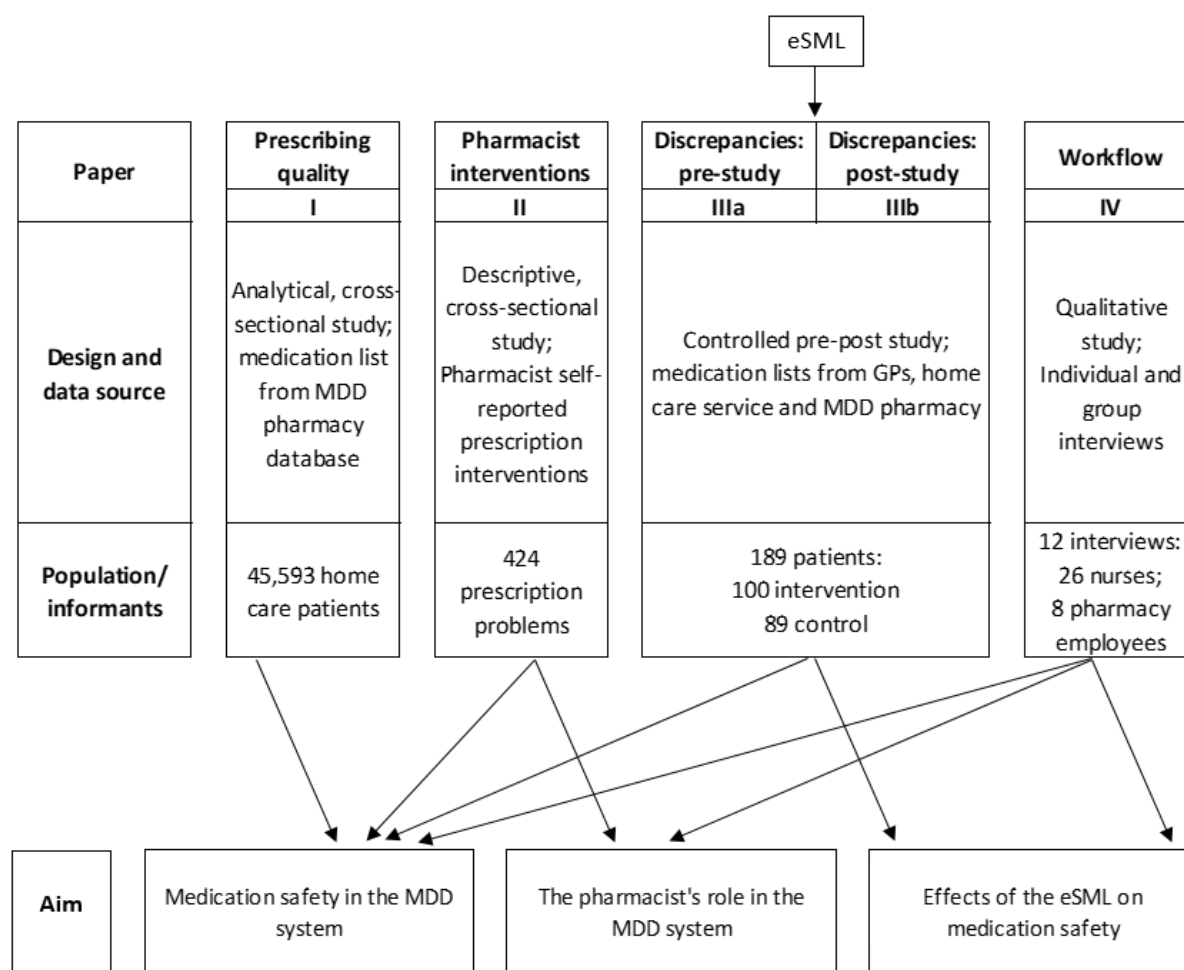


Figure 4: Aim, design, setting and study participants of the included papers

This thesis studies a version of the eSML system only piloted on MDD patients. In this version, all prescribers have access to read the eSML, but only the GPs can update it (The Directorate of e-health, 2021). When hospital doctors prescribe medicines for a patient with an eSML they will do so with ordinary e-prescriptions, but unlike in the paper-based MDD system, the pharmacist is notified about these prescriptions. If a patient gets an e-prescription that is not included in the eSML, the current recommendation is that the pharmacist should wait until the GP has updated the eSML to dispense it in MDD. However, it is possible to dispense MDD on the e-prescriptions if the pharmacist deems it necessary. If prescriptions that are not included in the eSML are dispensed in MDD, the system automatically notifies the GP about this. When the studies in this thesis were performed, the home care services did not yet have access to the eSML, but got updated on the patients' medicines through the normal communication channels to the GP and the MDD pharmacy.



In the paper-based MDD system the medication list in the pharmacy is used for dispensing MDD, while the eSML is generated based on what is listed in the GP's medication list. During the first pilot testing of the eSML in 2014, it was revealed that there were many discrepancies between the medication lists of the pharmacy and the GP in the paper-based system (Mamen AV, 2016). To avoid unintended changes in the patient's medications during the transition, the Directorate recommended that the GP did a medication reconciliation prior to generating the first eSML. To support this reconciliation procedure, the pharmacy sent a printout of the MDD medication list to the GP approximately 1 month prior to turning on the eSML functionality. The GP should have then compared the list from the pharmacy to their own record, and generated the first eSML and e-prescriptions. Once the pharmacy received the eSML, they deleted the "prescription card" in their system and started dispensing MDD on the eSML and the accompanying e-prescriptions.

## **Paper I : Medication use and potentially inappropriate medications**

The first paper explores potentially inappropriate medication use for home care service patients with MDD.

### **Study design and sample**

Paper I was a cross-sectional study using the medication lists from the MDD dispensing pharmacy database, prescribed in June 2018. We contacted the main MDD supplier in Norway, who provided anonymous data on their MDD users. The original dataset consisted of 87,519 patients and 859,642 medicines. Patient information included age, gender and care setting (self-pay, home care service, or nursing home). The medication lists included details of drug names, strength, formulation, ATC code (WHO. Collaborating Centre for Drug Statistics Methodology, 2018), dosing schedule and dispensing type (regular drugs dispensed via MDD, regular drugs not dispensed via MDD, or *when needed* medication).

### **Measures and data analyses**

The main outcome measures of this study were the number of PIMs, the number of DDIs and the total number of prescription items per patient.

Prescription items were categorized as regular medications dispensed as MDD, regular medications not dispensed as MDD or medications used as required. All categories could include dietary supplements. Prescriptions on medical devices and consumables (e.g. diabetes

supplies; incontinence products) were excluded from this study. We excluded patients under the age of 70 because the Norwegian General Practice Criteria (NORGEP) used in this study are only applicable to elderly  $\geq 70$ -year-olds. We also excluded self-pay and nursing home patients because their medication lists were usually incomplete, only containing MDD dispensable medications and no other regular medication or medications used as required.

PIMs were assessed using the NORGEP criteria, a validated tool adapted to the Norwegian formulary (Rognstad et al., 2009). It consists of 21 single substances and 15 drug combinations to be avoided in patients  $\geq 70$  years old (Table 1). The tool is based on the American Beers Criteria (Fick et al., 2003), the National Swedish recommendations (Swedish National Board of Health and Welfare, 2017) and other literature (Rognstad et al., 2009). The four NORGEP criteria on antibiotics (criterion 23,24,30,35) were excluded from our analyses because antibiotics are usually only prescribed for shorter periods and are not listed on the MDD prescription card. For the two criteria on overuse (criterion 12,13) we could only analyse medicines dispensed as MDD because other regular medicines and when needed medicines did not have an available dosing schedule. For the remaining 29 NORGEP criteria, we defined the criterion to be met if the medication(s) were present in the list, regardless of whether it was listed as regular use or *when needed*.

DDIs were analysed by use of the Norwegian Electronic Prescription Support System (“FEST” in Norwegian). This is a national service of pharmaceutical data, available to all members of the prescription chain, including the GPs and MDD dispensing pharmacy. In this system, DDIs are classified as (A) No action necessary; (B) Precautions should be taken; (C) Should be avoided (The Norwegian Medicines Agency, Updated 2016). In this study, we screened for DDIs of types B and C.

We used Stata/MP 15 to perform the statistical analyses. Sample characteristics were described by use of means and standard deviations and a student’s t-test to compare means. We used binary logistic regression to assess whether PIMs (yes/no) and DDI (yes/no) varied with gender, age and number of medicines. We categorized age into 10-year intervals rather than having it as a continuous variable because previous studies had shown a non-linear relationship between age and PIMs (Nyborg et al., 2012).

Table 1: The NORGEP criteria, adapted from Rognstad et al., 2009

No.	NORGEP single substance criteria	Comments*
1.	Amitriptyline	Tricyclic antidepressants: Anticholinergic effects, risk of impaired cognitive function.
2.	Doxepine	
3.	Clomipramine	
4.	Trimipramine	
5.	Chlorpromazine	First-generation low potency antipsychotics: Anticholinergic effects, extrapyramidal effects.
6.	Chlorprothixene	
7.	Levomepromazine	
8.	Prochlorperazine	
9.	Diazepam	Long-acting benzodiazepines: Prolonged elimination half-life, risk of accumulation, muscular weakness, falls and fractures.
10.	Nitrazepam	
11.	Flunitrazepam	
12.	Oxazepam >30 mg/24 h	High doses of benzodiazepines and benzodiazepine-like agents: Risk of muscular weakness, falls and fractures
13.	Zopiclone >7.5 mg/24 h	
14.	Carisoprodol	Centrally acting muscle relaxants: Anticholinergic effects, risk of addiction
15.	Dextropropoxyphene	Analgesics: More toxic than its comparators
16.	Theophylline	Pulmonary drugs: Risk of arrhythmias, No documented effect in COPD
17.	Sotalol	Cardiovascular drugs: Risk of arrhythmias, poor safety record
18.	Dexchlorfeniramine	First-generation antihistamines: Anticholinergic effects, prolonged sedation
19.	Promethazine	
20.	Hydroxyzine	
21.	Alimemazine (trimeprazine)	
22.	Warfarin+NSAID	Warfarin combinations: Increased risk of intestinal bleeding
23.	Warfarin+ofloxacin or ciprofloxacin	Increased risk of bleeding due to inhibition of warfarin metabolism
24.	Warfarin+erythromycin or clarithromycin	
25.	Warfarin+SSRI	Increased risk of bleeding due to a direct platelet-inhibiting effect
26.	NSAID (or coxib)+ACE inhibitor (or ARB)	NSAIDs combinations: Increased risk of renal failure
27.	NSAID+diuretic	Reduced effect of diuretics
28.	NSAID+glucocorticoid	Increased risk of intestinal bleeding. Risk of fluid retention
29.	NSAID+SSRI	Increased risk of gastrointestinal bleeding
30.	Erythromycin or clarithromycin+statin	Other combinations: Increased risk of adverse effects of statins, including rhabdomyolysis, due to inhibition of statin metabolism. Highest risk for simvastatin and lovastatin
31.	ACE inhibitor+potassium or potassium-sparing diuretic	Increased risk of hyperkalemia.
32.	Fluoxetine or fluvoxamine+ TCA	Increased risk of adverse effects of TCAs due to inhibition of TCA metabolism.
33.	Beta blocker+cardioselective calcium antagonist	Increased risk of atrioventricular block and myocardial depression.
34.	Diltiazem+lovastatin or simvastatin	Increased risk of adverse effects of statins, including rhabdomyolysis, due to inhibition of statin metabolism.
35.	Erythromycin or clarithromycin+carbamazepine	Increased risk of adverse effects of carbamazepine due to inhibition of its metabolism.
36.	Concomitant prescription of three or more drugs within the groups centrally acting analgesics, antipsychotics, antidepressants and/or benzodiazepines	Increased risk of muscular weakness, falls, fractures and cognitive impairment.

\* Abbreviations: NSAID = non-steroid anti-inflammatory drug; ACE = angiotensin converting enzyme; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; COPD = chronic obstructive pulmonary disease; ARB = angiotensin receptor blocker.

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## **Paper II: Prescription problems and pharmacist's responsibilities**

The second paper investigates prescription problems pharmacists detect and the responsibilities they adopt while dispensing MDD prescriptions.

“MDD prescription” refers to the prescription card, not individual medicines on the prescription. The term “prescription problem” refers to any issue that required an action from the pharmacist before dispensing, and included errors, ambiguities, omissions, or other problems with the prescription that are potentially harmful to patients or interfered with the dispensing process. “Pharmacist intervention” is the action the pharmacist took to resolve these prescription problems.

### **Development and testing of the self-completion form**

The self-completion form used in this study (see Appendix 3) was based on a form originally developed in the USA (Kennedy & Littenberg, 2004), that was later translated and adapted to Norwegian legislation (Haavik et al., 2006; Milenkovic et al., 2017). We adapted this form further for use on MDD prescriptions. In the form, prescription problems were categorized as either formal, medication-related or related to the MDD order. The two former categories are presented in this paper. In addition, the form recorded basic information about the patient, such as gender, age and type of MDD patient (self-pay, home care service, or nursing home), the intervention done by the pharmacist, result of the intervention and time spent correcting errors. The form was mostly check-box based..

We also developed a teaching manual for the self-completion form (see Appendix 4). This contained information about the study, examples of common prescription problems and accompanying completed forms for these problems. In 2017, I piloted the manual and form on 100 prescription problems in the pharmacy where I worked. These pilot interventions were excluded from the final study, but they gave us important input to the design and content of the form and teaching manual, in addition to an estimated frequency of interventions (10%). Each of the first three pharmacies in the study also provided feedback on the form, which led to minor adjustments. The eight consecutive pharmacies used the same version of the form.

## Participants

We asked the main MDD supplier in Norway for a list of pharmacies they thought were suitable for this study. The only criteria was that the pharmacy had to serve a minimum of 500 MDD patients. We set this cut-off to get a minimum number of interventions per pharmacy. Data from the MDD supplier shows that 12% of MDD patients have changes in their medication regimen between MDD orders (Mamen AV, 2016). Serving 500 MDD patients would then equal 60 MDD prescription checks per week. Based on the frequency of interventions in the pilot (10%), this gives an estimated six interventions per pharmacy.

The MDD supplier provided a list of 35 pharmacies. We purposefully selected pharmacies from all the different counties in Norway and pharmacies with different workloads in terms of number of MDD patients they served. We sent an e-mail to the 20 selected pharmacies with a short description of the study and an invitation to participate. When a pharmacy accepted the invitation, we sent them the teaching manual and the self-completion form and allocated a date for participation.

## Data collection and analyses

The study ran from February to October 2018. Each pharmacy registered prescription problems for two consecutive weeks. We chose this time frame because most MDD bags are dispensed for two weeks at a time. During a two-week period, the pharmacy will then have dispensed MDD for all their patients. If we had extended the period, we would have risked the same problems for one patient being registered several times. We also chose that no pharmacies should collect data during the same weeks. This was done partly to leave time for adjustments of the self-completion form between the periods, but also because of frequent drug shortages during this period. If a drug shortage arises on an MDD dispensable medicine, the pharmacist has to intervene on all MDD prescriptions with this medicine within a two-week period. We thus wanted to avoid collecting all our data during the same two weeks. One week before the allocated study period, I called the pharmacy to answer any questions they had about participation and to check that all personnel handling MDD prescriptions had read and understood the teaching manual.

During the allocated two-week period, the pharmacy personnel used the self-completion form to register all prescription problems and interventions on MDD prescriptions. The completed forms were returned by post after the study period at each pharmacy. I contacted

the MDD supplier and they extracted the total number of MDD prescriptions dispensed per pharmacy. Because MDD is subscription based and the pharmacist only has to be involved in the dispensing when there are changes to the prescriptions, defining the number of prescriptions dispensed as the number of MDDs dispensed would give a too low estimate of pharmacist interventions (Pottegård et al., 2011). For this study, we therefore defined the number of prescriptions dispensed as the number pharmacist checks.

The data from the forms was entered into Microsoft Office Excel 2016. Frequencies and means were used to describe the data. I later examined all the cases to identify different responsibilities the pharmacist adopts while dispensing MDD, and to categorize the reason for the pharmacist to intervene on MDD prescriptions into broader categories than what was reported in the self-completion form.

### **Paper III: Discrepancies in medication records**

The third paper investigates whether the electronic prescribing system for MDD decreases the number of discrepancies between the medication lists of the GP, home care service and the community pharmacy.

#### **Study design and sample**

Paper III had a controlled pre-post design. The Directorate of e-health provided contact details for the health care personnel who were piloting the eSML system in Oslo the spring of 2018: 3 GP offices with 17 GPs in total, one home care service district and one community pharmacy. We contacted all these health care personnel by fax or e-mail and asked them to participate in our study. The control group were recruited from the same or a neighbouring district in Oslo who were not starting the eSML. We recruited GPs from these districts until we had the same number of estimated patients in the control group as in the intervention group. The home care services in the neighbouring district were also contacted. The same community pharmacy provided MDD to both districts.

#### **Data collection**

Using the pharmacy dispensing program, we compiled a list of all MDD patients in the two districts who were registered with one of the participating GPs. One week before the first data collection, we sent a letter to all participants (all GPs, the home care services and the pharmacy) consisting of the list of patients under their care, a generated serial number of each patient and

detailed descriptions on how to print and anonymize the patient lists. The following week, the participants printed out the medication lists for the MDD patients in their care and replaced any patient identifying information with the generated serial number. The lists were posted or collected in person by me.

The first collection of medication lists was done in March 2018 for the intervention group and June 2018 for the control group. The medication lists were collected again in September and October 2019 for both groups.

### **Analyses**

First, we recorded the number of unique prescription items on each medication list into four groups: 1) regular prescription items dispensed as MDD; 2) regular prescription items not dispensed as MDD; 3) medications prescribed to be used as required; 4) medical devices and consumables (e.g. diabetes supplies; incontinence products). We defined a unique prescription item by an ATC code for medicines (WHO. Collaborating Centre for Drug Statistics Methodology, 2018), an active ingredient for dietary supplements and a product group for medical devices and consumables (Blue Prescription Regulation, 2007, §5, §6). We excluded medicines listed as ‘courses’ in the GP’s EHR (e.g. short antibiotic courses).

To assess discrepancies in the medication lists, we compared the medication lists in pairs: GP-list – Home-care-list; GP-list – Pharmacy-list; Pharmacy-list – Home-care-list. Two researchers compared each set separately. Based on a previous classification system (Heier et al., 2007a; Mamen AV, 2016; Wekre et al., 2010), we categorised discrepancies in the following categories: medication lacking from one of the two lists; different dosage; prescriptions listed as ‘regular use’ in one list and ‘as required’ in the other; different administration formula; others. Both missing and discordant information in the medication lists were recorded. If the researchers recorded different discrepancies or did not agree on the classification, I checked the lists a third time. Lastly, we compared all three lists to register the number of unique prescription items per patient and the number of prescription items present in all three lists (mutual prescription items).

We registered the data in Microsoft Office Excel 2016 and imported them in Stata/MP 16.1 for the analyses. To test the significance of differences between groups and changes in time we used the student’s t-test for continuous data, a chi-square test for categorical data and a McNemar test for paired nominal data. The significance level was set to 0.05.

To estimate the effect of the eSML on discrepancies we used a difference in difference method. With this method, we take the change in discrepancies in the intervention group from before to after the intervention, minus the corresponding change in the control group. This method assumes “parallel trends”, i.e. that the development of discrepancies is the same in the two groups in absence of the intervention (Dimick & Ryan, 2014). Since the method uses changes in the outcome rather than absolute values, it allows for differences in the outcome at baseline. The method also assumes that time-varying factors, such as a national information campaign to make GPs reconcile their medication lists, do not confound results because they would affect both groups equally.

#### **Paper IV: Changes in workflow**

The fourth paper explores how the e-prescribing of MDD affects the work and workload of pharmacy and home care employees.

##### **Participants**

The recruitment of participants in this study was done by the research group evaluating the effects of the electronic prescribing system for MDD at the Norwegian Centre for E-health Research. When this study began, I was working at the pharmacy where I was responsible for the teaching and support of the pharmacies involved in the pilot testing. Because of my connection with the participants in this study, I was not part of the recruitment or interview process. I have, however, contributed to making the interview guides as well as analysing the data for this paper.

After each new pilot of the e-prescribing system, the Directorate of e-health provided us with e-mail addresses to contact persons at each pilot site. We consecutively sent e-mails to the contact persons at the pharmacy and home care service asking them to forward the invitations to the persons involved in the pilot. The invitations included a short description of the project and the main themes of the interviews. We sent one reminder to non-responders. Between 10 months and 2 years after initiation of the e-prescribing system at each site, we sent invitations for follow-up interviews.

Twenty-six home care service employees and 8 pharmacy employees accepted our invitation (see Table 2). The interviews were conducted from November 2016 to February 2020. Twelve



of the interviews were conducted in person, 6 were group interviews with up to 6 participants and 3 were individual interviews. The two follow-up interviews were done by phone.

We chose group vs. individual interviews based on practical considerations of the informants. For our purpose, we considered group interviews to provide sufficient depth for the information we wanted to collect.

*Table 2: Details about interviews and participants*

No	Participants	Number of participants (n)	Setting	Follow-up interview
1	Pharmacist	3	Pharmacy 1	
2	Nurse	6	Home service 1	
3	Nurse	6	Home service 2	
4	Nurse	5	Home service 3	
5	Pharmacist	1	Home service 4	Yes n = 1
6	Nurse	2	Home service 4	
7	Pharmacist	4	Pharmacy 2	Yes n = 2
8	Nurse	1	Home service 5	
9	Nurse	5	Home service 6	
10	Nurse manager	1	Home service 6	

### Data collection

The interviews were semi-structured and included both open-ended and follow-up questions. The interviews focused on how MDD affected work practice, the users' experienced benefits with the system, the risks, the challenges and suggestions for improvement. The questions were categorized according to the phases of the implementation: prior to (preparations), during (the first MDD orders) and after start-up (See Appendix 6 and 7).

The in-person interviews took place at the informants' workplace and were conducted by two researchers (a sociologist and a registered nurse). The phone interviews were done by one researcher. Each interview lasted 30-45 minutes. The interviews were recorded and later transcribed by a professional agency.

### Data analysis

In this paper, we focused on changes in workflow that persisted after the initial start-up. Challenges directly related to the transition have been published elsewhere (Bergmo et al., 2019). To facilitate the analyses we used NVivo 12 software. We conducted a thematic

analysis based on the systematic text condensation method described by Malterud (2012), a method inspired by Giorgi's phenomenological analysis (Giorgi, 2009). Both authors (a pharmacist and a registered nurse) read the transcripts to obtain an overall impression and discussed emerging themes related to changes in workflow. Based on these themes, we independently identified and coded meaning units representing different aspects of the participant's experiences of workflow changes. The contents of each coded group were then condensed and summarized to make generalized descriptions of the participants' experiences.

### **Ethics**

The Data Protection Officer at the University Hospital of North Norway approved all four studies (Project No. 02003, Appendix 1). The objective of this project was quality assurance of a new system rather than generating new knowledge about health or disease. This means that the project falls outside the scope of the Health Research Act and did not have to be approved by the Regional Committee for Medical Research Ethics (REK) (see Appendix 2). However, for Paper III, REK waived the need to obtain consent from the participants for the collection and analyses of the medication lists in this study (2017/1393/REK Nord, Appendix 5). This decision was based on difficulties contacting home care service patients and an anticipated high dropout rate in this population (57% dropout in a similar study of MDD patients (Wekre et al., 2010)). For the other papers, no personally identifiable information was recorded and did not require approval from REK.

## RESULTS

### Paper I

In this cross sectional study we had a dataset with approximately 64,400 home care patients using MDD. We included the 45,593 (71%) users aged  $\geq 70$  years. The MDD patients used on average 10.6 (SD = 5.0) medications; of these, 6.1 were dispensed via MDD. In addition, 20% used dietary supplements. One-third used 10 or more medications regularly. Medicines on the cardiovascular and nervous system were the most commonly prescribed medication groups. More specifically, antithrombotics (70% of patients), non-opioid analgesics (58%), beta-blockers (47%), lipid-modifying drugs (41%) and hypnotics/sedatives (39%) were the most commonly prescribed therapeutic subgroups.

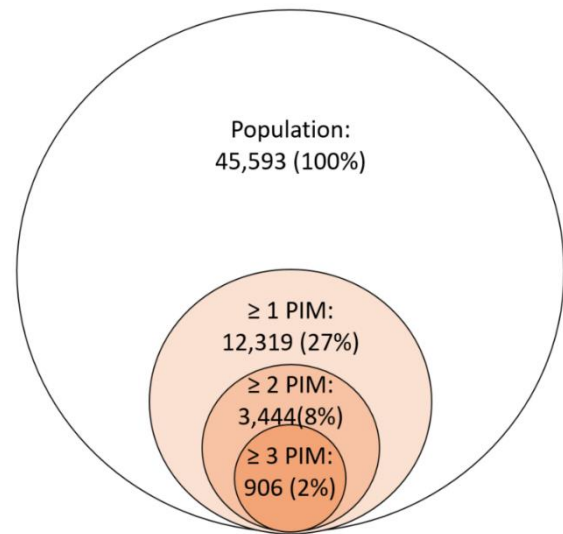


Figure 5: Prevalence of potentially inappropriate prescriptions (PIMs) <sup>1</sup>

PIMs were common in MDD patients. As shown in Figure 5, 12,139 (27%) of patients used one or more PIMs according to the NORGEP criteria; 906 (2%) had 3 or more PIMs. Concomitant use of three or more psychotropic and/or opioid drugs was the most common PIM (10.8%), followed by the prescribing of diazepam (6.4%). DDIs were present in 27,012 (59%) of the patients. Of the total number of DDIs, 97.7% were classified as “type B – precautions should be taken”, and 2.3% as “type C – should be avoided”.

The risk of both PIMs and DDIs decreased with patient age, increased with the number of medicines prescribed and was more prevalent in women than in men.

<sup>1</sup> Adapted from Josendal, A. V., Bergmo, T. S., & Granas, A. G. (2020). Potentially inappropriate prescribing to older patients receiving multidose drug dispensing. *BMC geriatrics*, 20(1), 272. doi:10.1186/s12877-020-01665-x

## Paper II

In this cross-sectional study, 11 pharmacies dispensing between 47 and 1,813 MDD prescriptions per week registered prescription problems encountered while dispensing MDD. We found that the community pharmacists clarified problems on 464 of 4121 MDD prescriptions (11.3%). The intervention rate varied from 2.2% to 38.2% between the pharmacies. As shown in Figure 6, half of the interventions were related to formal problems with the prescription, about one-third to medication issues, and one-fifth to drug shortages.

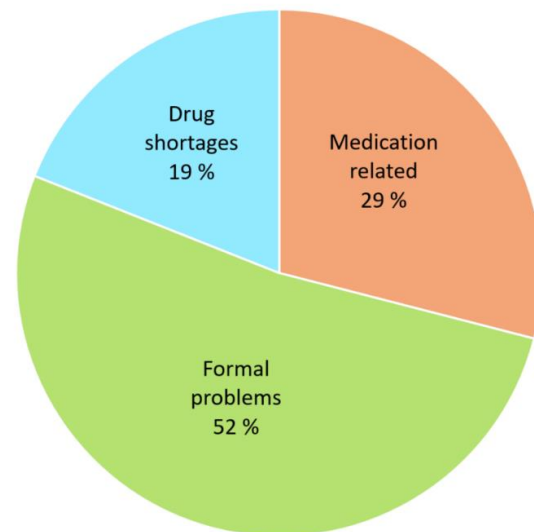


Figure 6: Type of prescription problems detected on MDD prescriptions (n=464)

For 55% of the problems, the pharmacist contacted the prescriber to get the problem resolved; for 17% they contacted the home care service; and for another 17% the pharmacist used their professional judgement to resolve the problem. As for ordinary prescribing, the pharmacists checked prescriptions for clinical appropriateness and verified the validity of prescriptions. Compared to when dispensing ordinary prescriptions, the pharmacist took on additional responsibility for getting prescriptions renewed. The number one cause for the pharmacist to contact the prescriber was prescriptions that were expired or about to expire. Still, for most formal prescription problems (54%), the pharmacist dispensed emergency refills because they did not obtain a valid prescription before sending the MDD order.

The most common reason for why the pharmacist detected a problem on a prescription was the patient's medication dispensing history (16%), followed by computer-generated warnings (mostly DDIs) (15%), conflicting information about the patient's medication use from different sources (e.g. prescriptions from doctors other than the GP, discharge notes from hospitals, messages from home care services, etc.) (13%) and incomplete prescriptions (mostly due to handwriting) (13%). Due to increased access to medication information about the patient, and active use of medication dispensing history, the pharmacists identified certain problems that would be difficult to detect with ordinary prescribing: e.g. a sudden stop in medication treatment.

### Paper III

In this controlled pre-post study, we included 189 patients (100 intervention; 89 control) and compared their medication lists held at the GP, the home care services and the MDD pharmacy. This was done twice: 3 months before the implementation of the eSML system and 18 months after.

Before the intervention, the number of prescriptions items present in all three lists was 60 % and 77 % in the control group and the intervention group, respectively. The congruence was greater between the home care service and the pharmacy, than the home care service and the GP in both groups (C: 98% vs. 60%; I: 99% vs. 77%)

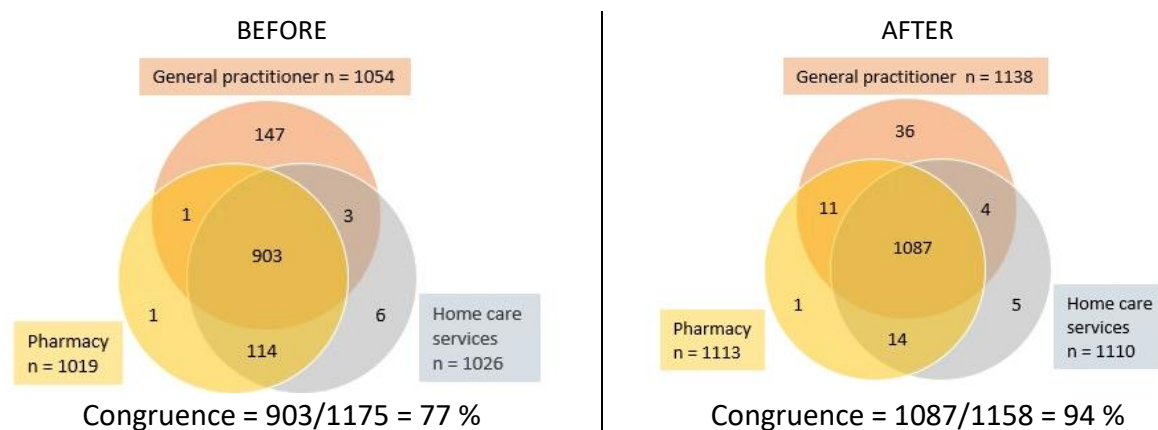


Figure 7: Number of prescription items present in the lists at the GP, home care service and the pharmacy, before and after implementation of an electronically shared medication list.  $N=100^2$

In the intervention group, we found that discrepancies were reduced from 389 to 122 ( $p < 0.001$ ) after the intervention. The share of mutual prescription items increased from 77% to 94% (See Figure 6). The number of patients with discrepancies in their lists was reduced from 75% to 56%. Missing prescriptions for psycholeptics, analgesics and dietary supplements were reduced the most. No significant reduction in the total number of discrepancies was found in the control group.

## Paper IV

In this qualitative study, we included 8 pharmacy and 26 home care employees about their experiences with the eSML system. The overall impression from both groups was that the eSML system increased medication safety, but also workload. We categorized the changes in workflow into three themes: local workflow changes, change in collaboration and communication patterns, and increased access to information.

### Local workflow changes

The pharmacists described an improved local workflow with the electronic system, where they did not have to check incoming faxes and where transcribing prescriptions was no longer necessary. However, they also experienced that when they first had to do manual corrections to the prescriptions, this was more difficult:

*“We are more vulnerable if the GP makes a mistake on the e-prescriptions (. . .) on a regular paper list we can make the change ourselves and ask the GP to sign it afterwards(. . .), but now (with e-prescribing) we must have a completely new e-prescription (if the medicines are to be dispensed)” Pharmacy 2*

The nurses experienced that the new system led to faster changes in the MDD bags and thus fewer manual corrections to them. However, some home care nurses described that medications were more frequently missing from the MDD bags, and some described new routines for double-checking the bags on the MDD delivery days.

*“Before (the electronic system), it was not necessary to check if, for example, the prescriptions needed a renewal (...). Before, it was the norm that all medicines were included, but now we have to check all the time that ok, the medicine is missing. Why is it missing?” Home service 4*

### Change in collaboration and communication patterns

Although many of the steps in the work process were more efficient, both the nurses and pharmacists felt that the new system increased their workload. This was mostly due to an increased need to contact the prescriber to get prescriptions renewed

*“ . . . we have to contact the GP much more frequently and say: you have prescribed medications for ten days, a multi-dose roll is for 14 days, and we need more tablets.”*

*Pharmacy 2*

Similarly, the home care nurses described having to contact the pharmacy and GPs more frequently to get information about the prescriptions for the patient. On the positive side, the pharmacy reported that the electronic system improved communication with the GP, both in terms of faster replies and less misunderstandings.

### **Increased access to information**

Because the MDD prescriptions and ordinary prescriptions were stored in a common database, everyone in the prescription chain had access to both prescriptions types. This had both advantages and disadvantages. The pharmacists described incidents where the patients had collected the MDD prescriptions at a local pharmacy, resulting in delays, as the pharmacist would need to clarify if this medicine was still meant to be dispensed in MDD.

Though having direct access to the prescriptions from the hospital led to the MDDs being updated faster, it could also increase the need for clarifications as the GP and hospital doctors sometimes issued new prescriptions without withdrawing the old ones, resulting in the pharmacist having to clarify which was the correct one. The eSML system was also described to increase the pharmacists' workload as they were notified of all changes in a patient's medication treatment, regardless of whether the prescriptions were dispensed in MDD or not, meaning that the pharmacist had to check more prescriptions even though they did not dispense on them:

*“ (..) “The disadvantage is that (...) all transactions in the Prescription Mediator are flagged as a change for us. On paper multidose, this course of antibiotics would never have been noticed because it was not reported to us. So, the safety is much better with electronic multidose because you will notice all changes. But the workload increases. It increases a lot.” Pharmacy 1*





## DISCUSSION

### **Methodological considerations**

This thesis has used a variety of methods, including both qualitative and quantitative research designs, to explore different perspectives of medication safety in the MDD system. Through Paper I, II and III we have investigated three different aspects of medication safety in the MDD system: PIMs in MDD patients, pharmacist interventions on MDD prescriptions and discrepancies in medications lists. In Paper IV we have captured important experiences nurses and pharmacists have with the MDD system, but these findings have also been used to complement, elaborate and illustrate the findings from Paper I-III (Greene et al., 1989). Specifically, we have used the self-reported pharmacist interventions in Paper II and the qualitative interviews in Paper IV to investigate the pharmacist's role, work practices and responsibilities in the MDD system from different perspectives. By combining the results from the before-after study on medication discrepancies (Paper III) with the interviews with nurses and pharmacists piloting the eSML system (Paper IV) we have achieved a more complete picture of how the eSML system influences medication safety.

In this section, I will address some methodological considerations that apply to all the studies, and then go into the strengths and limitations of each paper individually.

### **Conflict of interest and reflexivity**

My position at the pharmacy has been listed as a conflict of interest in all the included papers. However, this position does not include selling or advertising MDD in any way. I have mostly worked with the practical and technical aspects of implementing the eSML system in our pharmacies. This has included mapping work processes and adapting the MDD dispensing program at the pharmacy, as well as attending regular meetings with the Directorate of e-health to share experiences from our MDD pharmacies and discuss how the eSML could best be implemented from a pharmacy perspective. I would therefore argue that this position is not really a conflict of interest, because my interests are the same in both positions: to improve the MDD system in terms of improving medication safety and increasing efficiency for the health care workers involved.

However, the pharmacy position has affected my approach to and the focus of this research. As described, my aim with these studies has been to identify challenges with the MDD system

and find ways to improve it. This means that I have focused on the areas that I think could be improved upon and those most likely affected by the eSML system, based on my understanding of how the MDD system works. In what way my understanding could have affected my interpretation of results in the different papers will be discussed below.

### **Selection bias – MDD patients and the eSML**

Selection bias refers to error in a measure resulting from pre-existing differences in the groups under study, or the study group not accurately reflecting the target population (Polit & Beck, 2008, p. 244). All of the studies in this thesis have focused on MDD patients, specifically MDD patients who receive help from home care services to manage their medications. Though comparisons to the general elderly population are made, MDD patients have greater care needs than the general elderly population and none of the studies in this thesis can conclude whether MDD is the reason for differences we see between these groups.

When selecting patients for these studies we only contacted one of the two MDD suppliers in Norway and only one of three major pharmacy chains. Since the decision to start MDD is made by the municipality and not the pharmacy chain, there should not be any systematic differences between the MDD patients who get MDD from the different suppliers. In addition, the pharmacy chain and MDD supplier who participated in these studies was delivering 80–90% of all MDDs in Norway at the time of the studies, and the decision to include only these has probably introduced a very limited bias. In Paper II, however, we looked not at the patients, but the pharmacists working with MDD. Because routines and work practices differ between pharmacy chains, this selection might have biased the results, and we might not have recorded all the different types of interventions the pharmacists do.

In Papers III and IV, we conducted research related to the introduction of the eSML system. The selection of areas to pilot the eSML was based on the GP's EHR system. This means that all participating GPs had one of the two EHR systems that could generate eSMLs. The design and interface of computer systems can influence workflow (Zadeh & Tremblay, 2016) and in the interviews with the GPs piloting the eSML system they described several issues related to the interface of their EHR systems (Johnsen et al., 2018). If the different EHR systems have different ways of displaying the medication list to the GP, affect how easily the GP can do medication reconciliations etc., this again might affect the results of Papers III and IV. It was also voluntary for the GPs to pilot the eSML system, which has likely introduced additional

selection bias. The GPs who agreed to pilot the system were likely more positive towards technology than those who did not, and were motivated to test the new system, something that would not necessarily be the case when the system is implemented on a national level.

### **Paper I**

One of the major strengths of Paper I is the unique dataset used, which represented almost 90% of all MDD users in Norway. MDD prescriptions have an advantage over data from the national prescription database because they include information about prescription medicines as well as dietary supplements and over-the-counter medicines. Another advantage with the dataset is that patients receiving home care services and MDD prescriptions cannot be specifically identified in the Norwegian Prescription Database. Our study is thus one of few large-scale studies on the medication use in home care patients in Norway.

Information from the Norwegian Prescription Database represents dispensed medicines, as do the medications listed as MDD in the medication lists in Paper I. However, for the other regular medications and *when needed* medications in Paper I, this represents prescribed medicine. These data are thus prone to “primary non-adherence”, meaning that some of the prescriptions in our study might never have been filled by patients, which in turn could give a too high estimation of the number of medications and number of PIMs used. However, as we find in Paper III, the medication list of the home care service and the MDD pharmacy are almost identical. Since these patients get help managing their medications it is unlikely that many of them are collecting other prescription medicines from the pharmacy themselves, and the lists analysed in this paper are probably a good representation of what the patient is given. This is also supported by a recent study from Denmark that showed that patients receiving home care services had significantly less discrepancies between what was listed in the Danish eSML and what the patients reported using, compared to patients without home care (Bülow et al., 2021).

To analyse PIMs, we chose to use the NORGEP criteria. This has the advantage of being adapted to the Norwegian formulary; however, only a few studies have used these criteria previously, which makes comparison to other studies difficult. In addition, since the NORGEP criteria have not been updated since they were published in 2009, some of the items are now outdated (e.g. three of the medications have been withdrawn from the Norwegian market)

and they do not include newer therapies that can be considered inappropriate for elderly patients. The number of PIMs are therefore probably underestimated. Because our study is register-based we cannot know if the PIMs we found led to actual DRP for the patients. In fact, a recent study looking at multimorbid patients acutely admitted to the hospital, found that strict adherence to the NORGEP criteria could have prevented only 15% of the serious ADEs (Wang-Hansen et al., 2019). Lastly, we did not have any clinical information about the patients in this study nor information on whether the GP had assessed the overall medication use, PIM or DDI and taken necessary precautions. Drug-specific criteria like the NORGEP criteria do not capture all aspects of prescribing quality; specifically they do not address problems like under-prescribing, which we know is also a common problem in elderly patients (Belfrage et al., 2014; Tommelein et al., 2015). It is thus likely that we have underestimated the number of PIMs in our study and that some of the PIMs may not have caused any reactions in the patients.

Overall, this means that the data in Paper I gives a good representation of the actual medication use of Norwegian MDD patients, as well as age and gender distribution in this patient group. However, the number of PIMs have probably been underestimated, and we do not know whether these PIMs would have had any clinical impact on the patients.

## **Paper II**

To our best knowledge, the study presented in Paper II is the first to investigate problems on MDD prescriptions during the dispensing process specifically, and one of few that has investigated the pharmacists' role in the MDD system. In a previous study by Pottegård et al. (2011) problems with both MDD and ordinary prescriptions were analysed, and they found an intervention rate of 0.85% on the MDD prescriptions. This is considerably lower than the 11.3% we found. However, the authors describe that their rate is an underestimation as they have used the number of dispensed MDDs (i.e. one prescription every two weeks for each patient) as the number of prescriptions dispensed, while we have used the number of pharmacist checks (i.e. whenever there are changes on a prescription).

A strength of this study is that we used a registration form from previous studies (Haavik et al., 2011; Volmer, 2012). Though this form had to be adapted to MDD prescriptions, we piloted the form before the study. Because the categorization of responsibilities was not a part of the form, but done by me after the data was collected, there is uncertainty in this

classification. In addition, as interventions were self-reported by the pharmacists, and not completed by independent observers, the number of interventions is also probably underreported. Since we did purposeful sampling of pharmacies for this study, the study pharmacies are probably not representative for MDD pharmacies in Norway. We chose purposeful sampling because this was one of the first studies on pharmacist's interventions on MDD prescriptions, and we found it more relevant to detect the range of different problems than to get an accurate estimation of their frequency. However, because we only included pharmacies from one pharmacy chain, there might be problems and responsibilities we did not record in this study, as the different chains might have different routines for handling prescriptions.

We do however see that the number of interventions varied greatly (from 2.2% to 38.2%) between the pharmacies included in this study, which indicates that routines also varies between pharmacies in the same chain. Large differences in intervention rates between pharmacies and individual pharmacists at the same pharmacy have also been shown previously on ordinary prescriptions (Haavik et al., 2006; Mandt et al., 2010). We have not investigated why intervention rates vary in this study, but parts of it can be explained by drug shortages that affected the pharmacies differently. In addition, there were several small pharmacies included in this study, with the smallest dispensing only 47 MDD prescriptions per week. A small change in the number of interventions would thus give a large change in the rate of interventions.

To summarize, because we purposefully recruited pharmacies from all parts of the country this study gives a broad overview of a range of different problems that pharmacists detect on MDD prescriptions. However, there is uncertainty related to the frequency at which these different problems occur. In addition, my knowledge of the work processes might have affected how the responsibilities of the pharmacists have been categorized.

### **Paper III**

The study presented in Paper III investigates discrepancies in medication lists in the MDD system, and is one of few studies that investigates the effect of an eSML in primary care. A unique feature about this study is that we have done a three-way comparison of the GP, the home care service and the pharmacy medication list, while other studies investigating discrepancies have only compared two lists.

All GPs who were piloting the prescribing system in the municipality we studied agreed to participate. This means we did not have a selection bias based on who agreed to participate in our study. However, as described, there is likely a selection bias in who agreed to pilot the eSML in the first place. Our results indicate that there are differences between the two groups of GPs, as there were fewer discrepancies in the intervention group's lists at baseline. Possible explanations for this are that the intervention group started preparing for the new prescribing system before the actual implementation, or it might be that the GPs in the intervention group already had better routines for updating the medication list prior to the implementation. If the latter is the case, this has implications for the statistical analysis in this study. The main assumption of the difference in the difference analysis we have used is that of parallel trends. If the two groups had different routines for reconciliation prior to the implementation, the number of discrepancies might also have evolved differently in the two groups without the interventions, and then we would not have parallel trends. This means that there is uncertainty related to the size of the change in discrepancies that are due to the intervention.

Another important aspect to be aware of when interpreting these results is how the different GPs approached the initiation of the eSML, and to what extent this included a medication reconciliation. When the GPs started using the eSML, the official recommendations were that they should do a medication reconciliation and compare their own medication list to what the pharmacy had listed. The GPs were reimbursed if they also documented it as a medication review, a procedure that every GP in Norway can be reimbursed for up to three times a year for patients with four or more medications (Regulation relating to a municipal regular GP scheme, 2013, §25). However, we do not know if this was actually done, and if they distinguished medication reconciliation from medication reviews. During the implementation, the pharmacists and nurses reported that it seemed like some patients' medication lists had not been reconciled, though this could also be explained by unsatisfactory communication regarding the reconciliation process (Josendal & Bergmo, 2019). Because this recommendation was only given to the GPs in the intervention group, however, it is not possible to distinguish the effect of the reconciliation from that of having an eSML. Nevertheless, even after a medication reconciliation, discrepancies remain in medication lists, or quickly arise again (Bayoumi et al., 2009; Tam et al., 2005). The effects of the single

medication reconciliation during the initiation are likely to have dissipated after 16 months. As a result, the decreased number of discrepancies we see in this study is most likely due to how the eSML system supports the processes of keeping medication lists updated. However, the total effect of the eSML on discrepancies might have been lower if a reconciliation was omitted at initiation.

In summary, this study shows that the eSML is likely to reduce discrepancies in medication records, as has also been indicated previously (Josendal & Bergmo, 2018; Stock et al., 2008). However, because this study has only been done in one municipality and there is a likely selection bias regarding who was included in this pilot, there is uncertainty related to the size of the effect and generalizations should be made with caution.

#### **Paper IV**

Qualitative studies usually rely on purposeful sampling, where the researchers select cases/informants that is thought to benefit the study the most (Polit & Beck, 2008, p. 516). Considering that this study was conducted in an early phase of implementing the eSML, we instead used a pragmatic approach when recruiting participants: we invited everyone involved in piloting the system and interviewed all who accepted.

We feel that the interviews captured the most important experiences of the participants in our study. Considering that participants from all the different sites involved in the pilot testing were included, we argue that our findings gives a good picture of the experiences the home care nurses and pharmacy employees have had with the system thus far. However, there have been few people piloting the eSML system, and the number of interviews conducted in this study has been a consequence of the available number of informants rather than a matter of reaching data saturation (Polit & Beck, 2008, p 521). Because the eSML is still in an early phase, there are constant changes to both the technology and the routines for implementation, this means that the experiences of our informants might not apply to health care personnel piloting the system later. It is thus likely that new experiences will emerge in later interviews.

An important aspect of qualitative research is if the researcher will influence the findings and interpretation of the findings. As described in the Methods, I did not participate in these interviews because I knew many of the participants, but I did provide input for the interview

guides used. However, knowledge of my participation in the MDD research project might still have affected the informants' answers, especially in terms of being less open about problems with their dispensing program, or lack of information and teaching at the pharmacy prior to the pilot.

The interviews were done by an experienced qualitative researcher (a sociologist) and a registered nurse, and the analyses were performed by the same registered nurse who participated in the interviews, and by me (a pharmacist). Though we were two researchers analysing the interviews, my preconceptions might have affected the analyses process, particularly when looking at changes in workflow. Having worked in an MDD pharmacy myself and having helped develop best practice guidelines for working with MDD patients, I know how the workflow *should* be. When the informants described how they worked in the eSML system, this might have led me to emphasize how the workflow changed compared to the guidelines rather than how it changed in the included pharmacies.

Having extensive knowledge about the technical parts of the eSML system, what kind of training the actors had received prior to starting, common work practices, etc. has also been an advantage. This made it possible for me to distinguish between the different causes of the challenges the informants experienced such as technical problems, inappropriate work processes, challenges in communication with other actors, or other practical problems with the eSML system.

In summary, this study does not aim to give a complete picture of the pharmacists' and nurses' experiences with the eSML system, but focuses on changes in work and aspects that we think could be improved. My pre-understanding of workflow and challenges in the pharmacies might have influenced the analyses and the focus of this paper. However, the results from this paper have complemented, elaborated on and illustrated findings of Paper I-III (Greene et al., 1989), as discussed above, resulting in a more complete picture of how the eSML system influences medication safety.



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## Discussion of main findings

This research shows that MDD affects several aspects of medication safety. PIMs and DDIs are common in elderly patients receiving MDD, particularly co-prescribing of psychotropic and opioid drugs. In addition, MDD patients have a higher overall medication consumption than the general elderly population. The community pharmacist seems to contribute to safe and effective medication use by clarifying problems in one of every nine MDD prescriptions dispensed. Half of the problems were related to formal errors with prescriptions, one-third to medications and one-fifth to drug-shortages. Compared to ordinary prescriptions, the pharmacists take on an additional responsibility for renewing prescriptions. After implementation of the eSML system, discrepancies between the medication lists of the GP, the home care service and the pharmacy for the MDD users were significantly reduced: the number of medications that were present in all three lists increased from 77% to 94%. Despite great improvement, 56% of patients still had discrepancies, showing that the eSML does not eliminate the need for medication reconciliations. The eSML system led to faster information exchange and easier access to updated information about the patient's medication use for the nurses and pharmacists. However, it could also cause misunderstandings as health care personnel who had previously not been a part of the MDD system could now directly influence the prescribing and dispensing of MDD. Most informants reported that the overall workload increased with the eSML system due to an increased need for clarifications. On the positive side, they also reported the eSML to improve medication safety.

### The MDD patient

From Paper I, we find that MDD patients are generally elderly patients using a high number of regular medicines. We find an average of 10.6 medications, of which 6.1 were dispensed via MDD. This is higher than in the general elderly population (Nyborg et al., 2012). Since MDD patients also receive home care services they probably have a greater care need than the general population and the high consumption of medication might simply be a reflection of this. A high number of prescribed medications increases the risk of being exposed to PIMs (Tommelein et al., 2015). From Paper I, we see that one-fourth of the patients were exposed to PIMs and half to DDIs, which is in line with results from previous studies. A systematic review by Tommelein et al. (2015) found a prevalence of PIMs of 22.6% in European

community-dwelling older adults. Looking specifically at home care clients, the systematic review by Meyer-Masseti et al. (2018) found frequencies ranging from 19.8% to 48.4%. The prevalence varies greatly due to different study populations and quality indicators used in the studies. As described in the Introduction, several studies have shown that the prescribing quality in MDD patients is poorer than in patients with ordinary prescribing (Belfrage et al., 2014; Sjoberg et al., 2011; Wallerstedt et al., 2013). In Paper I, we have not done a direct comparison between patients with MDD and patients with ordinary prescribing. However, a previous Norwegian study by Nyborg et al. (2012) has analysed PIMs in the entire elderly home-dwelling population of Norway using the same quality criteria as us. These studies use different data sources, with Nyborg et al. (2012) using dispensed medications and Paper I prescribed medications. However, comparing the results from these two studies do not indicate that the prescribing quality is poorer in MDD patients than in patients with ordinary prescribing in Norway, as Nyborg et al. (2012) found PIMs in 37.8% of the patients and we found 27.0%, despite our study population using more medications.

Antithrombotic agents, non-opioid analgesics, beta blockers, lipid-modifying drugs and hypnotics/sedatives were the most commonly prescribed medication groups both in MDD patients (Paper I) and the general elderly population (Berg et al., 2018); however, we find that the overall prevalence is higher in MDD patients. For example, antithrombotic agents were used by 70% in Paper I and 47% in the general elderly population; analgesics 58% in Paper I versus 25% in the general elderly population (Berg et al., 2018), though the latter might be explained by over-the-counter medications being registered in our study and not in data from the general elderly population. These medication groups are also frequently involved in ADEs (Alqenae et al., 2020; Beijer & De Blaey, 2002; Thomsen et al., 2007).

The only study on the prescribing quality of MDD patients in Norway had been done by Halvorsen et al. (2012) on data from 2009. Using the NORGEP criteria, they found a prevalence of 24.6%. Despite increased focus on medication reviews and deprescribing in elderly patients (O'Mahony et al., 2015; The Norwegian Directorate of Health, 2015); it does not then seem that the prescribing quality for MDD patients has improved over the last decade. This means that MDD patients remain a very vulnerable patient group, being among the oldest home dwelling patients, with the highest medication consumption and thus being most at risk of experiencing PIMs and other DRPs.

### Information and overview

One of the positive aspects of the MDD system is that it gives an increased overview of the patients' medications. This has also previously been expressed by nurses and GPs (Bardage et al., 2014; Bell et al., 2015; Frøyland, 2012; Wekre et al., 2012). From Paper I, we see that the medication lists includes dietary supplements and over-the-counter medicines, information one does not have at the pharmacy for patients with ordinary prescribing. A more comprehensive overview of the patients' medications might explain the relatively low frequency of serious DDIs found in Paper I (Sjoberg et al., 2011).

Paper II also shows that pharmacists had access to more information about the patients' medication use, such as discharge notes from the hospital, and actively used the medication dispensing history of the patients when checking the prescriptions. Increased access to information about the patient has shown to increase the pharmacist's ability to detect errors (Buurma et al., 2001; Chen et al., 2005; Johnell & Fastbom, 2008), and in Paper II the pharmacists detected medication-related problems with 3.3% of the total MDD prescriptions dispensed. This is high compared to studies on ordinary prescriptions (Buurma et al., 2001; Chen et al., 2005; Ekedahl, 2010; Haavik & Ekedahl, 2013; Haavik et al., 2006; Knapp et al., 1998; Pottegård et al., 2011). When the electronic system was implemented, the pharmacists describe having access to even more information about the patients' total medicine use and how they feel that this increases medication safety (Paper IV).

Though the pharmacist might be in a better position to evaluate the total medication use of the patient, we see from Paper III that the medication list they evaluate is not the same the GPs use, as 75-90% of the patients had at least one discrepancy when comparing these lists. Discrepancies between medication records is not just a problem for MDD patients, and this degree of discrepancies is in line with what is found in home care in general (Meyer-Masseti et al., 2018). In fact, one study indicates that MDD might reduce discrepancies between medication lists in primary care, an improvement mostly attributed to increased cooperation and communication between the health care personnel (Wekre et al., 2012; Wekre et al., 2011). Similarly, studies that find that MDD patients are more exposed to errors and discrepancies in medication records during care transitions attribute these errors to insufficient communication and collaboration between primary and secondary health care personnel (Bergkvist et al., 2009; Caleres et al., 2020; Midlöv et al., 2005).

The communication of medicines information seems to improve after the implementation of the eSML. In Paper IV, the pharmacists describe how their communication with the GPs improved, and how GPs updated medication lists faster after hospital stays. We also see that the number of discrepancies is significantly reduced: from an average of 3.8 discrepancies per list to 1.2 after the implementation. It would thus seem that the electronic MDD system further improves the overview of patients' medication treatment compared to the paper-based system by increasing access to medicines information and reducing discrepancies.

### **The effect of eSML on medication safety**

The eSML system can lead to the reduction in discrepancies we find in Paper III in several ways. First, e-prescribing has shown to increase the legibility, completeness and clarity of prescriptions (Kaushal et al., 2010; Lanham et al., 2016; Odukoya & Chui, 2013; Zadeh & Tremblay, 2016). Errors such as missing prescriber signatures, missing patient information and illegible handwriting are likely to be eliminated with e-prescriptions. From Paper II we see that almost one-fifth of the pharmacist's interventions were due to incomplete prescriptions. Secondly, when the pharmacist detected a problem and contacted the GP, they described in Paper IV that the eSML system forced the GP to update their own system and issue a new prescription, while with the paper-based system the pharmacist could make the changes on the paper prescriptions and inform the GP about the change afterwards. Thirdly, the use of a common system for ordinary prescriptions and MDD prescriptions eliminates the need for double prescribing routines for GPs, and reduces the chances that the GP will forget to fax the prescriptions to the pharmacy. In addition, as described by the pharmacists in Paper IV, the manual routines for sorting faxes and transcribing prescriptions are reduced with the eSML system.

Despite a significant decrease in discrepancies, 56% of the patients still had at least one discrepancy after the implementation. This shows that the eSML does not eliminate the need for reconciliations. There is also conflicting evidence on whether a reduction in discrepancies actually affects outcomes such as re-hospitalizations and deaths (Daliri et al., 2021; Lehnбом et al., 2014; Redmond et al., 2018). However, medication reconciliation is a time consuming process, and having a more updated and accurate list will most likely reduce the amount of time health care personnel use on medication reconciliations. That said, both the nurses and

the pharmacists in Paper IV described the eSML as being more time consuming overall, though this was not related to medication reconciliations.

In particular, two aspects of the eSML system caused more work for the participants in Paper IV: increased access to information, which again led to more clarifications, and frequent renewals of prescriptions. The frequent renewals are in the electronic system by design: there are individual e-prescriptions for each medication on the list. In the paper-based system, there was one complete prescription card, valid for a one year supply, and with only one expiry date. It was thus only necessary to renew the prescription once per year. In the eSML system, however, a patient with 10 medicines will have 10 prescriptions. Though each prescription is valid for a year, they can be issued at different times resulting in a potential of 10 renewals per year. In addition, the e-prescription contains the quantities of a medication, which means they can be emptied out before a year has passed. In fact, prescribing the wrong quantity of a medicine is among the most common errors in e-prescribing (Gilligan et al., 2012; Kauppinen et al., 2017; Odukoya et al., 2014), and this might then result in each prescription having to be renewed more than once per year.

That the process of renewing prescriptions is more automated in the MDD system has been suggested as a possible explanation for why the prescribing quality for MDD patients is poorer than for patients with ordinary electronic prescribing (Sjoberg et al., 2011; Sjoberg et al., 2012; Wallerstedt et al., 2013). If this is the case, more frequent renewing of prescriptions might improve prescribing. However, renewing prescriptions can also be a technical task in many situations and does not necessarily include a review of the current treatment (Oravainen et al., 2021). One of the nurses in Paper IV said that medicines were more frequently missing from the MDD bags after the implementation of the eSML system, because the prescriptions were not renewed in time. Some had also started double-checking the MDD deliveries because of this. It is thus uncertain whether increased renewal of prescriptions really increases medication safety, especially considering how much extra time the GPs, the home care services and the pharmacists used on this task in the eSML system.

The other aspect that was more time consuming was the increased access to medicines information. Though this was generally viewed as positive and increasing medication safety, it also caused uncertainty and misunderstandings about the patients' current treatment. Despite the guidelines being that a physician should withdraw old prescriptions when issuing

new ones, it has recently been estimated that 13% of patients have at least one duplicate prescription in the Norwegian prescription database (Norwegian Healthnet - Public Enterprise, 2021b). Outdated prescriptions in this database were also an issue mentioned by the pharmacists in Paper IV, causing an increased need for clarifications. Similar concerns were raised by the GPs piloting the system, who expressed uncertainty about the status and validity of the current medication list, now that all physicians could influence prescribing (Gullslett & Bergmo, 2022; Johnsen et al., 2018). Although more actors being able to influence the MDD prescribing process seems to improve medication safety in terms of increased access to updated information and fewer errors, this also ultimately makes the process more complex. We find that if the roles and responsibilities were more clearly defined and understood by all the actors in the medication use process, this would improve many of the challenges the nurses and pharmacists experienced with the eSML system.

### **Responsibilities in the MDD system**

The MDD system has previously been criticized for unclear division of responsibilities and unclear routines across professional borders (Herborg et al., 2008; Hjelle, 2015; Johnsen et al., 2018). This is no surprise since MDD has traditionally been viewed as a means to reduce dispensing errors compared to manually filled dosettes, and as an adherence aid to help patients take their medicines at the right time. There has thus been limited need for specific guidelines separating MDD from ordinary prescribing. However, there is a growing body of evidence showing that MDD also affects other phases and actors of the medication use process, and my thesis is one of the first looking at the pharmacist's role in the MDD system.

The main responsibility of the community pharmacist is to check prescriptions, both for clinical appropriateness as well as validity of the prescription (Norwegian Pharmacy Association, 2017; Rule on Requisition and Distribution of Medicines from Pharmacies, 2019, §6-8). Paper II shows that this is also regularly done on MDD prescriptions. In addition, the pharmacist should assess whether the medication label is clearly written and whether the patient needs any additional information about their medications (Norwegian Pharmacy Association, 2017; Rule on Requisition and Distribution of Medicines from Pharmacies, 2019, §6-8). Considering that MDD is dispensed in individual bags for each administration time, and as such contain more information than a typical medication label, this need might be reduced for MDD patients. For example, there is less need to clarify complex dosing schedules,

informing the patients that the medications should be taken at specific times of the day or be taken some hours apart. However, it is difficult for the pharmacist to assess whether the patient needs more information about their medicines in this setting considering that they have no direct contact with the patient. Any patient counselling would then have to be done via the home care services. In Paper II, however, most problems are resolved by contacting the GP, and only 17% of the problems were resolved by contacting the home care nurses. On ordinary prescriptions, the pharmacist resolves up to half of the prescription related problems by talking to the patient or caregiver (Buurma et al., 2001; Haavik et al., 2006; Haavik et al., 2011; Maes et al., 2018). It would thus seem that there is limited patient counselling during the dispensing of MDD. Reduced patient counselling from the pharmacist could be a possible explanation as to why patients using MDD have less knowledge about their medications than patients with ordinary prescriptions (Kwint et al., 2013). Our findings call for a clearer placement and division of responsibilities for patient counselling between the pharmacy and the home care service, to ensure that patients have enough information to take their medicines correctly.

Another step where responsibilities do not seem to be clearly defined is in the renewing of prescriptions. For patients with ordinary prescribing, it is the patient's responsibility to get prescriptions renewed. When a patient gets MDD from home care services, the home care is responsible for handling the patients' medications, which includes ensuring that valid prescriptions are available for the patient (The Norwegian Directorate of Health, 2019b). However, in Paper II we find that prescriptions that were expired or about to expire was the number one reason for the pharmacist to contact the GP, showing that the pharmacy staff also take on this responsibility for MDD patients.

Empty or expired prescriptions can have more severe consequences for an MDD patient than patients with ordinary prescribing. This is because stopping an MDD prescription involves stopping all medication distributed in MDD, not just a single medication. In addition, by the time an MDD order is placed, the patient usually has only a few days left of medication supply. This might explain why the pharmacist adopts additional responsibility for renewing prescriptions, and why the pharmacist continues to dispense void prescriptions in the majority of cases (Paper II). In this sense, we see that pharmacists function as a safety net in the MDD system, preventing the patient from having unintentional gaps in their treatment.

However, the frequency at which they dispense emergency refills is worrying, especially if the practice is continued for longer periods for each patient as this might ultimately reduce medication safety due to patients not getting regular medication reviews. If this is the case, this might also explain why MDD users seem to have fewer changes in their medication treatment than patients with ordinary prescribing (Sjoberg et al., 2012; Wallerstedt et al., 2013). The fact that expired prescriptions is the most common cause for the pharmacist to contact the GP, and that pharmacists still frequently dispense void prescriptions shows that there is a major gap in communication or collaboration between the GP and the pharmacy in this matter.

Paper IV shows that the communication between the GP and the pharmacy is improved with the eSML system, and that the GPs renew prescriptions more frequently. Though the pharmacists still contact the GPs to get prescriptions renewed, the responsibility for renewing prescriptions seems to be shifted more towards the home care, as the nurses also describe new routines for ensuring valid prescriptions. The reason for these new routines was, however, that they had experienced medications to be more frequently missing from the MDD bags. It would thus seem that renewing prescriptions is an even bigger challenge in the eSML system than in the paper-based one. There are several possible explanations for why expired prescriptions would lead to more medications missing from the MDD bags in the eSML system. First, the prescriptions need to be renewed more often. More renewals mean more chances for mishaps in the renewal process. Secondly, the pharmacist might do emergency refills less often. In the paper-based system the entire MDD delivery is stopped if the prescription is expired, with individual e-prescriptions it is just the one medication and the threshold for how often the pharmacist has to do emergency refills might thus be raised compared to the paper-based system. Thirdly, the pharmacists expressed that errors from the GP were more difficult to correct on e-prescriptions. Expired prescriptions might thus have been more difficult to correct or do emergency refills on, resulting in the medication not being dispensed.

That e-prescriptions can be more difficult to correct and require more contact with the prescribers than paper prescriptions, has also been shown previously (Ekedahl, 2010; Smith & Sprecher, 2017; Vik et al., 2020; Åstrand et al., 2009). When the prescriptions are more structured and systems more integrated, this tightens some of the gaps where errors arise



today, but it also seems to make corrections more difficult. This emphasizes the need to get the input correct and puts additional pressure on the first step in the chain: prescribing. Though nurses and pharmacists should continue with their roles as safety nets, identifying and resolving errors to prevent them reaching the patient, a more effective approach might be to be more involved in the initial prescribing to ensure the quality of the input, thus reducing errors and clinical queries at later stages.

### **Implications, recommendations and future research**

This thesis contributes to reducing the knowledge gaps in the following three research fields: medication safety in home care services (Meyer-Masseti et al., 2018), the use of MDD systems in primary care (Sinnemäki et al., 2013) and the effects of the national shared medication list (Manskow et al., 2019). Though it is an early version of the eSML system that has been investigated, this research indicates a number of aspects that could be improved with an eSML system, and the challenges and factors to be aware of when implementing such a system. Lastly, this thesis illustrates that MDD systems used in primary care are more than just a way of dispensing medicines, but also affect other steps of the medication use process and collaboration between the actors.

#### **MDD systems in home care services**

Patients receiving home care services commonly suffer from complex chronic somatic or psychiatric problems and require long-term, coordinated health care services (St.meld.nr47 (2008-2009)). Consistent with previous studies, this thesis find that home care patients are mostly elderly, take a high number of regular medicines, and are frequently prescribed PIMs (Meyer-Masseti et al., 2018). The council of Europe recommends that patients with MDD get regular medication reviews to assess the appropriateness of medication use (European Directorate for the Quality of Medicines, 2018). Norwegian GPs can presently be reimbursed up to three times a year when they do medication reviews for patients with more than 4 regular medications (Regulation relating to a municipal regular GP scheme, 2013, §25) and in 2020 GPs did on average 140 such reviews per year (The Norwegian Directorate of Health, 2019a, 2020). However, these medication reviews can be done by the GP alone, and do not have to involve other health care personnel or the patient. This thesis shows that the MDD system gives a better overview of the patient's current medication and increased access to

medicines information for the pharmacist and there seems to be an unfulfilled potential of using the medication lists to systematically identify PIMs and target high-risk patients for medication reviews. As the eSML system also improves communication between the GP and the pharmacy and enables direct feedback between these two, the system has many of the prerequisites needed to improve prescribing quality in these patients. The next step might be to integrate interventions such as medication reviews in the MDD system, as is currently being tested in Finland (Tahvanainen et al., 2021).

This thesis also emphasizes the work of the community pharmacists in the MDD system. We see that the pharmacists adopt responsibilities that has not been documented previously. Knowledge of work processes is important when digitalizing systems, as there can be “hidden” work that is vital to safe medication use. Specifically, we see in this thesis that the pharmacists are preventing gaps in the medication treatment, both by reminding the GPs to renew prescriptions, and by frequently dispensing emergency refills. Paper IV also indicates that the latter has become more difficult in the eSML system, resulting in medications more frequently missing from the MDD bags. This calls for clearer placement of responsibilities and/or improved systems regarding renewing of prescriptions. One option to resolve this could be allowing pharmacists to renew prescriptions. Another, more long-term solution, could be to shift the focus away from single prescriptions and, rather, focus on the medication treatment and the eSML as a whole, removing the need to renew each prescription individually and instead focus on reviewing the medication treatment at set intervals.

The other area where the work processes for the pharmacist seem to differ for patients with ordinary prescribing and MDD is patient counselling. Previous studies have shown that MDD patients seem to have less knowledge about their prescribed medicines (Kwint et al., 2013; Modig et al., 2009), and reduced patient counselling might be a possible explanation for this. Dosing aids being filled by a third party can be disempowering for the patient, which has also been shown by others (Rohan Andrew Elliott, 2014). Increased use of e-health technology, such as video consultations between the patient and the pharmacist, could be considered as a means to ensure that patients get necessary information about their medicines to use them optimally. With the eSML system, the MDD patient also gets access to the updated medication list online. Future studies should focus on the patient’s experiences with the MDD

system, how they are affected by the electronic prescribing system and the means of involving patients in the MDD system.

### **Implementation of an eSML**

This thesis adds to the existing evidence that e-prescribing and a shared medication list has the potential to reduce medication errors (Josendal & Bergmo, 2018; Kaushal et al., 2010; Odukoya & Chui, 2013; Stock et al., 2008; Zadeh & Tremblay, 2016). The goal of the Norwegian eSML is to improve medication safety by generating one structured and complete medication list, by increasing access to medicines information for all health care professionals involved in the care of MDD patients, by improving the quality of medication treatment and by reducing the time used on medication reconciliation (The Directorate of e-health, 2021). This research shows that these aims have only been partly met so far.

In the paper-based MDD system the medication list at the pharmacy is used to dispense medicines. When the eSML is implemented, this is created based on the GP's medication list. Since 75% of patients had discrepancies when comparing these lists, this emphasizes the need to do a medication reconciliation before implementing the eSML to avoid unintended changes in patient's medication treatment. Further studies should focus on how GPs, in collaboration with other health care professionals and the patient, should create the first eSML based on the many medication lists that are available today.

If a medication reconciliation is not done, and there are errors in the first eSML, this can result in patients and health care personnel losing trust in the system. This was experienced in the previous testing of the eSML system for MDD patients: home care nurses identified many errors in the first eSML generated, and this seemed to compromise their trust in the system, at least short term (Josendal & Bergmo, 2019). We see similar findings in Paper IV, where the nurses added extra control routines and described feeling increased responsibility after the implementation. If users lose trust in the system, the eSML will not achieve its goals of improving medication safety.

When the eSML is used for MDD patients, errors in the first list might not actually reach the patient. The chance of detecting errors increases with the number of actors involved in the process (Leape et al., 1995) and for MDD patients both the pharmacy and home care nurses check the first eSML. When the eSML is implemented for patients without MDD, however,

this safety net is not present. This puts additional responsibility on the GP. We know from previous studies that the medication list at the GP office is not accurate compared to what the patient is actually taking (Bikowski et al., 2001; Ekedahl et al., 2011; Heerdink et al., 1995; Tulner et al., 2009), and we also know that there are many duplicate and outdated prescriptions in the prescription mediator (Norwegian Healthnet - Public Enterprise, 2021a). It is thus necessary for the GP to reconcile the list and remove these outdated prescriptions when generating the first eSML, and that they dedicate enough time for this work (Bergmo et al., 2019). Though much of the work is done at the initiation, it is also important to recognize that this process has to be done regularly. As this thesis shows, there are still discrepancies in the medication lists after the implementation, and the eSML does not eliminate the need for medication reconciliations. In order for the eSML to achieve its goals, all prescribers have to take responsibility for the medication list, withdraw outdated prescriptions, including those prescribed by physicians other than themselves. If physicians are reluctant to delete prescriptions issued by other doctors (Gillespie et al., 2018; Rahmner et al., 2010) this might, with time, result in more polypharmacy, inappropriate prescribing and decreased medication safety. Future studies should focus on this shared responsibility for common patients, especially at care transitions where the eSML system has the most potential to prevent errors. In addition, further research needs to be done measuring the eSML's effect on hard outcomes such as hospitalizations and death, as well as health services use.

## CONCLUSIONS

This thesis is based on four published papers that illuminate different aspects of medication safety in an MDD system used in home care services.

We find that one of the benefits of the MDD prescribing system is increased access to information about the patient's medication use. This includes dietary supplements and over-the-counter medicines — an overview one does not have for patients with ordinary prescribing — in addition to access to information such as discharge notes from the hospital. This increased overview enables pharmacists to identify and intervene on a range of problems with MDD prescriptions, including problems that would be difficult to detect on ordinary prescriptions, such as the sudden stop of a medication that should have been tapered. As for ordinary prescribing, we find that the main responsibility of the pharmacist is checking prescriptions for clinical appropriateness and verifying the validity of prescriptions. In contrast with ordinary prescribing, however, the pharmacist seems to provide little patient counselling and take on an additional responsibility to get prescriptions renewed. Reminding GPs to renew prescriptions seems to remain a responsibility for pharmacists in the eSML system, and more renewing of prescriptions is one of the main reasons why pharmacists find the eSML system more time consuming.

With the eSML system, the practice of having a complete medication list is continued, and the overview this list gives seems to be improved. In terms of medications present in the medication lists of the GP, the home care service and pharmacy, this is shown to increase from 77% to 94% after the implementation. The pharmacists also describe improved communication with the GP and having easier access to new prescriptions from the hospital, resulting in changes being initiated faster in MDD.

Though increased access was mostly viewed as improving medication safety, direct access to the hospital's prescriptions could also cause new challenges and this was another reason why the pharmacists reported that the eSML system was more time consuming. The increased access meant that they needed to make more clarifications before dispensing MDD, such as clarifying dosing schedules when hospital doctors and the GP had written prescriptions on the same medicine. This example also illustrates that the responsibility for updating prescriptions needs to be more clearly placed. When the eSML is implemented, the last physician changing

the medication treatment for a patient should take responsibility for the entire medication list. This means they have to delete prescriptions that are no longer relevant or appropriate, including those prescribed by other doctors.

Looking at the patient group that receives MDD also emphasizes the need to assess the medication treatment. We find that these patients are among the oldest patients still living at home, a patient group at high risk of experiencing PIMs and other DRPs. MDD patients have a higher medication consumption than the general elderly population, with one-third of the patients using 10 or more medications regularly, about one-fourth being prescribed PIMs and half exposed to DDI.

The eSML seems to reduce errors in the MDD system, but more emphasis should be placed on accuracy in the prescribing phase. For the eSML to achieve its goals of increasing medication safety in this vulnerable patient group there is a need to define the responsibilities of all the actors in the medication use process, including the responsibility of reviewing the entire medication treatment for the patient as a whole.

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## Appendix

### Appendix - the MDD project

1. Godkjenning Personvernombudet ved Universitetssykehuset Nord-Norge
2. Vedtak REK – ikke helsetjenesteforskning

### Appendix Paper II

3. Self-completion form for pharmacist interventions on MDD prescriptions
4. Opplæringsmateriell for studie om intervensjoner i MDD apotek

### Appendix Paper III

5. Godkjenning REK fritak fra samtykke

### Appendix Paper IV

6. Intervjuguide hjemmesykepleie
7. Intervjuguide apotek



Appendix 1





Trine Bergmo  
Nasjonalt senter for e-helseforskning

Deres ref.:

Vår ref.:  
2017/6695

Saksbehandler/dir.tlf.:  
Eva Henriksen / 95731836

Dato:  
12.12.2017

## GODKJENNING AV BEHANDLING AV PERSONOPPLYSNINGER

Det vises til Meldeskjema for forskningsprosjekt, kvalitetsprosjekt og annen aktivitet som medfører behandling av personopplysninger som er melde- eller konsesjonspliktig i henhold til helseregisterloven og personopplysningsloven med forskrifter, mottatt 22.11.2017.

Meldingen gjelder prosjektet/registeret:

**Nr. 02003**

**Navn på prosjektet:** *Forskning på elektronisk multidose – pasientsikkerhet, erfaringer og prosessevaluering*

Prosjektet er et **forskningsprosjekt** hvor Universitetssykehuset Nord-Norge HF er behandlingsansvarlig.

**Formål:** *«Vi skal undersøke om multidose i e-resept gir økt kvalitet på legemiddellistene og om det gir færre avvik mellom legemiddellister hos fastlege, hjemmetjeneste og apotek, opp mot dagens papirbaserte rutiner. Studien skal gjennomføres som en kontrollert før-etter studie, der samme pasienters legemiddelliste undersøkes før innføring av e-multidose og 12 måneder etter. Listene analyseres i forhold til kvalitet, og type og antall avvik mellom apotek, lege og hjemmesykepleien. Samme undersøkelse skal gjøres i parallell i en kommune som ikke får innført multidose i e-resept i studieperioden og skal fungere som kontrollgruppe.»*

REK har vurdert prosjektet, og finner at behandlingen av personopplysningene **ikke faller inn under medisinsk- og helsefaglig forskning etter Helseforskningsloven**. Behandlingen vil være regulert av § 7-27 i Personopplysningsforskriften og hjemlet etter Helseregisterloven § 6, jf. Personopplysningsloven § 11. Forskningsprosjekt vil som hovedregel kreve samtykke, men REK har gitt fritak for samtykke.

PVOs anbefaling forutsetter at prosjektet gjennomføres i tråd med de opplysningene som er gitt i henhold til Personopplysningsloven og Helseregisterloven med forskrifter.

PVO har på bakgrunn av tilsendte meldeskjema med vedlegg registrert prosjektet. Prosjektet har opplyst om at alle sensitiv data, også aidentifiserte, vil bli lagret hos Tjeneste for sensitive data (TSD) som er en sikker forskningsserver hos UiO.

Tilgang til dette området skal begrenses til kun å omfatte prosjektleder og den som prosjektleder definerer.

PVO gjør oppmerksom på at dersom registeret skal brukes til annet formål enn det som er nevnt i meldingen, må dette meldes særskilt.

PVO skal ha melding når registeret er slettet. PVO skal også ha melding dersom registeret ikke er slettet eller ikke ferdig behandlet innen 3 år.

Med hjemmel i Personopplysningsforskriften § 7-12 godkjenner PVO at behandlingen av personopplysningene settes i gang som beskrevet.

Med vennlig hilsen

UNIVERSITETSSYKEHUSET NORD-NORGE HF

PVO-teamet  
e.f.

Kopi: Senterleder Stein Olav Skrøvseth



Appendix 2



Region:  
REK nord

Saksbehandler:

Telefon:

Vår dato:

29.08.2017

Vår referanse:

2017/1393/REK nord

Deres dato:

13.06.2017

Deres referanse:

Vår referanse må oppgis ved alle henvendelser

Trine Strand Bergmo  
Nasjonalt senter for ehelseforskning

### **2017/1393 Innføring av elektronisk multidose – innvirkning på kvalitet og pasientsikkerhet i legemiddelkjeden.**

**Forskningsansvarlig institusjon:** Universitetssykehuset Nord-Norge HF

**Prosjektleder:** Trine Strand Bergmo

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK nord) i møtet 17.08.2017. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10.

#### **Prosjektleders prosjekttale**

*Multidosepakkelegemidler gir pasienter i kommunal pleie- og omsorgstjeneste en bedre og tryggere legemiddelbehandling. I dag ordineres multidose på papir via brev/faks. Det er planlagt å innføre elektroniske rutiner for forordning av multidose. Prosjektet er et samarbeid mellom Direktoratet for eHelse og NSE. Direktoratet er ansvarlig for innføring av løsningen. Vi skal undersøke om multidose i e-resept gir økt kvalitet på legemiddellistene og om det gir færre avvik mellom legemiddellister hos fastlege, hjemmetjeneste og apotek, opp mot dagens papirbaserte rutiner. Studien skal gjennomføres som en kontrollert før-etter studie, der samme pasienters legemiddelliste undersøkes før innføring av e-multidose og 12 måneder etter. Listene analyseres i forhold til kvalitet, og type og antall avvik mellom apotek, lege og hjemmesykepleien. Samme undersøkelse skal gjøres i parallell i en kommune som ikke får innført multidose i e-resept i studieperioden og skal fungere som kontrollgruppe.*

#### **Vurdering**

##### **Om prosjektet**

PhD-prosjektet er organisert som et samarbeidsprosjekt mellom Nasjonalt senter for e-helseforskning (UNN), UiT og UiO, og gjøres i samarbeid med Direktoratet for e-Helse.

I søknaden vises det til forprosjekt gjennomført høsten 2016 med tittel «Samstemming av legemiddellister ved bruk av elektronisk multidose» hvor formålet var å finne om avvik øker eller reduseres etter innføring av multidose i e-resept. Prosjektet ble vurdert å ikke omfattes av helseforskningsloven og det ble gitt dispensasjon fra taushetsplikt.

### **Framleggingsplikt**

De prosjektene som skal framlegges for REK er prosjekt som dreier seg om "medisinsk og helsefaglig forskning på mennesker, humant biologisk materiale eller helseopplysninger", jf. helseforskningsloven (h) § 2. "Medisinsk og helsefaglig forskning" er i h § 4 a) definert som "virksomhet som utføres med vitenskapelig metodikk for å skaffe til veie ny kunnskap om helse og sykdom". Det er altså formålet med studien som avgjør om et prosjekt skal anses som framleggelsespliktig for REK eller ikke.

I dette prosjektet er formålet å evaluere pasientsikkerheten i det nye systemet opp mot det gamle. Selv om dette er en helsefaglig studie og funnene i studien indirekte vil kunne gi en helsemessig gevinst faller ikke prosjektet inn under definisjonen av de prosjekt som skal vurderes etter helseforskningsloven.

Prosjektet faller ikke inn under helseforskningsloven, men prosjektet skal bruke personopplysninger fra helsesektoren i forbindelse med forskningen og det søkes fritak fra samtykke for å identifisere pasienter som får multidosepakkede legemidler og for innhenting av deres legemiddellister direkte fra apotek, fastlege og hjemmesykepleie (som er ansvarlig for behandlingen av den enkelte pasient).

### **Innhenting av data**

Data som skal innhentes og sammenlignes er antall avvik i legemiddellister før og etter innføring av multidose i e-resept, sammenlignet med kontroller (multidose i papirresepter) og man vil også analysere kvaliteten på forskrivningene.

For å identifisere og få laget lister over pasienter som får multidose må det gjøres oppslag i apotekenes multidoseprogram i de aktuelle kommunene. For å kunne identifisere en kontrollgruppe til denne studien ønskes det også å gjøre oppslag for en kommune der det nye systemet ikke innføres i studieperioden. Disse listene vil gi den komplette oversikten over alle pasienter som skal inkluderes i studien, og det vil ut fra disse listene lages løpenummer per pasient som fungerer som koblingsnøkkel mellom listene i senere analyser. Ordinasjonskortene/legemiddellistene for alle pasientene vil avidentifiseres av forskerne.

Det søkes om dispensasjon fra taushetsplikt for to navngitte forskere med begrunnelse at man ikke vet hvem pasientene er før etter at det er gjort oppslag i dataprogrammene og at det vil være store praktiske utfordringer å innhente samtykke fra brukerne også etter at de er identifisert.

### **Vurdering om det kan gis dispensasjon fra taushetsplikten etter helsepersonelloven § 29 og forvaltningslovens § 13 d.**

Prosjektet faller ikke inn under helseforskningsloven, men prosjektet skal bruke personopplysninger fra helsesektoren i forbindelse med forskningen. REK er delegert myndighet til å gi dispensasjon fra taushetsplikten etter helsepersonelloven § 29 og forvaltningslovens § 13 d.

I vurderingen av om det kan gis unntak for samtykke må komiteen vurdere alle sider av prosjektet, herunder om det er av vesentlig interesse for samfunnet og om hensynet til deltagerens velferd og integritet er ivarettatt. Komiteen skal også vurdere om det vil være vanskelig å innhente samtykke i denne studien.

I vurdering av om det vil være «vanskelig å innhente samtykke», fremgår det både av forarbeidene og av departementets kommentarer til helseforskningsloven at kvalifiserte og legitime årsaker til dette kan være dersom deltager er død, flyttet, sykdom, stort antall deltagere, samt at et stort frafall vil svekke forskningens validitet.

Selv om dette prosjektet har en del til felles med P REK 2016/2065, der det ble gitt dispensasjon, vurderer komiteen også prosjektene som ulike. Komiteen imøteser derfor en bedre begrunnelse for hvorfor det bør innvilges dispensasjon fra samtykke.

### **Vedtak**

*Etter søknaden fremstår prosjektet ikke som et medisinsk og helsefaglig forskningsprosjekt som faller innenfor helseforskningsloven. Prosjektet er ikke framleggelsespliktig, jf. hfl § 2.*

*Med hjemmel i forskrift av 02.07.09 nr. 989, der REK er delegert myndighet til å gi dispensasjon fra taushetsplikt etter helsepersonelloven § 29 første ledd og forvaltningsloven § 13 d. imøtesees prosjektleders tilbakemelding.*

*Den videre behandling av søknad om dispensasjon fra taushetsplikt vil bli foretatt av komiteens leder/nestleder og/eller sekretær, med mindre det reises spørsmål som må behandles av samlet komité.*

Vennligst benytt skjema for tilbakemelding som sendes inn via saksportalen til REK  
<http://helseforskning.etikkom.no>. Tilbakemeldingen må være oss i hende innen seks måneder

Med vennlig hilsen

May Britt Rossvoll  
sekretariatsleder

**Kopi til:** [stein.olav.skrovseth@ehealthresearch.no](mailto:stein.olav.skrovseth@ehealthresearch.no); [rek-svar@unn.no](mailto:rek-svar@unn.no)



Appendix 3





Date.....

Technician sign.....

Pharmacist sign.....

## REGISTRATION OF INTERVENTIONS ON MULTIDOSE PRESCRIPTIONS

### 1. BACKGROUND INFORMATION

- Type of patient:**       Private                       Nursing home                       Home care service
- RX Reception:**    NA    Fax    E-mail    Telephone    Electronic    Other:.....

### 2a. ERRORS ON THE MDD ORDER

- Missing       Missing shipping address       Illegible       Other:.....

### 2b. FORMAL ERRORS ON PRESCRIPTION(LIST)

- Date       Patient's date of birth/name       Missing approval for compassionate use       Unknown MD
- Missing       Missing signature       Other:.....

### 2c. ERRORS ON PRESCRIPTION ITEM

#### Drug-shortage

- Patient:**                      Year of birth:.....                      Sex:.....
- Prescriber:**                       MD Community                       MD other
- Prescription type:**       Medication list                       Single prescription

**Description of problem:** .....

.....

.....

#### **Problem (include information on drug, dose and use):**

- Drug or strength      .....
- Dose/schedule      .....
- Dosage form      .....
- Quantity/duration       Drug-drug interactions       Reimbursement       CAVE
- Other: .....

### 3. INTERVENTION

- Contacted prescriber       Contacted nursing home       Contacted home care service
- Pharmacist's own judgement       Patient profile/prescription history reviewed

**Prescriber informed retrospectively:**       Yes       No

### 4. RESULT:

- Added, discontinued or clarified drug or strength       Received necessary documentation
- Changed or clarified dose/schedule       Dispensed as prescribed/informed
- Changed or clarified dosage form       Drug not dispensed
- Changed of clarified quantity/duration       Dispensed without correction/clarification
- Changed or clarified reimbursement information
- Other:.....

**5. TOTAL TIME SPENT(ca):** ..... min



## Appendix 4





# Reseptfeil og farmasøytiske intervensjoner på multidoserecepter

Informasjonspakke til deltakende apotek



## Innhold

---

- Introduksjon
- Bruk av skjema
- Praktisk informasjon
- Vedlegg
  - Registreringsskjema for reseptavvik
  - Ettpunktsleksjon for innfylling av skjema
  - Eksempler for utfylling av skjema

## Om studien

---

Nasjonalt senter for e-helseforskning skal i samarbeid med direktoratet for e-helse undersøke om elektronisk multidose bidrar til riktigere/bedre legemiddelbehandling. Ett av målene er å undersøke hvordan elektronisk multidose påvirker andel avklaringer mellom apotek og lege og antall intervensjoner apoteket gjør på reseptene før pakking av multidose.

Kontroll og ekspedisjon av resepter er en av hovedoppgavene til apotekfarmasøyten. Generelt er det blitt gjort få studier i norske primærapotek over reseptintervensjoner, og det er ikke funnet noen som har undersøkt andelen intervensjoner på multidoseresepter spesielt. Formålet med denne studien er å registrere antall intervensjoner apotekene gjør på multidoseresepter. Det vil også være aktuelt å gjenta studien etter at multidose i e-resept er blitt innført for å se hvilke effekter e-resepter har på arbeidsflyt og antall intervensjoner i apotek.

## Bruk av skjema

---

I dette dokumentet ligger skjemaet som skal brukes for registrering av reseptavvik, en ettpunktsleksjon og eksempler for utfylling. Selve registreringskjemaet er også vedlagt i en egen PDF fil. Det anbefales å skrive ut en liten bunke med skjemaer før studien starter og legger på alle arbeidsplasser der man jobber med multidose, slik at skjemaet er lett tilgjengelig.

Det er ønskelig at alle avklaringer som må gjøres rundt enten en bestilling eller forskrivning registreres i skjemaet. Dette innebærer at det også skal registreres dersom man for eksempel ringer og informerer om at en vare igjen er pakkbar etter den har stått som utsolgt i Nagara, dersom man må ringe og informerer om at ordinasjonskortet *snart går ut*, dersom man etterlyser bestillinger fra sykehjem osv.

Dersom det er flere feil på samme resept/bestilling som krever *ulike tiltak* skal dette registreres på separate skjema, slik at man kan se hvilket tiltak og resultat og hører til hvilken feil. Dersom det er feil på flere ulike resepter som har samme tiltak (typisk utsolgt vare til flere pasienter på samme sykehjem) kan dette registreres på samme skjema så lenge det oppgis antall pasienter det gjelder

## Praktisk informasjon

---

Perioden for registrering skal være på *2 sammenhengende uker*. Ved studiens slutt skal utfylte intervensjonsskjema sendes til:

Apotek 1 Kundesenter Storkunde  
v/Anette Vik Jøsendal  
Postadresse: Postboks 243  
1471 Lørenskog

Vennligst skriv på **hvilket apotek** som er avsender, samt periode for innsamling.

Etter skjemaene er mottatt vil det fra Nagara hentes ut antall ordinasjonskort endret og antall bestillinger gjort i studieperioden på det enkelte apotek. Apoteker vil ca 1 måned etter avsluttet studie få en samlerapport over de intervensjonene som er gjort på sitt apotek i studieperioden

Dersom dere har noen spørsmål så er det bare å ta kontakt med meg på telefon: 97 67 19 38, eller e-post: e-post: [anette.vik.josendal@ehealthresearch.no](mailto:anette.vik.josendal@ehealthresearch.no)



Dato.....

Tekniker sign.....

Farmasøyt sign.....

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 1. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie

Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler

Ukjent lege  Savnes  Annet:.....

### 2c. FEIL MED ORDINASJONER Utsolgt vare

Pasient: Kjønn:..... Fødselsår:.....

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

.....

#### Problem (kort beskrivelse av problem):

Legemiddel eller styrke .....

Dosering/administrering .....

Legemiddelformulering .....

Mengde/varighet  Refusjon  Interaksjon  CAVE

Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste

Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke  Mottatt nødvendig dokumentasjon

Endret eller avklart dosering/administrering  Ingen endring/informert

Endret eller avklart formulering  Bestilling/resept avvist

Endret eller avklart mengde/varighet  Pakket med mangel/feil

Endret eller avklart refusjonspunkt

Annet:.....

5. TOTALT TIDSBRUK (ca): ..... min



Dato .....  Tekniker sign.....  Farmasøyt sign.....

1. Dagens dato

2. Stilling ved apoteket

## REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 1. BAKGRUNNSINFORMASJON

Type pasient:  Privat

Sykehjem

3. Pasienttype: hjemmesykepleie, sykehjem eller privat

Mottak:  Ikke

4. Bestillingsmottak: "Ikke relevant" skal brukes hvis feilen ikke gjelder en mottatt bestilling. For eksempel ved restnotert vare eller dersom feilen er manglende resept.

2a. FEIL PÅ BESTILLING  Savnes

Mangler gruppeinformasjon  Annet:

2b. FORMELLE FEIL MED

Dato/klokke  Mangler fødsels

5. Fyll inn ENTEN 2a ELLER 2b ELLER 2c .  
Alt som gjør at forskriver eller bestiller må kontaktes skal registreres

Ukjent lege  Savnes

2c. FEIL MED ORDINASJONER

Utsolgt vare

Pasient: Kjønn:..... Fødselsår:.....

Hvis "utsolgt vare" fylles ut trenger man ikke fylle inn resten av 2c

Forskriver:  Fastlege/primærlege

Type resept:  Legemiddelliste

Alle kategorier med fet skrift skal fylles ut: pasient, forskriver, type resept, ordinasjon og problem.

Ordinasjon: (informasjon om legemiddel, dose og bruk):

Problem (kort beskrivelse av problem):

Legemiddel eller styrke

Dosering/administrering

Legemiddelformulering

Mengde/varighet

Refusjon

Interaksjon

CAVE

Annet: .....

6. Hva ble gjort for å rette opp i feilen?

Hvis en av disse tre fylles inn, skal det også være en liten forklarende tekst til hva problemet er

### 3. TILTAK

Kontaktet forskriver

Kontaktet sykehjem

Kontaktet hjemmetjeneste

Farmasøytisk skjønn

Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:

Ja

Nei

7. Hvis forskriver ikke ble kontaktet som "tiltak": Ble forskriver informert i ettertid?

### 4. RESULTAT:

8. Resultat av intervensjonen

Lagt til, seponert eller avklart legemiddel eller styrke

Mottatt nødvendig dokumentasjon

Endret eller avklart dosering/administrering

Ingen endring/informert

Endret eller avklart formulering

Bestilling/resept avvist

Endret eller avklart mengde/varighet

Pakket med mangel/feil

Endret eller avklart refusjonspunkt

Annet: .....

5. TOTALT TIDSBRUK (ca): ..... min

9. Ca tidsbruk på intervensjonen





**Apotek 1 Gruppen AS, Avd. for Dosepakking**

<b>ORDINASJONSKORT</b>		<b>OBS/ INFO</b>	<b>CAVE</b>
5 PB Parken Bofellesskap Navn og fødselsnummer <b>LINN O. LEUM</b> Adresse <b>99.99.99 35570</b>		Standard pakkeintervall <b>2 uker</b> Første dose <b>Torsdag lik uke</b> Endingsfrist	-Cipralex. Annen mindre alvorlig reaksjon (grøt, oppspilt).
Lepentr. 4168708	Versjonsnr. 3	Side 1 av 1	Ord. Legge R Resept- og * refusjonskode
<b>DOSERING</b>			
07:00:08:00:09:00	12:00:13:00	17:00:20:00	21:00
Bruksområde, dosering, administrasjonsmåte etc.			
1	1	1	1
24.08.16	19.08.16	19.08.16	19.08.16
<b>Flux sugetab 0,75mg peppmynte</b> <b>Levaxin tab 100mcg</b> <b>Nycoplus D3-vit tab 20mcg</b> <b>Sertralin hexal tab 50mg</b> <b>Zolofit tab 25mg</b> <i>Simvastatin</i>			
fluor tilskudd, sugetabletter Mot lavt stoffskifte 400 D vitamin =Zolofit 50mg. i alt 75 mg i alt 75 mg <i>1 kolesterolsenkende</i>			
<b>JBO</b>			
<b>JBO T T86/ICPC</b>			
<b>JBO T -73/ICPC</b>			
<b>JBO T -73/ICPC</b>			
<b>JBO T -73/ICPC</b>			

Simvastatin er oppgitt uten styrke

Primærlege	[signatur e removed]	Sist validert av lege	14.07.2016	Ordinerende leger JBO = Boevink, Jon Hans	Kontaktperson (navn/tlf)	Ikke godkjent, 07.09.2017
				1. kontroll	2. kontroll	



\* Det settes inn dato for siste MED dosering og

\*R- Reservasjon mot generisk bytte. A=Apotek, K=Kunde, L=Lage.



Dato..... 12/09-17

Tekniker sign.....

Farmasøyt sign.....

AL

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 4. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie

Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler

Ukjent lege  Savnes  Annet:.....

### 2c. FEIL MED ORDINASJONER

Utsolgt vare

Pasient: Kjønn: *K* Fødselsår: *1999*

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

*Simvastatin 1 tbl kveld*

Problem (kort beskrivelse av problem):

Legemiddel eller styrke *Mangler styrke*

Dosering/administrering

Legemiddelformulering

Mengde/varighet  Refusjon  Interaksjon  CAVE

Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste

Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke  Mottatt nødvendig dokumentasjon

Endret eller avklart dosering/ad  Endring/informert

Endret eller avklart formulering  Bestilling/resept avvist

Endret eller avklart mengde/varighet  Pakket med mangel/feil

Endret eller avklart refusjonspunkt

Annet:.....

7

5. TOTALT TIDSBruk (ca): ..... min



Lu  
Føt  
id  
Fas  
Me

5. SEP. 2017 14:32

Morgen Middag Kveld Natte Ved behov Ma Ti On To Fr Le Sø Ordinert Siste endring Seponert

25.04.2017  
Mefia Novo

Laxoberal dråper 7,5mg/ml  
10  
Dråper  
Merknad: Første uke hver kveld senere x3/døka  
Viscoteas øyegel endos 2  
Dråper  
Merknad: Dryppes i begge øyrene

**Diagnostiske undersøkelser (multidose):**  
I  
Merknad: Tas til måltid  
Tolvon tab 30mg  
M T O T F L S 02.12.2014  
Hanne Subehan

Merknad: Mef sevringsster og firs tref.  
Spirix tab 25mg  
M T O T F L S 02.12.2014  
Hanne Subehan

Merknad: Tekst er lagt til 07.06.2016 - 10:09 - Aisha ( Lege Furuset sykehus ) Akthar  
Ved BT <10000  
M T O T F L S 02.11.2015  
Ali Kamal Ahmed Al-A

Rainiprill nycomed tab 2,5mg  
MULTIDOSE Tabliett  
M T O T F L S 02.11.2015  
Ali Kamal Ahmed Al-A

Burinex tab 1mg  
MULTIDOSE Tabliett  
M T O T F L S 26.09.2016  
Sykehuslege

Somac SA enterotab 20mg  
MULTIDOSE Tabliett  
M T O T F L S 28.09.2016  
Sykehuslege

Targiniq depottab 20/10mg  
MULTIDOSE Tabliett  
Merknad: Tekst er lagt til 20.06.2017 - 09:19 - Mefia Novo  
Morgen dose administreres kl 07:00  
M T O T F L S 12.10.2016  
Sykehus

Har kun mottatt side 1 av  
legemiddelliste fra lege

Skrivet ut



Dato..... 12/09-17

AG  
□Tekniker sign.....

□ Farmasøyt sign.....

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 5. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie  
Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler  
 Ukjent lege  Savnes  Annet:.....

### 2c. FEIL MED ORDINASJONER Utsolgt vare

Pasient: Kjønn:..... Fødselsår:.....

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

### Problem (kort beskrivelse av problem):

Legemiddel eller styrke .....  
 Dosering/administrering .....  
 Legemiddelformulering .....  
 Mengde/varighet  Refusjon  Interaksjon  CAVE  
 Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste  
 Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke  Mottatt nødvendig dokumentasjon  
 Endret eller avklart  Ingen endring/informert  
 Endret eller avklart  Bestilling/resept avvist  
 Endret eller avklart  Pakket med mangel/feil  
 Endret eller avklart refusjonspunkt  
 Annet:.....

4

5. TOTALT TIDSBruk (ca): ..... min



**Apotek 1 Gruppen AS, Avd. for Dosepakking**

<b>ORDINASJONSKORT</b>		<b>OBS/ INFO</b>	Standard pakteintervall <b>2 uker</b>
Navn og fødselsnummer <b>ANNE LEDES</b> <b>99.99.99 63139</b>		<b>CAVE</b>	Første dose <b>Fredag lik uke</b>
Adresse		<b>CAVE</b>	Endringsfrist <b>Torsdag ulik uke 10.00</b>
Første dose *	Siste dose *	LEGEMIDDEL Navn og styrke	Ordningsfrist
09.07.14	27.09.13	FASTE ORDINASJONER I MULTIDOSE	Torsdag ulik uke 10.00
27.09.13	27.09.13	Escitalopram actavis tab 10mg	
27.09.13	27.09.13	Kalsium mvit D3 tytab 500/400	
21.10.13	21.10.13	Simvastatin sandoz tab 20mg	
		Toviaz depottab 8mg	
		<i>Alendronat 70mg</i>	
		<i>Menlag</i>	
		<i>195</i>	

Alendronat er lagt i morgenposen kl 9, men bør tas minst 30 min før andre medisiner

Sist validert av lege	20.07.2016	Ordirerende lege	PKR = Kripas, Per-stein	Kontaktperson (navn/lif)	Ikke godkjent, 18.06.2016
				1. kontroll	
				2. kontroll	

[signature removed]

\* Det settes inn dato for første og eventuelle dato MED dosering og vil være datoen for  
\*R- Reservervejen mot generisk bytte. A=1







Dato 12/09-17

Tekniker sign.....

Farmasøyt sign..... AL

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 2. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie

Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler

Ukjent lege  Savnes  Annet:.....

### 2c. FEIL MED ORDINASJONER

Utsolgt vare

Pasient: Kjønn: K Fødselsår: 1999

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

Alendronat 70 mg, 1 tbl mandag kl 9

Problem (kort beskrivelse av problem):

Legemiddel eller styrke .....

Dosering/administrering Alendronat ligger sammen med andre LM

Legemiddelformulering .....

Mengde/varighet  Refusjon  Interaksjon  CAVE

Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste

Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke  Mottatt nødvendig dokumentasjon

Endret eller avklart dosering/administrering

Endret eller avklart formulering

Endret eller avklart mengde/varighet

Endret eller avklart refusjonspunkt

Annet:.....

Farmasøyten har endret kl slett på  
alendronat til 8.00.

Pakket med mangler/rett

1

5. TOTALT TIDSBruk (ca): ..... min



**Apotek 1 Gruppen AS, Avd. for Dosepakking**

<b>ORDINASJONSKORT</b>		<b>OBS/!INFO</b>	Standard pakkeintervall <b>2 uker</b>
5 <b>Apotek1 Askim</b>			
5HAS-AA Hjemmetjenesten Askim Rode A S-AA			
Navn og fødselsnummer <b>UNNI VERSELL</b>		Første dose <b>Torsdag lik uke</b>	
Adresse		Endringsfrist <b>Onsdag ulik uke</b>	
99.99.99 48427		<b>CAVE</b>	
Lepernr. 4061265	Versjonsnr. 25	Side 1 av 1	
<b>DOSERING</b>			
07.00 08.00 09.00 12.00 13.00 17.00 20.00 21.00	Bruksområde, dosering, administrasjonsmåte etc.		
16.04.12	1		IBO
=Acetyratio. =Albyl-E 75mg Forebygger blodpropp			
28.04.14	1		IBO
=Atorvastatin 40mg =Lipitor 40mg. kolesterolsenkende			
19.02.15	1		IBO
=Kaleorid dp 750mg =Kaleorid. kalium tilskudd sveiges hele			
16.04.12	1		IBO
=Mot lavt stoffskifte			
03.02.15	1		IBO
=Losartan 50mg blodtrykksenkende			
24.04.12	1		IBO
=mot urin inkontinens			
<i>Bucanil 25mg</i>			
<i>Apotekpakken. Oppstart DPS Askim</i>			
<b>FASTE ORDINASJONER UTENOM MULTIDOSE</b>			
16.04.12			IBO
Atrovent inh aer 20mcg/dose ff			
16.04.12			IBO
Serevent inh pulv 50mcg diskus			
<i>Ventoline diskus</i>			
<b>ORDINASJONER VED BEHOV</b>			
19.02.15			IBO
Acetylcystein sa brystab 200mg			
19.02.15			IBO
Vival tab 5mg			
Buronil er et uregistrert preparat. Apoteket har ikke mottatt registreringsfrakt sammen med ordinasjonskortet			
Primærlege	Endring/forte	Kontaktperson (navn/tlf)	ikke godkjent, 07.09.2017
	Dato: .....	1. kontroll	.....
	Legens sign	2. kontroll	.....
Sist validert av lege 21.06.2016			
Ordinerende lege		IBO = Bogurad, Inger Gunhilde	

[signature removed]

\* Det settes inn dato for første og ei dato MED dosering og vil være dat

\*R. Reservasjon mot generisk bytte





12/09-17

Dato.....

Tekniker sign.....

Farmasøyt sign.....

AL

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 7. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie

Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler

Ukjent lege  Savnes  Annet:.....

2c. FEIL MED ORDINASJONER  Utsolgt vare

Pasient: Kjønn:..... Fødselsår:.....

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

Problem (kort beskrivelse av problem):

Legemiddel eller styrke .....

Dosering/administrering .....

Legemiddelformulering .....

Mengde/varighet  Refusjon  Interaksjon  CAVE

Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste

Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke

Mottatt nødvendig dokumentasjon

Endret eller

Ingen endring/informert

Endret eller

Bestilling/resept avvist

Endret eller

Her har apoteket valgt å pakke  
Buronil til tross for at de ikke  
har mottatt reg.fritak

Pakket med mangel/feil

Endret eller avklart refusjonspunkt

Annet:.....

10

5. TOTALT TIDSBRUK (ca): ..... min





## Ordinasjoner for ordinasjonskort: 9999955552, ALF ARVEI, versjon 21 - P (nyeste)

Detaljer Ordinasjoner Seponerte ordinasjoner Vurderinger Historikk Dokumenter

Neste bestillingsfrist: on 05.10.2016 10:00 Estimert pakkeperiode: ma 17.10.2016 - sø 30.10.2016

type reservasjon	DOSE første siste	LEGENMIDDEL varenavn og -styrke ordinerende lege	DOSERING							ANNET / SEPONERING anvendelse / sep.årsak årsak til ending	b.k.(hj.) / sep.ov pkt. / sep.dato	vedtak kontor	
			ma	ti	on	to	fr	lø	sø				frek
[Ikke satt]		Fekadu Tsegay Samudrio	✓	✓	✓	✓	✓	✓	✓	1 uke			
<b>Vare 447680 Magnesium tygg120mg er i rest.</b>													
I POSE	07.09.17	Nycoplus magnesium tytab 120mg							1		1		
[Ikke satt]			✓	✓	✓	✓	✓	✓	✓	1 dag			
<b>Vare 447680 Magnesium tygg120mg er i rest.</b>													
I POSE	22.04.14	Panodil tab 1g							1		1		
[Ikke satt]		Fekadu Tsegay Samudrio	✓	✓	✓	✓	✓	✓	✓	1 dag			
													T
													L89/ICPC

Magnesium er blitt restnotert og kan derfor ikke pakkes i multidose



Dato..... 12/09-17

Tekniker sign.....

Farmasøyt sign..... AL

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 9. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie

Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler

Ukjent lege  Savnes  Annet:.....

### 2c. FEIL MED ORDINASJONER Utsolgt vare

Pasient: Kjønn:..... Fødselsår:.....

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

Problem (kort beskrivelse av problem):

Legemiddel eller styrke .....

Dosering/administrering .....

Legemiddelformulering .....

Mengde/varighet  Refusjon  Interaksjon  CAVE

Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste

Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettetid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke

Mottatt nødvendig dokumentasjon

Endret eller avklart dosering/administrering

Ingen endring/informert

Endret eller avklart refusjonspunkt

Bestilling/resept avvist

Endret eller avklart refusjonspunkt

Pakket med mangel/feil

Annet:.....

5. TOTALT TIDSBRUK (ca): 5 min



## Bestillingsforslag for Sandøyheimen Korttid- og rehab



Liste

Bestillingslinjeforslag (best.frist: 05.10.2016)

Valg	Nr	Ordinasjonskort	Forrige pakking til	Ny pakking fra	Ny pakking til	Utskrift	Merknader
<input checked="" type="checkbox"/>	1	> 4101259, TIKX, KINE	21.09.2016	17.10.2016	30.10.2016	<input type="checkbox"/>	
<input checked="" type="checkbox"/>	2	> 4114177, ARVEI, ALF	21.09.2016	17.10.2016	30.10.2016	<input type="checkbox"/>	
<input checked="" type="checkbox"/>	3	> 4167412, PLEKS, PER	21.09.2016	17.10.2016	30.10.2016	<input type="checkbox"/>	
Ordinasjonskort er eldre enn 12 mnd. Blir avvist i HELFO - OPPGJØR							
ringt på klokke 25.08.							
<input checked="" type="checkbox"/>	4	> 4101230, GASKAR, MAGDA	21.09.2016	17.10.2016	30.10.2016	<input type="checkbox"/>	
<input checked="" type="checkbox"/>	5	> 4101293, RIKKE, ANE	21.09.2016	17.10.2016	30.10.2016	<input type="checkbox"/>	

Klokkemerknad på en pasient i Nagara fordi ordinasjonskortet ikke har blitt validert på over 1 år



12/09-17

Dato.....

Tu

Tekniker sign.....

Farmasøyt sign.....

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 1. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie  
Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL VED BESTILLING  Savnes  Uleselig  Mangler gruppeinformasjon  Annet:.....

2b. FEIL VED RESEPT  Savnes/mangler  Utsolgt  Utgått/klokke  
Forskriver:  Fastlege  Sykehuslege  Sykehjemslege  Andre:.....  
Type resept:  Enkeltresept/endringsmelding  Legemiddelliste  
Feil på resept:  Uleselig  Feil blankett  Mangler ID  Annet:.....  
 Ukjent lege  Signatur mangler

Kjønn:..... Fødselsår:..... Kort beskrivelse

Legemiddel  .....  Ikke pakkbar  
Styrke  .....  Ikke pakkbar  
Legemiddelformulering  .....  Ikke pakkbar  
Dosering/Administrering  .....  
Refusjon  .....  
Interaksjon  .....  
Mengde  .....  
Annet problem  .....

### 3. TILTAK

Kontaktet forskriver/ sykehjem  Ja  Nei  Fikk ikke tak i forskriver  
Hvis nei: andre tiltak:  Kontaktet hjemmetjeneste  Gjennomgått pasientprofil/historikk  
 Farmasøytisk skjønn  Annet tiltak: .....  
Hvis nei: Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel  Endret eller avklart mengde  
 Endret eller avklart styrke  Ingen endring/informert  
 Endret e  Mottatt nødvendig dokumentasjon  
 Endret e  Bestilling/resept avvist  
 Endret eller avklart refusjonspunkt  Pakket med mangel/feil  
 Annet:.....

12

5. TOTALT TIDSBRUK (ca): ..... min





12/09-17

RiM

Dato.....

Tekniker sign.....

Farmasøyt sign.....

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 6. BAKGRUNNSINFORMASJON

Type pasient:  Privat  Sykehjem  Hjemmesykepleie

Mottak:  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL PÅ BESTILLING  Savnes  Mangler gruppeinformasjon  Annet:.....

### 2b. FORMELLE FEIL MED RESEPT(LISTE)

Dato/klokke  Mangler fødselsnr./navn  Mangler registreringsfritak  Signatur mangler

Ukjent lege  Savnes  Annet:.....

### 2c. FEIL MED ORDINASJONER

Utsolgt vare

Pasient: Kjønn: *M* Fødselsår: *1999*

Forskriver:  Fastlege/primærlege  Annen forskriver

Type resept:  Legemiddelliste  Enkeltresept/endringsmelding

Ordinasjon: (informasjon om legemiddel, dose og bruk):.....

*Paracet 500mg brusetablet. 1\*3*

### Problem (kort beskrivelse av problem):

Legemiddel eller styrke .....

Dosering/administrering *Brusetablet ikke pakkbar*

Legemiddelformulering .....

Mengde/varighet  Refusjon  Interaksjon  CAVE

Annet: .....

### 3. TILTAK

Kontaktet forskriver  Kontaktet sykehjem  Kontaktet hjemmetjeneste

Farmasøytisk skjønn  Gjennomgått pasientprofil/historikk

Forskriver kontaktet/informert i ettertid:  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel eller styrke  Mottatt nødvendig dokumentasjon

Endret eller avklart dosering/administrering  Ingen endring/informert

Endret eller avklart formulering  Mottatt resept avvist

Endret eller avklart mengde/varighet  Mottatt resept avvist med mangel/feil

Endret eller avklart refusjonspunkt

Annet:.....

4

5. TOTALT TIDSBruk (ca): ..... min

Her har apoteket endret  
til vanlige tablett





## APOTEK 1

### Meldinger til Kundesenter/Apoteke 1 vedrørende multidoser

<b>Må fylles ut</b>	Antall sider:	
	Fra sone/Institusjon: Eidsberg 7	Gruppe/Avdeling: Sentrum 7
	Telefon:	
	Signatur Spl.: [signature removed]	Dato: 07/09-17
	Navn og ID/HPK-nr sykenjemsiege som nar godkjent endringer (bruk blokkbokstaver):	

Ingen endring – multidoser pakkes som forrige gang (sett kryss)

INNMELDING NY BRUKER Navn, f.dato., adr.	Ønsket oppstartsdate multidoserull:	Tidligere multidoserbruker?(Ja/Nei)
Anton Nym	snarest	<del>Ja</del> Nei

UTMELDING /FLYTTING/STOPP Navn, f.dato	Stoppes fra dato:	Kommentar (midlertidig stopp/endelig stopp, ny gruppe)

ENDRINGER/MELDINGER Navn, f.dato	Melding til apoteket; ekstra dose, feriepakking, endring av kl.slett, annen informasjon

HASTEBESTILLING (kontakt apoteket) Navn, f.dato	Ønsket pakkeperiode	Ønsket leveringsdate (dialog med apoteket)



Legge

Siste

Inger

Avde

Faste

A.N

14.09.22

Start	Legemiddel	Form/ Styrke	09:00	13:00	18:00	21:00	Dos.tekst	Sep
14.12.16 15:21	Asasantin retard SA	Kapsel med modifisert frisetti 200/25mg	1		1		Blodfortynnande	
14.12.16 15:24	Selo-zok Døgndose: 100mg	Depottabletter 100mg	1				MÅ HA METROPOLOL og ikkje anna synonympreparat. Blodtrykkssenkande.	
14.12.16 15:25	Sobril	Tablett 10mg	0,5		0,5		Angstdempande	

Eventuelle legemidler

Start	Legemiddel	Form/ Styrke	09:00	13:00	18:00	21:00	Dos.tekst	Sep
24.07.16 06:00	Corsodaily munnskyl	(ikke angitt)					Smerter i munn, rødhet rundt tannstump i nedre kjeve skylle x 2 daglig	
27.09.16 06:00	Laxoberal Døgndose: 0	Dråper 7,5MG					10-15 drp ved behov obstipasjon	
10.05.16 06:00	Movicol Døgndose: 0	Pulver til mikstur					1 dose om kvelden, startes som fast medisin ved obstipasjon	
28.08.12 06:00	Nitrolingual Døgndose: 0	Munnspray 0,4mg/dose					1-2 spray ved symptomer pga høy blodtrykk i form av hodepine, press på brystet m.m, ved BT over 200 sys eller 100 diastolisk	
27.08.15 06:00	OxyNorm	Kapsel 5mg					ved behov	
12.06.14 06:00	Paracet	Tablett 500mg					1-2 tbl inntil x 3 daglig mot smerter/feber	
28.03.17 06:00	Viscotears Døgndose: 0	Øyegel					x4-6 ved tørre øyne	
20.01.11 10:32	Zopiclone actavis Døgndose: 3,75mg	Tabletter 7,5mg					1 tbl ved søvnvansker	

Dato, signatur:

05/09/22

Fastlege:

Mottatt innmelding fra  
hjemmesykepleien, men verken  
innmeldingsskjema og legemiddellisten  
har de siste 5 sifrene i f.nr





12/09-17

Dato.....

TU

Tekniker sign.....

Farmasøyt sign.....

## SKJEMA FOR REGISTRERING AV INTERVENSJONER VED MULTIDOSE

### 1. BAKGRUNNSINFORMASJON

**Type pasient:**  Privat  Sykehjem  Hjemmesykepleie  
**Mottak:**  Ikke relevant  Faks  E-resept  Telefon  Annet:.....

2a. FEIL VED BESTILLING  Savnes  Uleselig  Mangler gruppeinformasjon  Annet:.....

2b. FEIL VED RESEPT  Savnes/mangler  Utsolgt  Utgått/klokke  
**Forskriver:**  Fastlege  Sykehuslege  Sykehjemslege  Andre:.....  
**Type resept:**  Enkeltresept/endringsmelding  Legemiddelliste  
**Feil på resept:**  Uleselig  Feil blankett  Mangler ID  Annet:.....  
 Ukjent lege  Signatur mangler

	Kjønn:.....	Fødselsår:.....	Kort beskrivelse
Legemiddel	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> Ikke pakkbar
Styrke	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> Ikke pakkbar
Legemiddelformulering	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> Ikke pakkbar
Dosering/Administrering	<input type="checkbox"/>	<input type="checkbox"/>	
Refusjon	<input type="checkbox"/>	<input type="checkbox"/>	
Interaksjon	<input type="checkbox"/>	<input type="checkbox"/>	
Mengde	<input type="checkbox"/>	<input type="checkbox"/>	
Annet problem	<input type="checkbox"/>	<input type="checkbox"/>	

### 3. TILTAK

**Kontaktet forskriver/ sykehjem**  Ja  Nei  Fikk ikke tak i forskriver  
**Hvis nei: andre tiltak:**  Kontaktet hjemmetjeneste  Gjennomgått pasientprofil/historikk  
 Farmasøytisk skjønn  Annet tiltak: .....

**Hvis nei: Forskriver kontaktet/informert i ettertid:**  Ja  Nei

### 4. RESULTAT:

Lagt til, seponert eller avklart legemiddel  Endret eller avklart mengde  
 Endret eller avklart styrke  Ingen endring/informert  
 Endret eller avklart formulering  Mottatt nødvendig dokumentasjon  
 Endret eller avklart dosering  Bestilling/resept avvist  
 Endret eller avklart personnummer  Pakket med mangel/feil  
 Annet:.....

5. TOTALT TIDSBruk (ca): ..... min



Appendix 5



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<b>Region:</b>	<b>Saksbehandler:</b>	<b>Telefon:</b>	<b>Vår dato:</b>	<b>Vår referanse:</b>
REK nord			29.09.2017	2017/1393/REK nord
			<b>Deres dato:</b>	<b>Deres referanse:</b>
			07.09.2017	

Vår referanse må oppgis ved alle henvendelser

Trine Strand Bergmo  
Nasjonalt senter for ehelseforskning

## **2017/1393 Innføring av elektronisk multidose – innvirkning på kvalitet og pasientsikkerhet i legemiddelkjeden.**

**Forskningsansvarlig institusjon:** Universitetssykehuset Nord-Norge HF

**Prosjektleder:** Trine Strand Bergmo

### **Prosjektleders prosjekttale**

*Multidosepakkelegemidler gir pasienter i kommunal pleie- og omsorgstjeneste en bedre og tryggere legemiddelbehandling. I dag ordineres multidose på papir via brev/faks. Det er planlagt å innføre elektroniske rutiner for forordning av multidose. Prosjektet er et samarbeid mellom Direktoratet for eHelse og NSE. Direktoratet er ansvarlig for innføring av løsningen. Vi skal undersøke om multidose i e-resept gir økt kvalitet på legemiddellistene og om det gir færre avvik mellom legemiddellister hos fastlege, hjemmetjeneste og apotek, opp mot dagens papirbaserte rutiner. Studien skal gjennomføres som en kontrollert før-etter studie, der samme pasienters legemiddelliste undersøkes før innføring av e-multidose og 12 måneder etter. Listene analyseres i forhold til kvalitet, og type og antall avvik mellom apotek, lege og hjemmesykepleien. Samme undersøkelse skal gjøres i parallelle i en kommune som ikke får innført multidose i e-resept i studieperioden og skal fungere som kontrollgruppe.*

### **Vurdering**

Prosjektsøknaden ble behandlet på komiteens møte 17.08.2017. Prosjektet faller ikke inn under helseforskningsloven, men prosjektet skal bruke personopplysninger fra helsesektoren i forbindelse med forskningen. REK er delegert myndighet til å gi dispensasjon fra taushetsplikten etter helsepersonelloven § 29 og forvaltningslovens § 13 d. I vurderingen av om det kan gis unntak for samtykke må komiteen vurdere alle sider av prosjektet, herunder om det er av vesentlig interesse for samfunnet og om hensynet til deltagerens velferd og integritet er ivaretatt. Komiteen skal også vurdere om det vil være vanskelig å innhente samtykke i denne studien.

I vurdering av om det vil være «vanskelig å innhente samtykke», fremgår det både av forarbeidene og av departementets kommentarer til helseforskningsloven at kvalifiserte og legitime årsaker til dette kan være dersom deltager er død, flyttet, sykdom, stort antall deltagere, samt at et stort frafall vil svekke forskningens validitet. Selv om dette prosjektet har en del til felles med P REK 2016/2065, der det ble gitt dispensasjon, vurderer komiteen også prosjektene som ulike. Komiteen fattet et utsettende vedtak hvor prosjektleder ble bedt om å gi en bedre begrunnelse for hvorfor det bør innvilges dispensasjon fra samtykke. Prosjektleders tilbakemelding datert 07.09.2017 ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK nord) i møtet 14.09.2017.

I tilbakemelding har prosjektleder utdypet søknad om fritak fra taushetsplikt slik:

«Det søkes om fritak fra samtykke for å identifisere pasienter som får multidossepakkede legemidler for å hente ut data på kvalitet og avvik i legemiddellistene. Vi søker fritak for å identifisere brukere for Anette Vik Jøsandal, stipendiat ved Nasjonalt senter for e-helseforskning og lege Torsten Risør ved Nasjonalt senter for e-helseforskning og UiT.

Hvorfor søkes det om fritak fra hovedregelen om å innhente samtykke?

Fritak fra samtykke for å identifisere pasienter:

For Direktoratets pilot er det i første rekke fastlegekontor (1) (at de har systemstøtte for løsningen) som avgjør hvor man kan prøve ut multidose i e-resept. Av praktiske og opplæringsmessige hensyn vil imidlertid også piloten begrenses til gitte kommuner (2) og apotek (3).

De fastlegene som deltar i pilot har ikke selv noen mulighet til å hente ut en enhetlig liste over alle pasientene han eller hun har som får multidose, og kan derfor ikke identifisere deltakere. I tillegg er ikke hjemmesykepleiesone eller kommune pasienten tilhører nødvendigvis oppgitt i fastlegens systemer.

Fordi det er pasientens fastlege som avgjør om en pasient vil gå over til nytt system vil det heller ikke være mulig å ta kontakt med hjemmesykepleie-kontorene og be disse invitere deltakere til studien, fordi det heller ikke fra disse systemene er mulig å få ut en enhetlig oversikt over alle multidossepasienter som har gitte fastleger. Det er heller ikke gitt at alle hjemmesykepleiesoner i en kommune faktisk har pasienter som vil bli berørt av piloten.

Fra Direktoratets pilot i 2015 ble det derfor erfart at eneste metoden for å identifisere deltakere til pilot var å gjøre oppslag i apotekets multidoseprogram, da det kun er her det fantes en enhetlig oversikt over hvilke pasienter som møter alle tre inklusjonskriteriene (1-3). Denne metoden sees derfor også på som den eneste som er praktisk gjennomførbar innenfor dette prosjektets rammer for å få identifisert deltakere til studien.

Fritak fra samtykke etter at pasientene er identifisert:

Studien må ha minimum 100 pasienter i hver gruppe for å identifisere en positiv effekt på avvik i legemiddellistene. Studien skal analysere avvik 6 måneder før innføring og sammenligne med avvik 12 måneder etter innføringen. I en annen studie av multidosebrukere i hjemmesykepleien i Trondheim kommune i 2006-8 var frafallsprosenten på 57% fra innsamling av før data til målinger 12 måneder etter innføring\*.

Noen av pasientene var døde, mens andre var flyttet på sykehjem. For å få 100 legemiddellister som kan utføres analyser på etter innføring, må vi derfor regne med å måtte rekruttere 200 pasienter i hver gruppe før innføringen. Pasientene vil være spredt rundt i flere kommuner og tilhøre mange ulike hjemmetjenestesoner. Den eneste aktuelle metoden for å innhente samtykke fra 400 pasienter i hjemmetjenesten er å sende en forespørsel hjem til pasienten i posten. Svarprosent på forespørsel om å delta eller svare på en undersøkelse sendt i posten generelt, kan være så lav som 35%. For gruppen hjemmeboende eldre kan frafallet være større. Vi anser derfor at frafallet, dersom vi må innhente samtykke fra pasientene, vil være så stort at det vil svekke forskningens validitet.

Det er også en begrensning i hvor mange pasienter som vil få multidose forordnet elektronisk i 2018. Det er planlagt opp mot 10 kontor i første fase. Det er mellom 5 og 50 multidosebrukere per legekantor/senter avhengig av størrelsen på kontoret.

Det er viktig for studien og for evalueringen av Direktoratets nye løsning for multidose, at vi får med alle eller så mange som mulig av de som tester ut den nye løsningen.»

I vurderingen av om vilkår for dispensasjon fra taushetsplikt var oppfylt tok et mindretall dissens i saken.

Mindretallet, bestående av Thorbjørn Riise Haagenen, slutter seg til flertallets vurdering av at prosjektet er av vesentlig interesse for samfunnet. Det kreves imidlertid i tillegg at det må være vanskelig å innhente samtykke. Det er ikke situasjonen her. Som det framgår av søknaden, kan forespørsel sendes hjem til pasienten i posten. Antall potensielle søkere er langt fra så høyt at dette skulle være noen hindring. Søkers bekymring synes å være risikoen for lav svarprosent. Det er i søknaden oppgitt at svarprosenten kan være så lav som 35

prosent for henvendelser sendt i posten. Dette er imidlertid ikke i samsvar med forskning på responsrate som har vært opplyst til komiteen i andre studier. Under enhver omstendighet kunne det vært vurdert å inkludere flere pasienter kommuner og apoteker – slik at ønskelig mengde deltakere kunne vært nådd.

Komiteens flertall har også vurdert at prosjektet er av vesentlig interesse for samfunnet. Prosjektets formål er ikke å studere pasientopplysninger som sådan men legemiddellistene og komiteen har vurdert at hensynet til deltagerens velferd og integritet er ivaretatt. Komiteen legger prosjektleders tilleggsopplysninger til grunn i vurderingen av om vilkårene for fritak fra taushetsplikt er oppfylt.

### **Vedtak**

*Med hjemmel i forskrift av 02.07.09 nr. 989, der REK er delegert myndighet til å gi dispensasjon fra taushetsplikt etter helsepersonelloven § 29 første ledd og forvaltningsloven § 13 første ledd, har komiteens flertall gitt dispensasjon fra taushetsplikt for Anette Vik Jøsendal og Torstein Risør for innhenting av de data, som er nevnt i søknaden.*

### **Klageadgang**

Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK nord. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK nord, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

May Britt Rossvoll  
sekretariatsleder

**Kopi til:** [stein.olav.skrovseth@ehealthresearch.no](mailto:stein.olav.skrovseth@ehealthresearch.no)





Appendix 6



## E-multidose intervjuguide hjemmesykepleien

Først vil jeg si mange takk for at dere stilte opp. Dere har erfaringer som er viktig for utviklingen og innføringen av multidose i e-resept-ordningen på landsbasis.

Vi heter xxxxxxxx. Vi jobber altså ved Nasjonalt senter for e-helseforskning og har fått i oppdrag av Direktoratet for e-helse å dokumentere erfaringer med eMD - (multidose i e-resept).

Vi er ute etter erfaringer med såkalt «MD i e-resept» i pilotkommunene blant fastlegene, hj.s.pl. og blant farmasøyter på multidoseapoteket – altså *elektronisk* kommunikasjon rundt MD i stedet for papirbasert. Både positive forandringer og forhold som dere opplever problematiske og/eller mener bør endres, er verdifullt å få høre om.

Vi ønsker å høre om forberedelsene før dere startet, selve oppstarten og hvordan det går nå.

Vi regner med at intervjuet varer fra 30-45 minutter. For å slippe å notere mens vi skal snakke med dere, ønsker vi å ta opp intervjuet. OK? Materialet blir behandlet konfidensielt, og ingen personer skal kunne gjenkjennes i vår skriftlige formidling.

### *Først dagens situasjon:*

- Kan dere først presentere dere og fortelle om oppgaver dere har i arbeidet med MD.
- Vet dere hvor mange MD-pasienter dere har, og antallet legekontorer dette angår?

Vi vet ikke i hvilken grad dere faktisk merker overgangen fra papirbasert til elektronisk basert kommunikasjon rundt MD. Men ...

- er det mulig kort å beskrive hj.tj.s rutiner for MD med og uten elektronisk kommunikasjon.
- Kan dere beskrive fordeler og ulemper for dere som følge av overgang til eMD.
  - Først, ser eller erfarer dere fordeler for hj.s.p. som følger overgang til eMD?
  - Enn negativt, er det ulemper eller problemer for hj.s.p som følger av å bruke eMD?
- Skjer det at dere mangler gyldige resepter når pakkingen skal skje? Et problem?
  - Hvis ja: Anslått antall per pakking?
  - Fordeling på legekontorer?
- Svarer legesentrene innen rimelig tid på henvendelsene fra hj.s.pl?
  - Henvender dere dere ofte til legene, ev. hvor ofte?
  - Purrer dere ofte på svar, ev. hvor ofte?
  - Hva er rimelig responstid? Avtalt?
- Hva er hj.s.pl.s praksis:
  - Hvordan henvender dere dere til legene – meldingsskjema, telefon, annet?
  - Hva utløser en henvendelse, gjør at dere henvender dere?
- Skjer det at hj.s.p. er usikre på om en MD-endring kan vente til neste pakking? Et problem?
- Får hj.s.pl. flere endringsbeskjeder m/eMD enn m/papirrutiner? Et problem?
- Forekommer doble resepter? Et problem?

- Har dere ideer eller tanker om endringer som kan gjøre eMD til et bedre redskap? Ev. hva/hvordan? (Smått og stort, teknologisk, pedagogisk, administrativt..)
- Ser dere endringsgrep som kan være nyttig i samhandlingen m/apoteket?
- Hva med endringer som kan være nyttig i samhandlingen med legene?
- Har dere ideer til nye krav til systemstøtte i eMD-ordningen?

*La oss nå gå tilbake til selve oppstarten og det som skjedde i forkant:*

- *Før:* Erfaringer og lærdommer fra tida før oppstart tanke på innføring av eMD på landsbasis?
  - Ble hj.s.pl. involvert i forberedelser, ev. hvordan?
  - Mht etableringen av korrekte MD-lister; var hj.s.p involvert v/oppstart av eMD?
  - Hva med opplæring av og informasjon til berørte i forkant? Først, f
  - Annet av betydning?
- Hvordan var den aller første tida etter oppstart?
  - Erfaringer og lærdommer å ta med m/tanke på innføring av eMD på landsbasis?
  - Hadde hj.s.pl. behov for support, ev. fra hvem?
- Til slutt, mener dere eMD er et framskritt eller tilbakeskritt mht pasientsikkerheten? `
  - Enn med tanke på egen arbeidssituasjon?
  - Hva foretrekker dere, MD med papirutiner eller i e-resept
- Til slutt, er det noe noen av dere mener at vi ikke har fått belyst?

Igjen takk for at dere stilte opp. Det er svært nyttig å kunne trekke veksler på deres erfaringer med eMD når ordningen skal rulles ut på landsbasis. Tusen takk.

Appendix 7



## E-dose intervjuguide apotek

Presentasjonsrunde.

Vi har hatt et prosjekt som har evaluert utprøving av multidose siden 2016. Først i Rogaland, så i Oslo og Larvik. Vi har snakket med både leger, sykepleiere og farmasøyt i hjemmetjenesten og farmasøyter på Skåresletta A1.

Vi er ute etter erfaringer med «MD i e-resept». Det er verdifullt å høre om både positive forandringer og forhold som dere opplever problematiske og/eller mener bør endres.

For å slippe å notere mens vi skal snakke med dere, ønsker vi å ta opp intervjuet. OK? Materialet blir behandlet konfidensielt, og ingen personer skal kunne gjenkjennes i vår skriftlige formidling.

**Først takk for at du stiller opp. Kan du si litt om din rolle?**

**Hvor lenge har dere hatt multidose i e-resept?**

### 1. Hvordan var selve oppstarten og det som skjedde i forkant

- Hvilke forberedelser ble gjort på apoteket?
- Hva med opplæring og informasjon til berørte i forkant?
- Andre berørte som ble involvert i forberedelser (fastleger NHN, ev. hvordan?)
- Annet som bør nevnes fra tida før oppstart?

### 2. Hvordan var den aller første tida etter oppstart?

- Var det mange feil som måtte rettes opp i begynnelsen? Hvilke feil?
- Brukte dere mye tid på avklaringer?
- Var det enkelt å rette opp hvis det ble feil?
- Hvordan var samhandling med de andre aktørene (legen, spl)?
- Har du forbedringsforslag eller tips til andre som skal starte?

### 3. Hvordan er det nå?

Kan du beskrive litt hvordan systemet fungerer?

- Skiller det nye systemet seg fra det gamle papirsystemet? Hvis ja hvordan?
- Er alt automatisert eller er det ennå noen manuelle rutiner?
- Skjer det endringer med e-dose i forhold til farmasøytenes mulighet til å gjøre selvstendige vurderinger?

Samhandling/kontakt med andre aktører

- Er det endringer for dere og fastlegene:  
Lettere/vanskeligere å ta kontakt - oppklare misforståelser - få svar?
- Hva med hjemmetjenesten? Skjer kontakten via telefon - meldingssystem?

- Hva skjer nå i forhold til resepter skrevet ut av sykehuslegene for multidosebrukerne? Enklere – vanskeligere?
- Andre forskjeller på papir og e-dose?
- A1 på skåresletta opplevde at det kunne mangle e-resepter? Opplever dere dette?

**4. Hva synes du er de største fordelene med e-dose?**

**5. Hva synes du er de største ulempene? Hvis det er noen?**

**6. Hva synes du er best mht. pasientsikkerhet, riktige medisinlister**  
Tidsbruk – bruker dere mer/mindre tid på e-dose i sum (effektivitet)  
Forbedringer du kunne ønske?

**7. Oppsummert vil du gå tilbake til det gamle papirsystemet?**

**8. Er det da noe som vi ikke har fått belyst?**

Takk for at dere stilte opp. Det er svært nyttig å kunne trekke veksler på deres erfaringer med multidose i e-resept ordningen skal rulles ut på landsbasis. Tusen takk.



Paper I

# Potentially inappropriate prescribing to older patients receiving multidose drug dispensing.

Josendal AV, Bergmo TS, Granas AG

*BMC Geriatrics* 2020 Aug 5;20(1):272. doi: 10.1186/s12877-020-01665-x



RESEARCH ARTICLE

Open Access



# Potentially inappropriate prescribing to older patients receiving multidose drug dispensing

Anette Vik Josendal<sup>1,2\*</sup> , Trine Strand Bergmo<sup>1</sup> and Anne Gerd Granas<sup>1,2</sup> 

## Abstract

**Background:** 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. Previous studies have suggested that the quality of prescribing, with time, is lower for MDD users, compared to patients receiving prescriptions dispensed as usual. This study aimed to examine the quality of prescribing to Norwegian elderly home care service patients receiving MDD.

**Methods:** A cross-sectional study comprising 45,593 MDD patients aged  $\geq 70$  years was performed. The proportion of potentially inappropriate medications (PIMs) was assessed using the Norwegian General Practice Criteria, and drug-drug interactions (DDI) were investigated using the Norwegian Medicines Agency database.

**Results:** On average, patients were prescribed 10.6 drugs (SD = 5.0), of which 6.1 were dispensed via MDD. Men used on average fewer drugs than women (10.7 vs 11.1). Twenty-seven percent of patients used at least one PIM. Concomitant use of three or more psychotropic drugs (10.8%), and prescribing of diazepam (6.4%) was the most commonly identified inappropriate prescribing. DDIs affected 59% of the patients, however, only 2.7% had serious interactions. Women were more frequently exposed to both PIMs and DDIs than men, with an odds ratio of 1.50 (95% CI: 1.43–1.58) and 1.43 (95% CI: 1.37–1.50), respectively.

**Conclusions:** Polypharmacy is common in elderly Norwegian patients using MDD. About one-fourth of the patients were exposed to PIMs, and over half were exposed to DDI.

**Keywords:** Multidose drug dispensing, Inappropriate prescribing, Elderly, Norway, Home care services, Drug-drug interactions

## Background

Multidose drug dispensing (MDD) is an adherence aid that provides patients with machine-dispensed medicines in disposable plastic bags, usually for 14 days. The MDD bags are labeled with the patient's name, the drug names and the time the medicines should be taken. Tablets and capsules can be dispensed via MDD, while medicines such as mixtures, inhalators, topical formulations,

etc., are dispensed in their original packaging. However, all medicines are usually issued on the same prescription as the MDD medicines, including other regular medication, pro re nata (p.r.n) medications, and dietary supplements.

MDD users are typically elderly patients with difficulties handling and administering their medicines, in addition to using several regular medicines [1–3]. This puts them at high risk of experiencing side effects, medication errors, and other adverse drug reactions. Even though the scientific evidence of the effects of MDD is limited [4, 5], the system is recommended by the

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Norwegian health authorities for use by homecare service patients [6]. The number of patients receiving MDD in Norway has grown from 15,700 patients in 2006 to 90,500 in 2017 [7]. The majority (76%) receive home care services (HCS), 21% live in nursing homes and the remaining 5% are home-dwelling patients who get MDD at their local pharmacy [7]. Most medicines for chronic conditions are reimbursed by the Norwegian National Insurance Scheme. For patients in HCS, the municipality pay the additional costs for the packing of MDD. In 2017, 240,000 patients received HCS; 132,000 were > 67 years [8]. HCS provide nursing care, such as assistance with personal hygiene, wound care and help to administer medicines, as well as practical help like cleaning, food delivery, and laundry, allowing patients to be able to live at home for as long as possible before moving into a nursing home [9].

Different tools can be used to investigate potentially inappropriate medications (PIMs). The Norwegian General Practice (NORGE) criteria assess the quality of prescribing to elderly patients in general practice [10]. According to these criteria, about one-third of the elderly Norwegian population is exposed to PIMs [11]. MDD users are, however, more likely to be exposed to PIMs than patients using ordinary dispensing [12–14]. A Norwegian study examined the quality of prescribing to patients receiving MDD in 2009, shortly after the MDD system was established in Norway, and found a prevalence of PIMs of 26% [2]. However, this study was carried out using an incomplete medication list.

In Norway, over 90% of prescriptions are electronic [15], however, the MDD prescriptions are still paper-based. The MDD prescriptions have to be faxed to the pharmacy, and GPs find the multidose system more time consuming than electronic prescribing [16, 17]. As a consequence, there are concerns that the MDD system might lead to the GP making fewer changes in the patients' prescribed medicines, and increase the risk of medication errors in the transition between primary and secondary care, as shown in Sweden [18, 19]. Patients can also get duplicate prescriptions when GPs prescribe electronic prescriptions in addition to MDD prescriptions [20]. There is, however, an electronic MDD prescribing system in the making, where the prescribing procedure will be the same for MDD prescriptions and ordinary prescriptions. This system is expected to improve the prescribing quality for MDD patients [15, 20].

This study aims to assess the prevalence of potentially inappropriate medication use among elderly patients receiving MDD in Norway, before the implementation of an electronic MDD prescribing system.

## Methods

### Study design and sample

We conducted a cross-sectional study using the medication lists from MDD patients in Norway, containing

medicines prescribed in June 2018. The MDD supplier delivered about 90% of all MDDs in Norway at the time of the study, and provided anonymous study data for all patients in their system, containing age, gender and care setting (home dwelling, home care service, or nursing home). From the medication lists, details of drug names, strength, formulation, ATC code [21], dosage schedule and dispensing type (regular drugs dispensed via MDD, regular drugs not dispensed via MDD, or p.r.n medication) were obtained. The original dataset consisted of 87,519 patients and 859,642 medicines. As the NORGE-criteria are applicable for elderly  $\geq 70$  years old, patients under the age of 70 were excluded. Self-pay patients and patients in nursing homes were also excluded because their medication lists are usually incomplete, only containing medicines dispensed as MDD, and no other regular medications and p.r.n. medications.

### Outcome measures

Each patient's drug list was systematically screened for drug-drug interactions (DDIs) using the Norwegian Electronic Prescription Support System where DDIs are classified as either (A) *No action necessary*, (B) *Precautions should be taken*, or (C) *Should be avoided* [22]. Our data were screened for interactions of types B and C.

The PIMs were analysed employing the NORGE criteria, a validated tool based on the updated American Beers Criteria [23] adapted to the Norwegian formulary, Swedish recommendations [24], and other literature [25]. The NORGE criteria consists of 21 single substances and 15 drug combinations to be avoided in patients  $\geq 70$  years old (Table 1). Seven of 36 criteria were handled separately in the analysis: Antibiotics are usually prescribed for short periods, and therefore not listed on MDD prescriptions. Four NORGE criteria on antibiotics (criterion 23, 24, 30, 35) were thus excluded from our analysis. One criterion (No 36) concerns concomitant prescription of three or more psychotropic medicines. In the analysis for this criterion, psychotropic medications had to be listed as *regular use* to be included, whereas p.r.n. psychotropic medications were excluded. For the two NORGE criteria on overuse (no. 12,13), we could only analyse medicines dispensed via MDD and not as other regular medicines or p.r.n., because the dosing schedule was only available for the MDD medication. For the remaining 29 criteria, the criterion would be met if the medication was present in the list, regardless of whether it was listed as regular or p.r.n.

### Statistical analysis

Statistical analysis was performed using Stata/MP 15. Means and standard deviation were used to describe the

**Table 1** Prevalence of potentially inappropriate medications in elderly (≥70 years) MDD users in Norway

	Study population (n = 45,593)		Female (n = 30,090)		Male (n = 15,503)		Age 70–79 (n = 11,435)		Age 80–89 (n = 21,633)		Age 90+ (n = 12,525)	
	n	%o	n	%o	n	%o	n	%o	n	%o	n	%o
<b>NORGE P single substance criteria</b>												
1. Amitriptyline	848	19	639	21	209	13	312	27	381	18	155	12
2. Doxepin	61	1	44	1	17	1	17	1	25	1	19	2
3. Clomipramine	74	2	64	2	10	1	31	3	33	2	10	1
4. Trimipramine	162	4	120	4	42	3	60	5	69	3	33	3
5. Chlorpromazine (withdrawn from Norw. market 2007)	5	0	5	0	0	0	4	0	1	0	0	0
6. Chlorprothixene	387	8	234	8	153	10	222	19	130	6	35	3
7. Levomepromazine	391	9	255	8	136	9	195	17	140	6	56	4
8. Prochlorperazine	288	6	230	8	58	4	59	5	133	6	96	8
9. Diazepam	2911	64	2175	72	736	47	1011	88	1269	59	631	50
10. trazepam	839	18	595	20	244	16	227	20	342	16	270	22
11. Flunitrazepam	15	0	12	0	3	0	7	1	4	0	4	0
12. Oxazepam > 30 mg/24 h	335	7	253	8	82	5	179	16	116	5	40	3
13. Zopiclone > 7.5 mg/24 h	142	3	98	3	44	3	65	6	52	2	25	2
14. Carisoprodol (withdrawn from Norw. market 2008)	1	0	0	0	1	0	0	0	1	0	0	0
15. Dextropropoxyphene (withdrawn from Norw. market 2009)	0	0	0	0	0	0	0	0	0	0	0	0
16. Theophylline	107	2	68	2	39	3	45	4	50	2	12	1
17. Sotalol	210	5	133	4	77	5	30	3	116	5	64	5
18. Dexchlorpheniramine	64	1	42	1	22	1	20	2	26	1	18	1
19. Promethazine	85	2	54	2	31	2	31	3	35	2	19	2
20. Hydroxyzine	766	17	472	16	294	19	252	22	306	14	208	17
21. Alimemazine/ trimeprazine	964	21	634	21	330	21	419	37	395	18	150	12
<b>NORGE P combination criteria</b>												
22. Warfarin + NSAID	36	1	23	1	13	1	8	1	19	1	9	1
23. Warfarin + ofloxacin/ ciprofloxacin	NOT ANALYZED: ANTIBIOTICS ARE NOT INCLUDED ON THE MDD PRESCRIPTIONS											
24. Warfarin + erythromycin/ clarithromycin	NOT ANALYZED: ANTIBIOTICS ARE NOT INCLUDED ON THE MDD PRESCRIPTIONS											
25. Warfarin + SSRI	348	8	229	8	119	8	83	7	183	8	82	7
26. NSAID + ACE inhibitor/ARB	573	13	407	14	166	11	195	17	270	12	108	9
27. NSAID + diuretics	633	14	454	15	179	12	181	16	272	13	180	14
28. NSAID + glucocorticoids	206	5	160	5	46	3	68	6	98	5	40	3
29. NSAID + SSRI	370	8	309	10	61	4	139	12	174	8	57	5
30. Erythromycin/ clarithromycin + statin	NOT ANALYZED: ANTIBIOTICS ARE NOT INCLUDED ON THE MDD PRESCRIPTIONS											
31. ACE inhibitor+ potassium /potassium-sparing diuretic	1035	23	625	21	410	26	324	28	457	21	254	20
32. Fluoxetine/ fluvoxamine + TCA	3	0	2	0	1	0	2	0	1	0	0	0
33. Beta blocker + cardioselective calcium antagonist	147	3	107	4	40	3	28	2	67	3	52	4
34. Diltiazem + lovastatin/ simvastatin	34	1	22	1	12	1	13	1	15	1	6	0
35. Erythromycin/clarithromycin + carbamazepine	NOT ANALYZED: ANTIBIOTICS ARE NOT INCLUDED ON THE MDD PRESCRIPTIONS											
36. Concomitant prescription of three or more drugs from the groups centrally acting analgesics, antipsychotics, antidepressants, and/or benzodiazepines	4906	108	3775	125	1131	73	1959	171	2047	95	900	72

sample characteristics, and student's t-test was applied to compare means. Binary logistic regression was used to assess the relationships between inappropriate medications (yes/no) for each patient, drug-drug-interactions (yes/no), and gender, age, and number of medicines. For the analysis, age was categorized into 10-year age intervals.

**Ethics**

The study was approved by the Data Protection Officer at the University Hospital of North Norway. All data were anonymous and deemed not to need approval by the Regional Committees for Medical and Health Research Ethics.

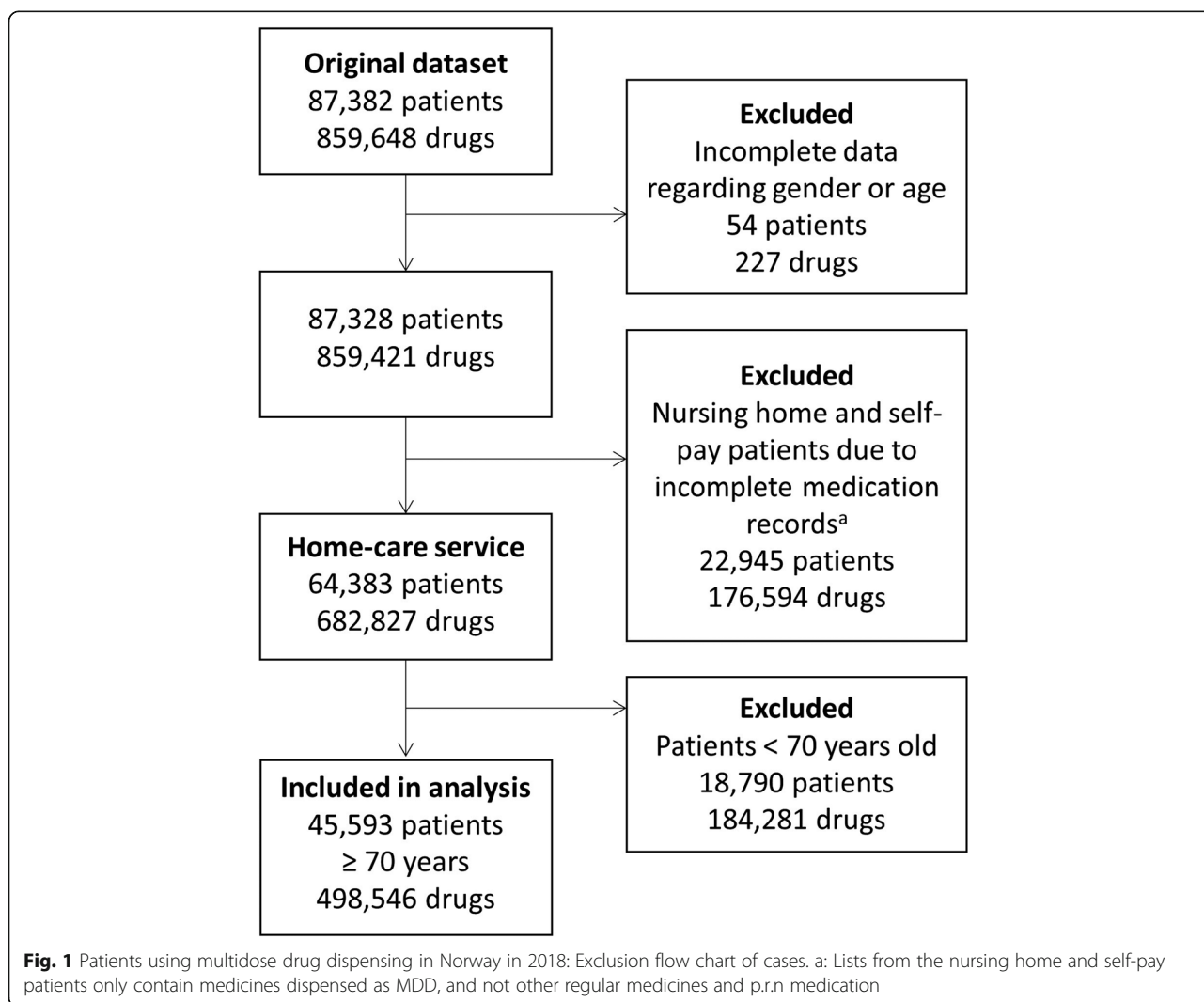
**Results**

As shown in Fig. 1, after exclusions the final analysis included 45,593 patients, i.e. approximately one-third of the patients ≥70 years old receiving home care services in Norway [8]. The study population characteristics are

shown in Table 2. The mean number of regular medications was 8.2 (median = 8), of which 6.1 (median = 6) were dispensed as MDD. The mean number of total prescribed medicines was 10.6 (median = 10). In total 85% used 5 or more medicines regularly and 33% used 10 or more medicines. In addition, 20 % of the patients used dietary supplements. The mean age was 84.7 (SD = 7.3). Women were on average older than men (85.5 vs. 83.1,  $p < 0.001$ ), and used a higher number of drugs (11.1 vs 10.7,  $p < 0.001$ ). Drugs for the cardiovascular and nervous-system were the most frequently used drug groups. The most commonly prescribed therapeutic sub-groups were antithrombotics (70% of patients), non-opioid analgesics (58%), beta-blockers (47%), lipid-modifying drugs (41%) and hypnotics/sedatives (39%) (Table 3).

**Potentially inappropriate medications**

According to the NORGEP-criteria, 12,319 patients (27%) received one or more PIMs (Fig. 2). Table 1 shows



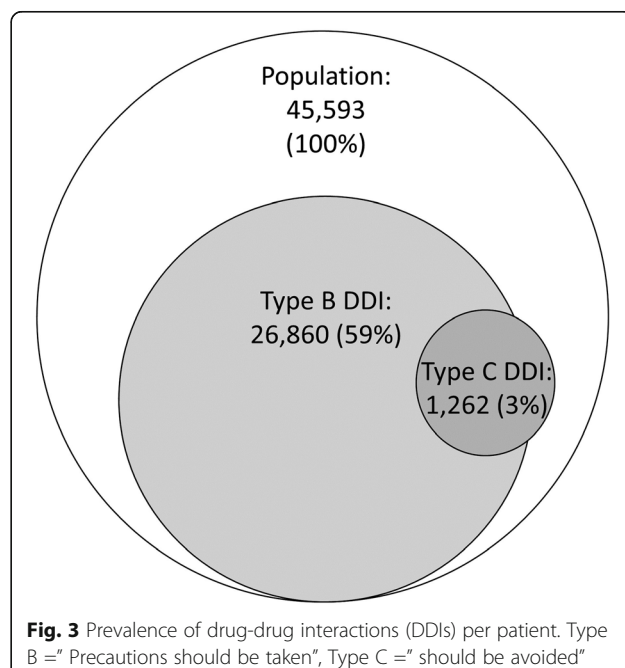
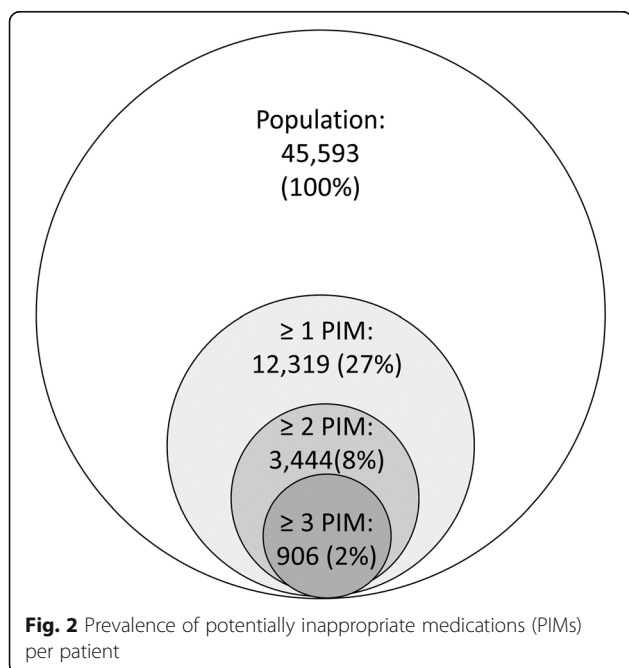
**Fig. 1** Patients using multidose drug dispensing in Norway in 2018: Exclusion flow chart of cases. a: Lists from the nursing home and self-pay patients only contain medicines dispensed as MDD, and not other regular medicines and p.r.n medication

**Table 2** Study population characteristics and drug use (N = 45,593)

	Study population		Regular drugs Dispensed as MDD		Regular drugs Not dispensed as MDD		P.r.n drugs		Total number of drugs	
	n	(%)	mean	(SD)	mean	(SD)	mean	(SD)	mean	(SD)
<b>Total</b>	45,593	(100)	6.3	(2.8)	2.2	(2.0)	2.4	(2.3)	10.9	(5.0)
<b>Age</b>										
70–79	11,435	(25)	6.9	(3.1)	2.3	(2.1)	2.4	(2.4)	11.6	(5.5)
80–89	21,633	(47)	6.4	(2.8)	2.2	(1.9)	2.4	(2.3)	11.0	(4.9)
90+	12,525	(27)	5.7	(2.6)	2.1	(1.9)	2.4	(2.2)	10.3	(4.6)
<b>Gender</b>										
Female	30,090	(66)	6.4	(2.9)	2.5	(2.3)	2.6	(1.9)	11.1	(5.1)
Male	15,503	(34)	6.2	(2.8)	2.2	(2.2)	2.2	(2.0)	10.7	(4.9)

**Table 3** The 25 most frequently used drug groups among MDD patients with home care services (N = 45,593)

ATC level 3	Therapeutic drug group	Regular drugs Dispensed as MDD		Regular drugs Not dispensed as MDD		P.r.n medications		Drug use female (n = 30,090)		Drug use male (n = 15,503)	
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
B01A	Antithrombotic agents	27,477	(60)	5744	(13)	65	(0)	19,845	(66)	12,004	(77)
N02B	Other analgesics and antipyretics	11,393	(25)	1448	(3)	16,024	(35)	18,829	(63)	7846	(51)
C07A	Beta blocking agents	21,522	(47)	79	(0)	174	(0)	13,796	(46)	7709	(50)
C10A	Lipid modifying agents, plain	18,545	(41)	133	(0)	10	(0)	10,911	(36)	7643	(49)
N05C	Hypnotics and sedatives	10,485	(23)	495	(1)	7426	(16)	12,841	(43)	5984	(39)
A02B	Drugs for peptic ulcer and gastro-oesophageal reflux disease	16,036	(35)	289	(1)	1599	(4)	11,371	(38)	5266	(34)
C03C	High-ceiling diuretics	13,832	(30)	136	(0)	1992	(4)	9962	(33)	4939	(32)
A06A	Drugs for constipation	578	(1)	8926	(20)	7918	(17)	9502	(32)	4727	(30)
N02A	Opioids	3771	(8)	3758	(8)	9375	(21)	9869	(33)	3695	(24)
N06A	Antidepressants	11,564	(25)	429	(1)	178	(0)	8807	(29)	3377	(22)
N05B	Anxiolytics	3999	(9)	219	(0)	7743	(17)	8205	(27)	3171	(20)
A12A	Calcium	10,328	(23)	336	(1)	19	(0)	8821	(29)	3155	(20)
C08C	Selective calcium channel blockers with mainly vascular effects	9055	(20)	79	(0)	81	(0)	6269	(21)	3060	(20)
R03A	Adrenergics, inhalants	1	(0)	6809	(15)	4651	(10)	5542	(18)	2901	(19)
A11E	Vitamin B-complex, including combinations	8262	(18)	173	(0)	36	(0)	5072	(17)	2721	(18)
B03B	Vitamin B12 and folic acid	2968	(7)	5792	(13)	192	(0)	5573	(19)	2698	(17)
C09A	ACE inhibitors, plain	7569	(17)	37	(0)	1	(0)	4539	(15)	2644	(17)
C01D	Vasodilators used in cardiac diseases	3359	(7)	372	(1)	5997	(13)	4851	(16)	2498	(16)
H03A	Thyroid preparations	7050	(15)	29	(0)	2	(0)	5839	(19)	1981	(13)
C09C	Angiotensin II receptor blockers (ARBs), plain	6466	(14)	41	(0)	2	(0)	4547	(15)	1958	(13)
A10B	Blood glucose lowering drugs, excluding insulins	5734	(13)	229	(1)	12	(0)	3328	(11)	1927	(12)
R06A	Antihistamines for systemic use	3630	(8)	133	(0)	1984	(4)	3975	(13)	1872	(12)
D07A	Corticosteroids, plain	1	(0)	989	(2)	4504	(10)	3354	(11)	1844	(12)
A11C	Vitamin A and D, including combinations of the two	4709	(10)	209	(0)	61	(0)	3144	(10)	1819	(12)
R05C	Expectorants, excl. Combinations with cough suppressants	15	(0)	1187	(3)	3820	(8)	3003	(10)	1622	(10)



the prevalence of the different PIMs. Concomitant use of three or more psychotropic and/or opioid drugs was the most prevalent PIM (10.8%), followed by prescribing of diazepam (6.4%). Criterion 1–8 and 18–21 concerns anticholinergic drugs; 3843 patients (8.4%) had one or more of those criteria. The number of PIMs was significantly correlated with the number of drugs prescribed ( $p < 0.001$ ). After adjustment for age, women had a higher risk of PIMs (OR = 1.50, 95% CI: 1.43–1.58). The risk of PIMs decreased with patient age (Table 4).

**Drug-drug interactions**

The screening for DDI revealed 59,414 interactions in 27,012 (59%) of the patients. Of the total number of interactions, 97.7% were classified as “type B – precautions should be taken”, and 2.3% as “type C- should be avoided”. Figure 3 illustrates the number of patients

with type B and C DDIs. DDIs increased with the number of prescribed drugs and decreased with patient age (Table 4). Women had a higher risk of DDIs than men (OR = 1.43, 95% CI: 1.37–1.50).

**Discussion**

The medication use in elderly patients using MDD in home care services in Norway is high, with about one-third of the patients using 10 or more drugs regularly. Approximately one-fourth received potentially inappropriate medications, and over half was exposed to drug-drug interactions. Females had a higher risk than men to experience both PIMs and DDIs, and both PIMs and DDIs were positively correlated with the number of medicines prescribed and negatively associated with patient age.

**Table 4** Factors associated with PIMs and DDIs in elderly (> 70 years) multidose users in Norway in 2018

Study population	Potentially inappropriate medications (PIM)					Drug-drug interactions (DDI)					Type B <sup>a</sup>		Type C <sup>a</sup>	
	n	n	(%)	OR	(95% CI)	n	(%)	OR	(95% CI)	n	(%)	n	(%)	
Age 70–79	11,435	4072	(35.6)	1	(ref)	7227	(63.2)	1	(ref)	7171	(62.7)	493	(4.3)	
Age 80–89	21,633	5449	(25.2)	0.61	(0.57–0.64)	13,000	(60.1)	0.90	(0.85–0.95)	12,935	(59.8)	543	(2.5)	
Age 90+	12,525	2793	(22.3)	0.55	(0.52–0.59)	6785	(54.2)	0.76	(0.72–0.81)	6754	(53.9)	226	(1.8)	
No. of drugs	45,593	NA		1.15 <sup>b</sup>	(1.15–1.16)	NA		1.30 <sup>b</sup>	(1.28–1.30)	NA		NA		
Male	15,503	8814	(22.6)	1	(ref)	8354	(53.9)	1	(ref)	8294	(53.5)	420	(2.7)	
Female	30,090	3505	(29.3)	1.50	(1.43–1.58)	18,658	(62.0)	1.43	(1.37–1.50)	18,566	(61.7)	842	(2.8)	

<sup>a</sup>: Type B = “Precautions should be taken”, Type C = “should be avoided”

<sup>b</sup>: Increase in odds for PIMs and DDIs for every one unit increase in the number of drugs



### Drug utilization

The most commonly prescribed medication groups are the same in the MDD population as in the general elderly population not receiving MDD, however, the overall prevalence is higher in MDD patients (Table 3) [26]. Antithrombotic agents (70% in the present study vs. 47% general elderly population) and analgesics (58% vs. 25%) are more frequently prescribed in MDD patients than the general elderly population. Women were more frequently prescribed medications acting on the nervous system and less cardiovascular drugs compared to men. The MDD patients used on average 8.2 drugs regularly, of which 6.1 were dispensed as MDD. In addition, 2.4 drugs were listed as p.r.n. medications. This is a higher number of medicines compared to the Norwegian elderly community-dwelling patients [26, 27], and thus supports previous findings that MDD patients tend to use more medicines than patients with ordinary dispensing [1, 3, 13]. However, since our study population receives HCS, they also have greater care needs than the general population.

Polypharmacy has been associated with negative health outcomes such as falls, adverse drug reactions, hospitalization, and mortality [28, 29]. However, lack of proper adjustment for confounders has been mentioned as a challenge in these studies [28–30]. The recent ESTHER study found no independent association between polypharmacy and non-cancer mortality when adjusting for confounding by indication [31, 32]. The high prevalence of polypharmacy in our study might thus be a reflection of a high morbidity in the study population. One previous study has shown that introducing an MDD system increases the number of medicines prescribed [13], though another observed the same increase in the control group where MDD was not introduced [33].

### Potentially inappropriate medications

In our study, 27% of the patients had at least one PIM. A systematic review of PIMs found an estimated prevalence of 22.6% in European community-dwelling older adults [34]. The prevalence, however, varied greatly between the studies due to different quality indicators used and differences in the study populations included. Nyborg et al. used the NORGE criteria and found a 34.8% prevalence of PIMs for the entire Norwegian home-dwelling elderly population [27]. This is higher than in our study, despite our study population using more medicines. An explanation is that we have excluded the criteria on the use of antibiotics. In addition, we used different data sources; Nyborg et al. used dispensed medicines while we used prescribed medicines (see strength and limitation).

Our prevalence of PIMs according to the NORGE criteria (27%) is comparable with Halvorsen et al. (24.6%) a decade ago [2]. Though our prevalence (27%) is somewhat higher, this is expected since we have looked at the entire medication list of the patients, and not just the medicines dispensed as MDD. The prescribing quality for MDD patients over the past decade does not seem to have improved, despite increased focus on medication reviews and deprescribing [35, 36].

Concomitant use of three or more psychotropic drugs is a PIM in the NORGE list, as this increases the risk of muscular weakness, falls, fractures and cognitive impairment [25]. Similar to our study, Halvorsen et al. found that this was the most prevalent PIM in MDD patients, with 9.0% meeting this criterion compared to 10.8% in our study. This is high compared to the general Norwegian elderly population, where the prevalence is 4.8% [27], however, it is lower in the Swedish studies of MDD patients, which found a prevalence of between 16.0 and 22.1% [3, 13, 14].

### Drug-drug interactions

The prevalence of DDIs in older patients vary greatly in the literature, from a few percent to almost 60% [2, 37, 38]. A prevalence of 59% as found in our study, is thus high. The majority of DDIs are “Type B – precautions should be taken” (Table 4). The suggested precautions for these DDIs include changing the ingestion time, increased monitoring of symptoms or side-effects and dose adjustments. The data in our study do not include information on whether precautions have actually been taken, however, the DDIs might not be clinically relevant if they have.

The prevalence of the most serious DDIs (type C) is more similar in our study and the literature. In our study, 2.7% of the patients had such interactions, while the prevalence is between 0.4 and 9.0% in previous studies of MDD patients [2, 3, 38, 39]. As the MDD prescriptions are systematically screened for DDIs using the same database we have used in this study, the GP is likely aware of these interactions at the time of the prescribing. Considering the low prevalence of the most serious DDIs we could thus question the clinical relevance of the interactions found in this study, as the doctor might already have judged the co-prescribing as necessary with no better alternatives available, and started appropriate monitoring of the patients.

### Predictors of PIMs and DDIs

We found that younger elderly (70–79 years) had a higher number of inappropriate drugs, a relationship confirmed by others [2, 39, 40]. However, Nyborg found that the age effect was not present in the multivariate analysis when in addition to age and gender, the number of prescribers was also included [27]. Information about

the number of prescribers was, however not available for our study. Women having a higher risk of experiencing DDIs and PIMs, is also consistent with previous findings [2, 27, 38, 40, 41]. This is partly explained by the fact that women are more commonly prescribed sedatives, analgetics and anxiolytics (See Table 3) [41], and many of the PIMs are related to these drugs.

### Strengths and limitations

A major strength of this study is that it represents almost 90% of the MDD users in Norway. In addition, the medication lists include dietary supplements. This data gives comprehensive information on drug use for these patients. HCS patients and MDD-prescriptions cannot be specifically identified in the Norwegian Prescription Database [42]. In that sense, our data on medicines use is unique. There could still, however, be errors or omissions in the data. The patient can get prescriptions on antibiotics and other short-term treatments or buy over-the-counter medicines, which are not listed on the MDD prescription. Most Nordic countries have databases over dispensed prescriptions [43] while the medication list used in our study represents prescribed medications. Our data thus includes prescriptions issued by a physician but not filled (“primary non-compliance”), which makes comparison to other Nordic studies difficult.

As with all register-based studies, one cannot conclude if PIMs have led to actual drug-related problems for the patients. A recent study looking at patients with multimorbidity acutely admitted to the hospital, found that strict adherence to the NORGEP-criteria could have prevented 15% of the serious adverse drug reactions [44]. The NORGEP-criteria was published in 2009. Changes in both prescribing patterns and the Norwegian formulary have led to some of the items on the NORGEP list to be outdated (e.g. Table 1 shows that three drugs have been withdrawn from the Norwegian market), and newer therapies which can be considered inappropriate for elderly have not been included. In addition, drug-specific criteria like the NORGEP-criteria do not capture all aspects of prescribing quality, as it, for example, does not address problems like under-prescribing like e.g. the START/STOPP criteria [35].

### Unfulfilled potential of the MDD system

Having all the patients’ medicines on the same prescription puts the pharmacist in a unique position to assess the prescribing and identify PIMs and DDIs. Having a complete overview over the patient’s medication use have been suggested as an explanation for why MDD patients seem to have fewer serious DDIs than patients with ordinary prescribing [14]. The systematic screening for DDIs for MDD patients might also explain the relatively low prevalence (2.7%) of serious DDIs in the

present study. However, there still seems to be an unfulfilled potential of using the MDD system to systematically identify PIMs. The screening could be used to identify high-risk patients who could be targeted for interprofessional medication reviews which again could raise awareness of inappropriate prescribing. When the electronic prescribing system is implemented, this also opens possibilities for the pharmacist to give direct feedback to the prescriber when problems are detected.

Further research is needed to explore whether high overall medication use is a result of the MDD system in itself, or whether it is due to differences in patient characteristics for patients with ordinary prescriptions compared to MDD.

### Conclusions

This study suggests that potentially inappropriate prescribing is common in elderly patients receiving MDD in Norway, as about one-fourth of the patients were exposed to PIMs, and over half were exposed to DDIs. However, previous studies suggest that both PIMs and DDIs are common also in patients not receiving MDD. Comparing our results to previous Norwegian studies, we do not find the same difference in prescribing quality between patients with MDD and patients with ordinary prescribing, as is shown in Sweden. However, we see that the overall drug consumption in MDD patients is higher than the general population, with about one third being prescribed 10 or more drugs regularly. In addition, there is more frequent co-prescribing of psychotropic and opioid drugs in MDD patients.

### Abbreviations

MDD: Multidose drug dispensing; PIM: Potentially inappropriate medication; DDI: Drug-drug interactions; HCS: Home care service; NORGEP-criteria: The Norwegian General Practice-criteria

### Acknowledgments

We thank Apotek 1 Gruppen AS for providing data for this study.

### Authors’ contributions

AVJ, AGG, TSB conceived the study design. Material preparation, data collection and the initial analysis were performed by AVJ. The first draft of the manuscript was written by AVJ. AVJ, TSB and AGG revised the manuscript. All authors approved the final version of the manuscript.

### Funding

This study was internally funded by the Norwegian Centre for E-health Research.

### Availability of data and materials

The data that support the findings of this study are provided by Apotek 1 Gruppen AS and are not publicly available. Data are however available from the corresponding authors upon reasonable request and with permission of Apotek 1 Gruppen AS.

### Ethics approval and consent to participate

The aim of the project falls outside the Health Research Act and the study was deemed not to need approval by the Regional Committees for Medical and Health Research Ethics. The study was approved by the Data Protection Officer at the University Hospital of North Norway and the Data Protection

Officer at Apotek 1 Gruppen AS. Because it was a retrospective study and all data was anonymised by Apotek 1, the need to obtain written informed consent was waived.

#### Consent for publication

Not applicable.

#### Competing interests

Apotek 1 Gruppen AS, a supplier of multidose dispensed drugs in Norway, provided data for this study. A.V. Jøsendal is employed by Apotek 1 Gruppen AS. The other authors declare no conflict of interest relevant to this study.

Received: 10 October 2019 Accepted: 22 July 2020

Published online: 05 August 2020

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Paper II

# The Practice Guidelines for Multidose Drug Dispensing Need Revision-An Investigation of Prescription Problems and Interventions

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*Pharmacy* 2021 Jan 6;9(1):13. doi: 10.3390/pharmacy9010013



Article

# The Practice Guidelines for Multidose Drug Dispensing Need Revision—An Investigation of Prescription Problems and Interventions

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**Abstract:** Multidose drug dispensing (MDD) is an adherence aid used by one-third of patients receiving home care services in Norway. The system can increase patient safety by reducing dispensing errors and increase adherence, however it has also been criticised for unclear routines and distribution of responsibilities. We investigated prescription problems which pharmacists have detected, and the responsibilities they adopt regarding MDD. For two consecutive weeks, 11 pharmacies used a self-completion form to register prescription problems identified with MDD. Of the 4121 MDD prescriptions, problems were identified on 424 (11%). The most common issues were expired prescriptions (29%), drug shortages (19%), missing prescriber signatures (10%) and unclear/missing medication names or strengths (10%). Compared to ordinary prescriptions, the pharmacist took on additional responsibility for renewing MDD prescriptions. However, because these patients received their medications via the home care service, there was limited patient counselling during dispensing. To increase the efficiency and patient safety of the MDD system, the roles and responsibilities of the pharmacist, GP, and home care nurses in the MDD system should be clearly defined. This seems most urgent for the renewal of prescriptions and patient counselling, where the responsibilities and work practice seem to differ from ordinary prescriptions.

**Keywords:** multidose drug dispensing; prescribing errors; pharmacy practice; pharmacist interventions; Norway



**Citation:** Josendal, A.V.; Bergmo, T.S.; Granas, A.G. The Practice Guidelines for Multidose Drug Dispensing Need Revision—An Investigation of Prescription Problems and Interventions. *Pharmacy* **2021**, *9*, 13. <https://doi.org/10.3390/pharmacy9010013>

Received: 25 November 2020

Accepted: 1 January 2021

Published: 6 January 2021

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## 1. Introduction

Prescribing errors commonly cause preventable medication errors and adverse drug events in primary care, many of which can lead to patient harm [1–3]. Pharmacists increase medication safety by resolving prescription errors and other prescription problems, such as drug shortages, issues with reimbursement, and drug–drug interactions [4–8]. Most studies from primary care show that pharmacists intervene on 0.5–9% of prescriptions dispensed [8–11], but some show frequencies up to 50% [9,12]. The great variation in these rates is probably due to differences in the definitions of pharmacist's intervention and in the methods used to register them.

Previous studies of prescription interventions have not included prescriptions for multidose drug dispensing (MDD). MDD, which is used by one third of patients receiving home care services in Norway [13,14], is an adherence aid where the patients' medications are machine-dispensed in disposable plastic bags, usually for 14 days at a time. MDD is believed to increase medication safety by reducing dispensing errors, reducing discrepancies between medication lists, and increasing adherence [15–19]. However, researchers have raised concerns that the MDD system increases the risk of inappropriate prescribing



and medication errors, due to the automation of prescribing procedures and insufficient routines for updating the MDD prescriptions [20–23].

The same laws apply to MDD and ordinary prescriptions, but there are some practical differences between the two prescription types. In Norway, over 90% of ordinary prescriptions are issued electronically [24], while MDD prescriptions are paper-based and faxed to the pharmacy. In addition, MDD prescriptions are often printouts from a GP's medical journal and contain a complete list of the patients' medications, including regular medications, as needed medications, and dietary supplements. This differs from ordinary electronic prescriptions, where a prescription consists of only one item at a time. The only legal difference between the two prescriptions is the timing of the pharmacist's check [25]. For ordinary prescriptions, the pharmacist checks the prescription at each dispensing, usually every three months for repeat prescriptions, while the MDD prescription is only checked when there are changes in the patient's medication treatment.

Regardless of prescription type, the pharmacist's checks ensure that the medication, dosage form, and the dose prescribed is in accordance with the patient's age, gender and indication written on the prescription. The pharmacist also checks for interactions, contraindications, and other available information about the patient. In addition, the validity of the prescription, including the prescriber's identity and right to prescribe medications is checked. Lastly, the pharmacist assesses whether the prescription label is clearly written and whether the patient needs any additional information [25,26]. If the prescription is incomplete, unclear or contains other problems, the pharmacist should try to correct the error and intervene. If this is not possible, an emergency refill can be dispensed if the pharmacist deems it necessary to prevent gaps in treatment and patient harm [25].

Most problems with the prescriptions are identified during the pharmacy check, however, the pharmacist's ability to detect and resolve problems on prescriptions is affected by factors such as patient age, care-setting, types of prescriptions and pharmacy [5,8–10,27–31]. Given the differences in format and routines for dispensing MDD and ordinary prescriptions, it is likely that the pharmacist's intervention rates vary between these two prescription types. Despite the MDD system being criticised for its vague distribution of responsibility and unclear routines across professional borders [17,32–34], no previous studies have investigated the pharmacist's responsibilities in the MDD system.

This study investigates: (1) the prescription problems in which pharmacists intervene; and (2) the responsibilities they adopt while dispensing MDD prescriptions in Norwegian community pharmacies.

## 2. Materials and Methods

### 2.1. The Development and Testing of the Registration Form

This cross-sectional study provides a descriptive analysis of prescription problems and pharmacist interventions on MDD prescriptions. The term "prescription problem" refers to errors, ambiguities, omissions, or other problems with the prescription that are potentially harmful to patients or interfere with the dispensing process. "Pharmacist intervention" refers to any action the pharmacist takes to resolve these prescription problems.

Based on a form used on ordinary prescriptions in previous studies [4,30], we developed a self-completion form for the registration of interventions on MDD prescriptions (See Supplementary Table S1). Prescription problems were grouped as either formal or medication-related (see Table 1) or relating to the MDD order (data not presented in this study). Information about the patient, prescription, interventions, the outcomes of the interventions and time spent on correcting errors were also recorded.



**Table 1.** Prescription problems detected ( $n = 464$ ), and the result of pharmacist interventions on multidose drug dispensing (MDD) prescriptions.

Problem with Prescription	Result of Intervention				Sum	Percentage of Total	
	<i>n</i> (Percentage of Problem Type)						
	Changed or Clarified Prescription	Dispensed as Prescribed	Prescription Not Dispensed	Other			
<b>Medication-related problems</b>	<b>104 (77%)</b>	<b>16 (12%)</b>	<b>2 (1%)</b>	<b>13 (10%)</b>	<b>135</b>	<b>(100%)</b>	<b>29%</b>
Medication name or strength	42	1	2	0	45	(33%)	10%
Dose or schedule	37	2	0	2	41	(30%)	9%
Drug–drug interaction	9	9	0	2	20	(15%)	4%
Administration formula	7	0	0	0	7	(5%)	2%
Treatment duration	6	1	0	0	7	(5%)	2%
Other	3	3	0	9	15	(11%)	3%
<b>Formal prescription problems</b>	<b>93 (39%)</b>	<b>131 (54%)</b>	<b>8 (3%)</b>	<b>9 (4%)</b>	<b>241</b>	<b>(100%)</b>	<b>52%</b>
Prescription date expired	8	125	0	0	133	(55%)	29%
Missing signature from the prescriber	39	1	7	1	48	(20%)	10%
Reimbursement	22	1	0	1	24	(10%)	5%
Missing prescriber data	9	0	0	2	11	(5%)	2%
Missing patient data	8	0	0	0	8	(3%)	2%
Other	7	4	1	5	17	(7%)	4%
<b>Drug shortages</b>	<b>52 (59%)</b>	<b>21 (24%)</b>	<b>13 (15%)</b>	<b>2 (2%)</b>	<b>88</b>	<b>(100%)</b>	<b>19%</b>
<b>TOTAL</b>	<b>249 (54%)</b>	<b>168 (36%)</b>	<b>23 (5%)</b>	<b>24 (5%)</b>	<b>464</b>	<b>(100%)</b>	<b>100%</b>

A teaching manual including examples of common prescription problems and completed forms was developed. These were piloted on 100 prescriptions in one pharmacy in 2017. The pilot provided important input to the design and content of the form and teaching manual. The pilot interventions are not included in this study. The first three pharmacies in this study provided feedback that led to minor adjustments in the self-completion form, which were used in the eight consecutive pharmacies.

## 2.2. Selection of Pharmacies

At the time of our study, one pharmacy chain dispensed 80% of all MDD prescriptions in Norway. We asked this pharmacy chain for a list of pharmacies with  $\geq 500$  MDD patients. This cut-off was set to obtain a reasonable number of interventions per pharmacy. About 12% of MDD patients have changes in their drug regimen between MDD orders [35], therefore 500 MDD patients equalled approximately 60 MDD prescription checks per week. The pharmacy chain provided a list of 35 pharmacies. We purposefully selected 20 pharmacies and invited them by email to participate in our study. We aimed to obtain a variety of geographical representation and workloads in terms of the number of MDD prescriptions dispensed.

### 2.3. Data Collection

The study was conducted from February to October 2018. Each pharmacy collected data for two consecutive weeks. We chose this time frame because most MDD bags last for two weeks, which means that the pharmacy will order a new delivery of MDD for all their patients within this period. To leave time for adjustments to the self-completion form between the periods, no two pharmacies collected data during the same weeks. Once a pharmacy accepted the invitation, a date for participation was allocated and the teaching manual and self-completion form were emailed to the pharmacy. A week before participation, we contacted the pharmacy to check whether the participants had read the teaching manual and we answered any questions they had about the study.

Using the self-completion form, the participants registered all prescription problems and interventions on MDD prescriptions for two consecutive weeks. The forms were sent back to the researchers by post. The pharmacy chain extracted the total number of MDD prescriptions dispensed from each pharmacy from their central dispensing database. We defined the number of prescriptions as the number of pharmacist prescription checks. This corresponds to the number of patients having changes in their medication treatment during the study period.

The data were analysed in Microsoft Excel 2016. No personally identifiable information was recorded, and thus the study did not require approval from the Regional Ethics Committee.

### 3. Results

Of the 20 pharmacies invited to participate, 11 accepted. The main reason for declining was a lack of time or resources. The participating pharmacies were located in 9 of the 11 counties in Norway, and dispensed between 47 and 1813 MDD prescriptions per week, with a median of 109. In total, the pharmacists intervened on 464 prescriptions, an intervention rate of 11.3% of all MDD prescriptions ( $n = 4121$ ). The intervention rate varied from 2.2% to 38.2% between the participating pharmacies.

As shown in Table 1, half of the interventions were related to formal problems with the prescription, about one-third to medication issues, and one-fifth to drug shortages. On average, the medication-related problems took 8.0 min to correct, drug shortages took 4.5 min and formal prescription problems took 3.6 min. Problems related to drug shortages varied from 0 to 55% of the problems detected in each pharmacy.

Missing or unclear information about medication names, strengths, doses, or schedules accounted for more than half of the medication-related prescription problems, in which the majority were corrected or clarified before dispensing. Table 2 shows that a patient's medication history was the most common reason for the pharmacist to intervene on a prescription, followed by computer-generated warnings and conflicting information about the patient's medication use from different sources (e.g., prescriptions from other doctors than the GP, discharge notes from hospitals, messages from home care services, etc.).

Table 1 illustrates that over 70% of the formal prescription problems were due to expired prescriptions or missing prescriber signatures. In addition, the prescribers were contacted regarding 42 prescriptions that were about to expire (data not shown). For the majority of formal prescription problems, the pharmacist did not obtain a valid prescription before sending the MDD order and, therefore, dispensed void prescriptions.

In total, 88% of the problems were resolved by a pharmacist and the remaining by pharmacy technicians. For 55% of the prescription problems, the pharmacist contacted the prescriber to resolve the problem; for 17%, the home care services were contacted; and for another 17%, the pharmacist used their professional judgment to resolve the problem.

Based on the problems detected and actions taken by the pharmacist, we have identified five different responsibilities the pharmacist adopts while dispensing MDD prescriptions: checking prescriptions for clinical appropriateness, verifying the validity of prescriptions, renewing prescriptions, patient counselling, and dispensing emergency refills.

**Table 2.** The five most frequent reasons for pharmacist intervention on medication-related problems on MDD prescriptions.

Reason for Intervention	Examples of Prescription Problems	n (%)
Patient medication history	The new prescription stated candesartan 32 mg, while the previous prescription was 8 mg. The pharmacist reacted to the sudden change in dose. The patient had used methylphenidate 54 + 36 mg daily, but the medication was missing on the new prescription. The pharmacist wondered if the stop was intentional.	21 (16%)
Computer-generated warnings (drug–drug interactions)	Iron tablets and calcium were prescribed to the same patient at the same time of day. Calcium reduces the absorption of iron, and these should be taken 2–3 h apart from each other. A patient started escitalopram while he was already using dabigatran. This increases the chances of bleeding.	20 (15%)
Multiple sources with conflicting information about the prescribed medicines	On the paper-based MDD prescription, ticagrelor was prescribed as 90 mg, one tablet daily. On an ordinary electronic prescription, the dosing schedule was 90 mg, two times daily. The pharmacist wondered which dose the patient should have. Discharge notes from the hospital stated a temporary reduction in the dose of apixaban. On the MDD prescription from the GP, the treatment of apixaban was stopped. It was unclear which of the prescriptions were the newest/correct.	18 (13%)
Incomplete prescriptions (due to handwriting)	A patient was prescribed valsartan, one tablet daily. No strength was given. Prescribed “iron tablets”. The strength and dose were lacking.	17 (13%)
Other inconsistencies	A patient was prescribed a high dose of prednisolone in MDD without a stop date. The pharmacist called to check if there should be a tapering schedule. A prescription contained two different dosing schedules for the same medication. Unclear which one was correct.	17 (13%)

## 4. Discussion

### 4.1. Pharmacist Interventions

One in nine of all MDD prescriptions needs an intervention or clarification by the pharmacist before dispensing. The most common prescription problems were expired prescriptions (27% of all problems), drug shortages (19%), and missing signatures (13%). For most of the medication-related problems, the pharmacist clarified or corrected the problem before dispensing. For the majority of formal prescription problems, the pharmacist reported dispensing MDD despite the prescription being invalid. Five percent of the prescription problems resulted in one or more medications not being dispensed.

To our knowledge, our study is the first to specifically investigate prescription problems on MDD prescriptions. A Danish study reported errors on MDD prescriptions as a part of a larger study and found an intervention rate of 0.85% [11]. This is considerably lower than our findings, but this is expected due to the differences in definitions of an MDD prescription. We have used the number of pharmacist checks (i.e., whenever there are changes on a prescription), while the Danish study used the number of MDD orders (i.e., one prescription every two weeks for each patient).

A prescription intervention rate of 11.3% is high compared to studies in community pharmacies, which usually show interventions on 0.5–9.0% of prescriptions [8–11]. For MDD prescriptions, the pharmacist usually has more information about the patients, including a complete medication list and the indication for use. This could contribute to a higher intervention rate [5,31]. Some evidence also suggests that intervention rates are higher on new prescriptions than repeat prescriptions [8,30,36]. We have used the number of pharmacist checks (i.e., whenever there are changes in the drug treatment) as

the number of prescriptions dispensed, which might also explain our high intervention rate. On the other hand, the pharmacist has less contact with the patients when supplying MDD prescriptions, which could contribute to a lower intervention rate [4,5,27,30,37].

#### 4.2. *The Pharmacist's Responsibilities*

##### 4.2.1. Checking Prescriptions for Clinical Appropriateness

The medication-related problems in our study constituted 29% of all problems; 3.3% of the total MDD prescriptions. In comparison, clinically relevant interventions are done on fewer than 1% of ordinary prescriptions [5–7,9,11,12,30,31]. “Medication-related interventions” is a broader definition than “clinically relevant interventions”, therefore it is expected that our rate is higher than what is shown in these studies. The types of problems detected are similar to other studies, where missing or unclear information about the medication name, strength, dose, or dosing schedule are among the most common problems [4,5,7,11,28,30].

In our study, the pharmacist identified certain problems which would be difficult to detect on ordinary prescriptions. When checking new MDD prescriptions, the pharmacist compares this with the previous MDD medication list. This enables the pharmacist to identify problems such as a sudden stop in medication treatment. In our study, 15% of the medication-related problems were identified using the patients' medication histories in this way. We also discovered that 13% of the medication-related problems were revealed because the pharmacist had access to different prescriptions with inconsistent information about the patient's current treatment. On ordinary prescriptions, the pharmacist rarely has access to other information about the patient, apart from the electronic prescriptions they are dispensing.

##### 4.2.2. Verifying the Validity of Prescriptions

The majority of prescription problems detected in our study were related to formal errors, in line with other studies regarding paper-based prescriptions [4,7,10,28,30]. Patient and prescriber data are fields that must be completed to enter prescriptions into the dispensing program, but this is not the case for a missing signature. The frequent detection of this problem indicates that the pharmacists actively check the validity of the MDD prescriptions before dispensing, and do not just detect the problems that physically hinder the dispensing.

##### 4.2.3. Renewing Prescriptions

Most prescriptions for regular medications are valid for one year, including MDD prescriptions. Normally, the patient contacts the GP to renew prescriptions when they are about to expire, but for MDD patients the home care service has this responsibility. However, as our study shows, the pharmacist partly takes on this responsibility. Informing that a prescription was expired ( $n = 125$ ) or about to expire ( $n = 43$ ) was the single most common cause of the pharmacist contacting the prescriber. It seems to have become a common practice for many pharmacies to contact the GPs directly to renew MDD prescriptions to prevent unintentional gaps in drug treatment [17].

##### 4.2.4. Counselling Patients on the Use of Prescription Medications

The pharmacists should assess whether the prescription label is clearly written and whether the patient needs any additional information about their medications [26]. The MDD bags contain more information than medication labels, therefore this might reduce the need for clarifying complex medication regimens, such as informing that medications should be taken some hours apart or at specific times of the day.

However, assessing the patient's need for information is more difficult in the MDD system than for ordinary prescriptions, because the pharmacist has no direct contact with the patient. Any medication counselling has to be conducted via the home care services. When dispensing ordinary prescriptions, contact with the patient or caregiver

can resolve up to half of the prescription-related problems [4,5,30,37]. Contact with the home care nurses resolved only 17% of the problems in our study, while the majority were resolved by contacting the GP. Our study indicates that the pharmacists only take limited responsibility for patient counselling when supplying MDD prescriptions. Reduced patient counselling about prescription medications upon dispensing might explain why patients using MDD have less knowledge about their medications than patients with ordinary prescriptions [16,18].

#### 4.2.5. Dispensing Emergency Refills

Although the pharmacist frequently intervened on formal prescription problems, only 40% of these problems were corrected before dispensing, while 54% were dispensed despite the prescription being invalid. Previous studies also show that for formal errors, the majority of prescriptions were dispensed as prescribed [4,30]. However, the problems detected in these studies were mostly reimbursement issues and missing patient information, which were not errors that made the prescriptions invalid.

We have not investigated why the rate of dispensing invalid prescriptions is so high in our study; however, there are some important differences between the MDD system and ordinary prescriptions that might explain this finding. Stopping an MDD prescription involves stopping all medications distributed in MDD, not just a single medication. Secondly, MDD patients usually only have a few days of medication supply left when the new MDD order is placed. The MDD bags have to be produced and shipped before the patient receives them, therefore this leaves the pharmacist with less time to correct errors and omissions on the prescriptions before the patient runs out of the medications. These factors might raise the pharmacist's threshold of stopping the dispensing.

According to legislation, a pharmacist can dispense an emergency refill only once per prescription, and only in amounts necessary until the prescriber can be reached and the error corrected [25]. If the emergency refill is only performed once for 14 days, this can prevent patient harm because it prevents gaps in the patient's regular medications. However, if this practice is continued for longer periods, it might ultimately reduce patient safety due to the patient not receiving regular medication reviews. If dispensing emergency refills is a common practice, this might also explain why MDD users seem to have fewer changes in their medication treatment than patients with ordinary prescriptions [20].

#### 4.3. Implications and Suggestions for Improvement

This study shows that pharmacists play an important role in detecting and resolving problems in MDD prescriptions. The pharmacist's responsibility and practice for checking clinical appropriateness and the validity of prescriptions seems to be similar for ordinary prescriptions and MDD prescriptions. However, one can speculate whether the pharmacist should have detected even more medication-related problems for these patients. MDD patients, in general, use many medications, and potentially inappropriate medications are common [20,38]. Pharmacists have access to the complete medication list for these patients; this puts them in a position to review the medication treatment as a whole.

The pharmacist is responsible for counselling patients on the use of prescription medications; however, this seems to happen only to a limited degree for MDD patients. There is no direct contact between the patient and the pharmacist upon dispensing, therefore increasing the use of E-health technology, such as video consultations between the patient and the pharmacist, could be considered. In the MDD system, the home care services are also responsible for patient counselling [39]. To ensure that the patients receive the information they need, the roles and responsibilities for patient counselling between these professional groups should be more clearly defined.

We see that pharmacists frequently dispense emergency refills for MDD patients, mostly due to prescriptions being expired. Additionally, pharmacists seem to have taken on the additional responsibility of contacting GPs to renew prescriptions, a responsibility which they do not take with ordinary prescriptions. This indicates that there is a lack



of clear guidelines or enforcement of such guidelines when it comes to the renewal of prescriptions in the MDD system. This highlights the need for clarifying the responsibility of the GP, home care nurses and the pharmacist in this setting.

#### 4.4. Strengths and Limitations of the Study

A strength in our study is that our registration form was based on those in previous studies, and was piloted before the study. However, a self-completed form means that problems might be underreported. Our selection of pharmacies is not representative for MDD pharmacies in Norway, which means that there is uncertainty in the frequency of different types of prescription problems. However, we feel that the purposeful selection helped us capture the different types of problems which pharmacists identified. We recruited pharmacies from all parts of the country, which increased the generalisability, although there might have been a selection bias because many pharmacies declined to participate. We were investigating routines for managing prescription problems, therefore only having pharmacies from one of three chains is a limitation. However, we found a great variation in both the number of problems detected and how they were solved, which indicates that there is still variation in routines within the pharmacy chain. We also lack the information of any clinical impact of the pharmacists' interventions.

## 5. Conclusions

Community pharmacists contribute to safe and effective drug use by clarifying problems in one of every nine MDD prescriptions. One-third of the problems were related to medications, half were formal errors with the prescriptions and the remaining problems were related to drug shortages. As for ordinary prescriptions, the pharmacists check prescriptions for clinical appropriateness, verify the validity of prescriptions, and dispense emergency refills when deemed necessary. However, the pharmacists seem to take on additional responsibilities for renewing prescriptions and counsel patients less than for patients without MDD prescriptions. The responsibilities of the pharmacist differ between ordinary prescriptions and MDD prescriptions, therefore there is a need for specific practice guidelines for dispensing MDD prescriptions. Clearly defining the roles and responsibilities of the pharmacist, GPs, and home care nurses, especially regarding the renewal of prescriptions and patient counselling, has the potential to increase efficiency and patient safety of the MDD system.

**Supplementary Materials:** The following are available online at <https://www.mdpi.com/2226-4787/9/1/13/s1>, Table S1: A self-completion form for registering interventions on MDD prescriptions.

**Author Contributions:** A.V.J., A.G.G., T.S.B. conceived the study design. Material preparation, data collection, and the initial analyses were performed by A.V.J. The first draft of the manuscript was written by A.V.J., A.V.J., T.S.B. and A.G.G. revised the manuscript. All authors have read and approved the final version of the manuscript.

**Funding:** This study was internally funded by the Norwegian Centre for E-health Research.

**Data Availability Statement:** The data underlying this article will be shared on reasonable request to the corresponding author.

**Acknowledgments:** The authors would like to thank all pharmacies who participated in this study.

**Conflicts of Interest:** A.V.J. is employed by Apotek 1 Gruppen AS, which presently provide services to about half of all MDD patients in Norway. The other authors declare no conflicts of interest relevant to this study.

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Paper III

# Implementation of a shared medication list in primary care - a controlled pre-post study of medication discrepancies

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*BMC Health Services Research* 2021 Dec 13;21(1):1335. doi: 10.1186/s12913-021-07346-8.



RESEARCH

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# Implementation of a shared medication list in primary care – a controlled pre-post study of medication discrepancies

Anette Vik Josendal<sup>1,2\*</sup>, Trine Strand Bergmo<sup>1,3</sup> and Anne Gerd Granas<sup>2</sup>

## Abstract

**Background:** Access to medicines information is important when treating patients, yet discrepancies in medication records are common. Many countries are developing shared medication lists across health care providers. These systems can improve information sharing, but little is known about how they affect the need for medication reconciliation. The aim of this study was to investigate whether an electronically Shared Medication List (eSML) reduced discrepancies between medication lists in primary care.

**Methods:** In 2018, eSML was tested for patients in home care who received multidose drug dispensing (MDD) in Oslo, Norway. We followed this transition from the current paper-based medication list to an eSML. Medication lists from the GP, home care service and community pharmacy were compared 3 months before the implementation and 18 months after. MDD patients in a neighbouring district in Oslo served as a control group.

**Results:** One hundred eighty-nine patients were included (100 intervention; 89 control). Discrepancies were reduced from 389 to 122 ( $p < 0.001$ ) in the intervention group, and from 521 to 503 in the control group ( $p = 0.734$ ). After the implementation, the share of mutual prescription items increased from 77 to 94%. Missing prescriptions for psycholeptics, analgesics and dietary supplements was reduced the most.

**Conclusions:** The eSML greatly decreases discrepancies between the GP, home care and pharmacy medication lists, but does not eliminate the need for medication reconciliation.

**Keywords:** Shared medication list, Multidose drug dispensing, Medication reconciliation, Medication discrepancies, Primary care, E-health, E-medicines management

## Background

Access to medicines information is important when treating patients. If treatment decisions are based on outdated medication lists this can lead to inappropriate prescribing, discontinuity of therapy and medication errors [1, 2]. Yet, discrepancies in medication lists are common, particularly during transitions of care [3]. A systematic review has shown that up to 60–67% of medication

histories recorded at hospital admissions contain at least one medication discrepancy, 11–59% of these were clinically important [2]. These discrepancies may not only result in inappropriate treatment during the hospital stay but also carry over to discharge, resulting in errors in the discharge letters to primary care providers [4, 5].

Also within primary care, discrepancies are common and studies show that up to 90% of patients have at least one discrepancy in their lists [6–8]. Poor communication between health care providers is a common cause of these discrepancies [1, 9–13]. In addition, there are many manual routines involved in the transfer of

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medicines information [8, 14, 15]. A recent Norwegian study shows that primary care nurses, pharmacists and GPs experience many challenges obtaining an accurate medication list. They find the current procedures very time consuming, complex and posing a risk to patient safety [15]. Technology such as e-prescribing, which can increase legibility and completeness of the prescriptions and increase access to medicines information, has been suggested to address these challenges [16, 17]. In addition, several countries are developing systems for sharing complete medication lists across care levels [18, 19]. These systems for sharing medication lists vary between countries, and the scientific evidence on the effects is still limited [19].

In Norway, e-prescribing in primary care was implemented in 2013, and today more than 90% of new prescriptions are sent electronically [20]. The Norwegian Directorate of eHealth is also currently developing a nationwide electronic Shared Medication List (eSML) [21]. The first patients to get an eSML are home care service patients with multidose drug dispensing (MDD), a system where patients get medicines dispensed as unit-for-use disposable bags. Today, MDD patients already have a complete medication list containing all regular medications, *when needed* medications and dietary supplements, but this list is paper-based and sent by fax between the actors. Though one Norwegian study has shown that the paper-based MDD system can reduce the number of discrepancies in medication lists [7], discrepancies between the community pharmacy, the home care services and the GPs still frequently occur in the paper-based system [7, 22, 23]. When eSML is implemented for these patients, the paper-based medication list will be replaced by a joint electronic list. In addition, e-prescriptions for each item on the eSML is necessary to dispense medicines. Both the e-prescriptions and the eSML are transferred via a national database accessible from all pharmacies and prescribers in the country.

The goal of the eSML is to generate one structured and complete medication list, to increase access to medicines information for all health care professionals involved in the care of MDD patients and to reduce the time used on medication reconciliation [21, 24]. In this study, we investigate whether the eSML system decreases the number of discrepancies between the medication lists of the GP, home care service and the community pharmacy.

## Methods

### Study setting

This study followed the implementation of the eSML for MDD patients in Oslo in 2018. The Directorate of eHealth was responsible for the implementation process and chose participants based on the GPs electronic health

record (EHR) system. All GPs with a specific EHR system in a given district in Oslo were asked to participate.

### Study design and sample

This study has a controlled pre-post design. The Directorate of eHealth provided contact details for the health care personnel who were starting the eSML in Oslo: 3 GP offices with a total of 17 GPs, one home care service district and one community pharmacy. GP offices located in the same or a neighbouring district in Oslo who were not using eSML served as a control group. GPs were recruited until we had the same number of estimated patients in the control group as in the intervention group. The home care services in the control district was also contacted. The same pharmacy provided MDD to both districts.

### The intervention

Before the intervention, all GPs used paper-based MDD-prescriptions, mostly printouts from the medication list in the GPs Electronic Health Record (EHR). These prescriptions are usually complete medication lists containing all regular medications, *when needed* medications, medical devices and dietary supplements, and are valid for 1 year supply of all items on the list. The GP sends the MDD prescription to the pharmacy via fax. The hospital doctors can also prescribe for these patients, but the main rule is that the GP approve these changes before they are dispensed in MDD. If the prescribing is done via ordinary electronic prescriptions, the MDD pharmacy will not automatically be notified about the prescription.

The eSML prescribing system is a function in the currently used EHR systems. After this functionality is turned on, the GP can define which patients should use eSML. The eSML by itself is only a medication list giving an overview of the patient's current treatment, but it cannot be used for dispensing directly. It is thus necessary to generate e-prescriptions for each item on the eSML. When a patient is defined as using eSML in the EHR system, the eSML will be generated and sent automatically when the GP generate e-prescriptions. Both the eSML and the e-prescriptions are valid for 1 year, however, the e-prescriptions also contain information about the quantity which can be dispensed on the prescription. This means that the e-prescriptions can be emptied before 1 year has passed. At present, all prescribers have access to read the eSML, but only the GPs can update the list [24]. When hospital physicians prescribe medicine, they will do so by ordinary e-prescriptions. They should also withdraw prescriptions that are no longer relevant or appropriate. As in the paper-based system, the current recommendation is that the pharmacy should wait to dispense MDD until the GP has updated the eSML, but it is

possible to dispense MDD on the e-prescriptions if the pharmacist deems it necessary. For MDD patients, the system also opens for electronic communication between the GP and the MDD dispensing pharmacy, where the pharmacist can suggest changes of the eSML directly to the GP. If the pharmacist dispenses a prescription that is not included in the eSML, e.g. a prescription from the hospital or a dietary supplement, the system will automatically send information about this to the GP.

During the first pilot testing of the eSML system in 2014, the nurses and pharmacists experienced many errors in the first eSML created. They retrospectively reported errors to the GPs asking them to correct the lists [23, 25, 26]. It was suspected that these errors were caused by the discrepancies in the medication lists. In our study, the Directorate of eHealth thus recommended medication reconciliation of the medication lists at the GP, pharmacy and/or home care before the actual creation of the eSML. To facilitate this, the MDD pharmacy sent a printout of their medication lists to the GPs approximately 1 month before start-up. After comparing this list to their own record, the GP created the first eSML and necessary e-prescriptions. The GPs could claim reimbursement for this work if they documented it as a medication review, a process that all GPs in Norway can be reimbursed for up to three times a year for patients with four or more medications [27]. Once the pharmacy received the eSML for the patients, they deleted the paper-based medication list in their system and started dispensing MDD based on the new eSML and e-prescriptions.

#### Data collection

A list of all MDD patients in the two districts who were registered with one of the participating GPs was compiled using the pharmacy dispensing programme. One week before data collection, a letter was sent to all participants (all GPs, the home care services and the pharmacy) with the list of MDD patients under their care and a generated serial number for each patient. The following week, the participants printed out the medication lists for the patients and replaced the patient identifying information with the serial number. The lists were posted or collected in person by AVJ. For the intervention group, the first medication lists were collected in March 2018, approximately 3 months prior to the implementation of eSML. For the control group, the first medication lists were collected in June 2018. For both groups, the lists were collected again in September and October 2019.

#### Analyses

The medication lists were compared in pairs: GP-list – Home-care-list; GP-list – Pharmacy-list; Pharmacy-list

– Home-care-services-list. Two researchers separately compared each set. First, the number of unique prescription items in each list were recorded into four groups: 1) regular prescription items dispensed as MDD; 2) regular prescription items not dispensed as MDD; 3) medications prescribed to be used as required; 4) medical devices and consumables (e.g., diabetes supplies; incontinence products). A unique prescription item was defined by an ATC code for medicines [28], an active ingredient for dietary supplements and a product group for medical devices and consumables [29]. Medicines listed as ‘courses’ in the GP journal system (e.g., short antibiotic courses) were excluded. Second, based on a previous classification system [7, 22, 23], discrepancies were classified in the following categories: Medication lacking from one of the two lists; different dosage; prescriptions written as ‘regular use’ in one list and ‘as required’ in the other; different administration formula; others (see Table 2). Both missing and discordant information in the medication lists were recorded. Lastly, all three lists for the patient were compared to register the number of unique prescription items per patient and the number of prescription items present in all three lists (mutual prescription items). These were used to calculate the congruence level = mutual prescriptions items/unique prescription items.

The three-way comparison of medication lists was only used for the overall congruence level. For the rest of the results, the number of discrepancies between the GP list and the home care service list was used. This was chosen because these were the lists most frequently compared in previous studies. Similarly, the number of items in the GP medication list was used when discussing the number of items prescribed.

Data was registered in Microsoft Office Excel 2016 and analyses were performed in Stata/MP 16.1. The student's *t*-test was used for continuous data to test the significance of differences between groups and changes in time, a chi-square test was used to compare categorical data and McNemar test for paired nominal data. The significance level was set to 0.05. To estimate the effect of the eSML on discrepancies a difference in difference (DID) method was used. The DID design is based on taking the difference in discrepancies before and after the introduction of the eSML, minus the corresponding change in the control group. The main assumption of this method is that of “parallel trends”: that the development of discrepancies would be the same in the two groups in absence of the intervention. Because the method looks at change and not absolute values, the groups can have different baseline levels of the outcome. It also implies that any time-varying factor, such as an information campaign to make GPs reconcile

their medication lists, would affect both groups equally and thus not confound the results.

**Ethics**

This study was performed in accordance with guidelines and regulations as stated in the study protocol approved by the Data Protection Officer at the University Hospital of North Norway (UNN) (Project No. 02003). Because the aim of the project was not to generate new knowledge about health or disease, but rather quality assurance of a new system, the project fell outside the scope of the Health Research Act. The Regional Committee for Medical Research Ethics (REK) has waived the need to obtain consent for the collection and analyses of the medication lists in this study, due to difficulties contacting home care service patients and an anticipated high dropout rate in this population (57% dropout in a similar study of multi-dose patients [7]) (2017/1393/REK Nord). Patient identifying data was stored separately from the anonymous medication list in a secure research server at UNN.

**Results**

In the intervention group, all 17 GPs who piloted the eSML participated. The data collection before implementation included complete sets of medication lists for 188 patients, the second 100 sets (53%). Of the dropouts, 82 were no longer eligible (moved to another municipality, moved to a nursing home, changed their GP or stopped using MDD); 6 still used MDD but were not available (missing or incomplete medication list from either home care service, GP or pharmacy). Of 12 GP offices contacted for the control group, five offices with 19 GPs accepted the invitation. The reason for declining was lack of time. The first data collection included complete sets for 178 patients, the second 89 (50%). Of the dropouts, 68 were no longer eligible, 21 medication lists were not available.

**Comparison of intervention and control group before implementation**

Table 1 shows the comparison of groups before the intervention; the participants in the control group were significantly older than those in the intervention group, but

there was not a significant difference in gender or number of items prescribed.

As seen in Fig. 1, the overlap of medicines information between the three lists was higher in the intervention group than in the control group before the intervention. The intervention group had on average 3.9 discrepancies in their medication lists before the intervention, while the control group had 5.9 (Table 2).

For both groups, when comparing the GP and the home care service list, the most frequent types of discrepancies were that medication was lacking or that different dosages were listed. The most frequent items lacking from the lists were N05-Psycholeptics (11% of missing items before implementation), N02 – Analgesics (10%), dietary supplements (9%), and medical devices and consumables (6%). Medicines acting on the cardiovascular system (ATC-code = C) constituted 10% of the discrepancies.

**Changes after the intervention**

Discrepancies in the intervention group were significantly reduced after the implementation of eSML. The share of mutual prescription items in all three lists increased from 77 to 94% (Fig. 1), and the total number of discrepancies was reduced from 383 to 122 ( $p < 0.001$ ) (Table 2). The most frequent types of discrepancies were still that medication was lacking and that different dosages were listed.

After implementation, medical devices and consumables constituted 30 of the 47 missing prescription items in the home care service list. Dietary supplements, which was the most frequently missing item from the GP list before implementation (16% of missing prescription items in the GP list), were not missing from any medication lists after implementation.

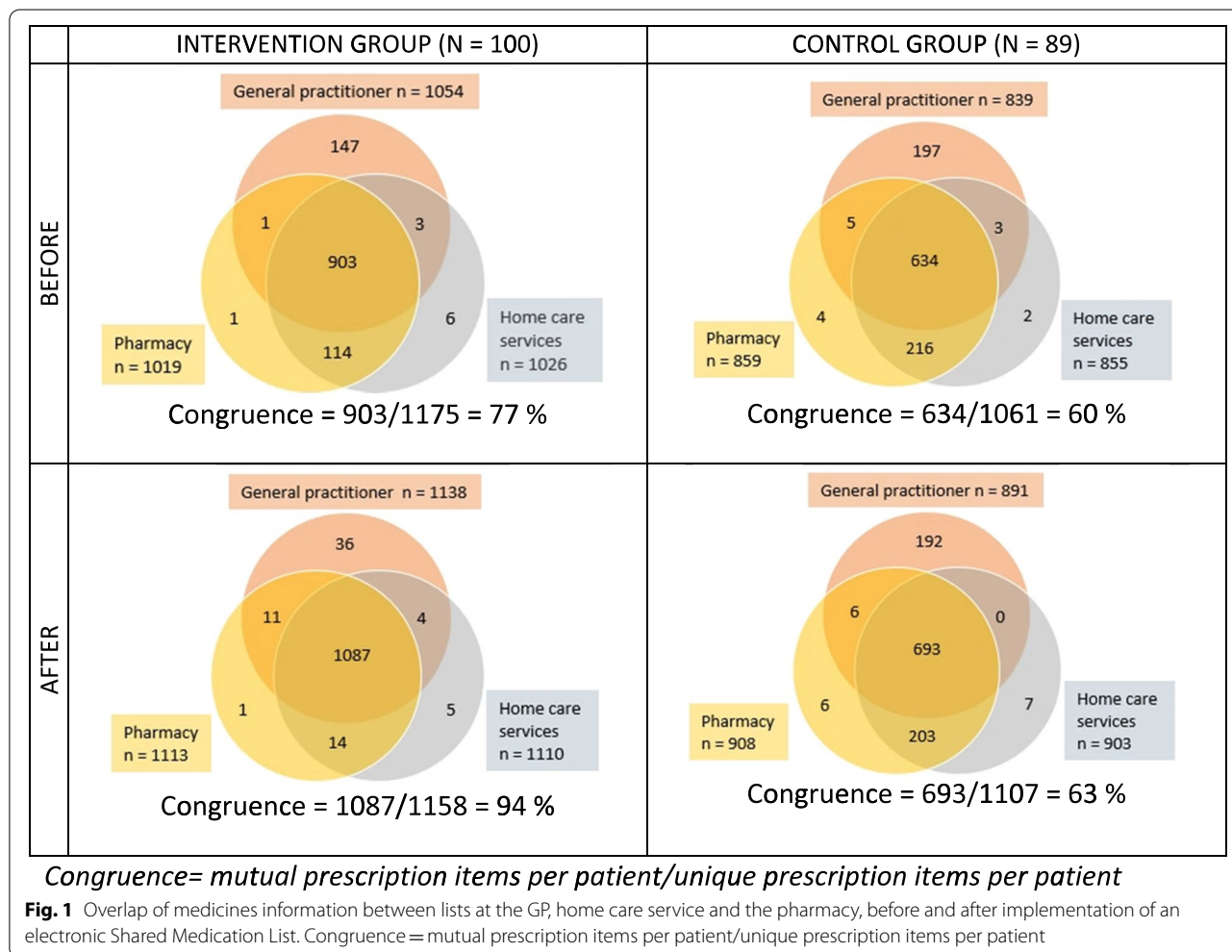
No significant reduction in the total number of discrepancies was found in the control group. The share of mutual prescription items in all three lists increased from 60 to 63% (Fig. 1), and the total number of discrepancies was reduced from 517 to 503, but the reduction was not significant ( $p = 0.734$ ) (Table 2). Like in the first data collection, the most frequent types of discrepancies in all list pairs were that a medication was lacking and that a different dosage were listed.

**Table 1** Pre-intervention comparison of age, gender and number of drugs

Parameter	Intervention, N = 100	Control, N = 89	P-value*
Age, mean (SD)	63.1 (20.6)	72.5 (19.2)	< 0.001
Gender Female, n (%)	52 (52)	53 (60)	= 0.297
Number of drugs, mean (SD)	10.5 (6.8)	9.4 (5.6)	= 0.891

\*p-values calculated with the use of a Chi-square test of independence and Student's t-test





The DID estimation ( $\Delta$ intervention -  $\Delta$ control) found the decrease in number of discrepancies attributable to the eSML to be  $-2.44$  ( $-3.70, -1.12$ ),  $p < 0.001$ .

As seen in Fig. 1 there is an increase in the number of items in all medication lists post-intervention. We analyzed the change in the number of prescribed items post hoc and found an increase of 0.25 in the intervention group relative to the control group, however, this was not statistically significant ( $p = 0.54$ ).

**Discussion**

This study shows that introduction of a shared medication list significantly reduces the number of discrepancies between the medication lists of the GP, pharmacy, and home care service: the number of discrepancies was reduced by two thirds and the share of patients with discrepancies in their lists decreased from 75 to 56%. The study thus adds to the existing evidence that e-prescribing has the potential to reduce medication discrepancies and prescription errors. It also adds to the limited

evidence about discrepancies in the home care setting [30]. Though our study is one of the first to investigate the effect of an eSML on discrepancies specifically [31], e-prescribing is known to increase the legibility, completeness and clarity of prescriptions [32–35], all of which one would also expect to reduce discrepancies.

**Limitations**

This study has some important limitations to be aware of when interpreting the results. When the eSML was implemented, the GPs in the intervention groups were recommended to do a medication reconciliation. No such recommendation was given to the GPs enrolled in the control group. It is thus difficult to separate the effect of the reconciliation from that of having an eSML. However, previous studies have shown that even after reconciliations, discrepancies remain or quickly arise again, and reconciliations need to be repeated regularly to keep the medication lists updated [236]. After 16 months, the effects of the single medication reconciliation that was

**Table 2** Type and frequency of discrepancies between the GP and home care services medication list, before and after the implementation of eSML for MDD patients

NUMBER OF DISCREPANCIES	INTERVENTION GROUP (N = 100)			CONTROL GROUP (N = 89)		
	BEFORE	AFTER	Mean difference (95%CI) <i>p</i> -value**	BEFORE	AFTER	Mean difference (95%CI) <i>p</i> -value**
Type of discrepancy	n (%)	n (%)		n (%)	n (%)	
Missing prescription	268 (69)	66 (54)		420 (81)	408 (81)	
Dosage	59 (15)	48 (39)		71 (14)	72 (14)	
Regular vs. as required*	50 (13)	5 (4)		18 (3)	19 (4)	
Pharmaceutical form	6 (2)	1 (1)		8 (2)	4 (1)	
Other	6 (2)	2 (2)		4 (1)	0 (0)	
Total	389 (100)	122 (100)	-2.6 (-3.57, -1.63) <i>p</i> < 0.001 <i>P</i> -value***	521 (100)	503 (100)	-0.16 (-0.76, 0.07) <i>p</i> = 0.734 <i>P</i> -value***
<b>NUMBER OF PATIENTS WITH DISCREPANCIES</b>						
Missing prescription	60 (60)	38 (38)		69 (78)	73 (82)	
Dosage	36 (36)	27 (27)		45 (51)	45 (51)	
Regular vs. as required*	30 (30)	5 (5)		17 (19)	17 (19)	
Pharmaceutical form	6 (6)	1 (1)		8 (9)	3 (3)	
Other	5 (5)	1 (1)		3 (3)	0 (0)	
Total	75 (75)	56 (56)	0.006	80 (90)	79 (89)	0.782

\* medicine listed as 'regular use' in one list and 'as required' in the other

\*\* paired t-test

\*\*\* McNemar test

done at implementation would probably have dissipated. It is thus likely that the decreased number of discrepancies is mostly due to how the eSML system supports the processes of keeping medication lists updated.

There were some differences between the control group and the intervention group before the implementation. A reason might be that the GPs started to prepare and perform a medication reconciliation before the implementation of eSML [23]. Also, the GPs who accepted to test the eSML may be more positive towards new technology. If this is the case, the effects of eSML on discrepancies might be larger than our results indicate.

The main assumption of a DID analysis is that of parallel trends, i.e., that the trend in the number of discrepancies would be the same for the intervention group in absence of the intervention as the trend in the control group. With this assumption, the differences in the groups at baseline do not necessarily confound the results, given that these differences represent a permanent difference between the two groups. If, however, the differences at baseline are related to e.g. the GPs in the intervention group having better routines for updating the medication lists in the paper-based system, the parallel trend assumption would be violated. Because we only had one data collection before the intervention, we could not test if the parallel trends assumption holds. There is thus uncertainty concerning the magnitude of the change

in discrepancies related to the intervention. Another limitation is that this is a relatively small study with patients from only two districts in one municipality, and generalizations should thus be done with caution.

**The effect of eSML on discrepancies**

Before the implementation of eSML, the patients had on average 3.9 discrepancies in their medication lists. In line with previous studies, cardiovascular agents, sedatives and analgesics, were among the medications most frequently involved in discrepancies [2]. Cardiovascular medicines and analgesics medicines are also frequently involved in adverse drug events [37–39]. Though reducing these discrepancies could reduce the potential harm, systematic reviews have shown conflicting results on outcomes such as re-hospitalizations and deaths [3, 40, 41]. However, considering the amount of time health care personnel use on medication reconciliation, a more accessible and correct medication list will probably reduce the workload related to these activities.

Much of the reduction in discrepancies were related to items of less clinical importance, such as dietary supplements and medical devices. Since many dietary supplements are dispensed in MDD, the patients will not get these dispensed if they are not listed in the eSML. For the medical devices and consumables, the patients need prescriptions on these items to get them reimbursed. If these



items are missing from the medication lists it might thus have economic consequences for the patients. After the implementation of eSML, one-third of missing prescription items in the home-care service list were related to “medical devices and consumables”. The great increase of this discrepancy type indicates a systematic error in the registration of these in the home care service list after the implementation. This error is probably related to the home care service not having access to the eSML in the prescription database. If this is the case, this problem will be resolved in time for further implementation of the eSML [21].

After implementing eSML, 56% of the patients still have one or more discrepancies in their list (Table 2). There are several potential reasons for these discrepancies. The pharmacists who piloted the eSML experienced that they had to intervene on the prescriptions more frequently in the new system, mostly because the GPs had prescribed an outdated item number or the wrong quantity of medication [42]. This is in line with previous studies showing that e-prescriptions increase the need for pharmacist interventions [43–45]. Such manual changes increase the chance of discrepancies in the medication lists. Another reason might be the delay of the discharge summary from the hospitals [11]. The GP will typically wait for the discharge summary before making changes to their medication list [46], the home care service and the pharmacy, however, will add medications to their lists based on the electronic nursing discharge notes from the hospital and new prescriptions in the national prescription database.

### Implications and further studies

Our study emphasizes the need to do a medication reconciliation and review before the implementation of the eSML, a need also expressed by the GPs who participated in the testing of the system [25]. In the paper-based system, the medications are dispensed based on the medication list in the pharmacy, while after the implementation, the eSML generated by the GP is used for dispensing. Our study found discrepancies in 75–90% of these medication lists. The transition from the paper-based to the electronic system can thus lead to unintended changes in the patient’s medication treatment if these discrepancies are not resolved before implementation.

To avoid errors in the eSML it is crucial with a clear placement of responsibility when it comes to keeping the list updated. In the current version, only the GP can update the list, but when the eSML is implemented nationwide, all prescribers will be able to make changes to the same list. The last physician adding, withdrawing or changing a prescription item will then have to take responsibility for the medication list as a whole. This

means they will have to delete prescriptions that are no longer relevant or appropriate, also those prescribed by other doctors. This is currently the case for ordinary e-prescriptions as well: a physician can delete a prescription another physician has written. However, this is often not done: in March 2021, it was estimated that 13% of patients have at least one duplicate prescription in the Norwegian prescription database [47]. These non-current and duplicate prescriptions pose a serious threat to the long-term trustworthiness of the eSML. Not only can these prescriptions lead to patients getting the wrong medicine or dose, but if physicians are reluctant to delete prescriptions issued by other doctors [48] this might with time result in more polypharmacy, inappropriate prescribing and decreased patient safety.

### Conclusions

This study suggests that an eSML reduces the number of discrepancies between the medication lists of the GP, the home care service and the pharmacy for MDD users. Before implementation, the overlap of unique prescription items in the tree lists was 77% in the intervention group; after, it had increased to 94%. For the control group, there was no change. Despite a great improvement, discrepancies were still present, showing that the eSML does not eliminate the need for medication reconciliations. The lessons learned from the MDD patients in our study is that medication reconciliation and medication review must go hand-in-hand to support the construction of the first eSML. Further studies, before the nationwide implementation should focus on how GPs, in collaboration with other health care professionals and the patient, create the first eSML based on the many medication lists that are available today.

### Abbreviations

eSML: Electronically Shared Medication List; MDD: Multidose Drug Dispensing; DID: Difference in Difference; EHR: Electronic Health Record.

### Acknowledgements

The authors would like to thank Eli Kristiansen and Sukumarie Sothinathan for their help in analyzing the medication lists. We would also like to thank all the GPs, home care nurses and pharmacists who participated in this study.

### Authors’ contributions

AVJ, TSB and AGG conceived the study design. Data collection and material preparation were performed by AVJ. AVJ and TSB performed the analyses. The first draft of the manuscript was written by AVJ. AVJ, TSB and AGG revised the manuscript. All authors have read and approved the final version of the manuscript.

### Funding

This study was internally funded by the Norwegian Centre for E-health Research.

### Availability of data and materials

Data are available upon reasonable request to the corresponding author.

## Declarations

### Ethics approval and consent to participate

The study was approved by the Data Protection Officer at the University Hospital of North Norway (UNN) (Project No. 02003), and the Regional Committee for Medical Research Ethics (REK) has waived the need to obtain consent for the collection and analyses of the medication lists (2017/1393/REK Nord).

### Consent for publication

Not applicable.

### Competing interests

AVJ is employed by Apotek 1 Gruppen AS, which currently provide services to about half of all MDD patients in Norway. The other authors declare no conflicts of interest relevant to this study.

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Received: 11 June 2021 Accepted: 23 November 2021

Published online: 13 December 2021

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Paper IV

# From Paper to E-Prescribing of Multidose Drug Dispensing: A Qualitative Study of Workflow in a Community Care Setting

Josendal AV, Bergmo TS

*Pharmacy* 2021 Feb 16;9(1):41. doi: 10.3390/pharmacy9010041



Article

# From Paper to E-Prescribing of Multidose Drug Dispensing: A Qualitative Study of Workflow in a Community Care Setting

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**Abstract:** E-prescribing is now widespread and, in some countries, has completely replaced paper prescriptions. In Norway, almost all prescribing is electronic, except for multidose drug dispensing (MDD), which is still sent to the pharmacy by fax or ordinary mail. MDD is an adherence aid used by one-third of all patients receiving home care services. In this paper, we present results from a qualitative study evaluating the introduction of e-prescribing for MDD in a community health care setting. The focus is on the work and workflow for the pharmacists and nurses involved in the medication-handling process. We used the pragmatic process evaluation framework and the systematic text condensation method to analyse the data. We conducted 12 interviews with 34 nurses and pharmacists. This study shows that the e-prescribing of MDD led to greater integration between systems, both within the existing MDD system and across care levels, potentially improving patient safety. However, the structured prescriptions increased the need for clarifications, resulting in an increased overall workload. A greater understanding of the roles and responsibilities of the different professionals in the medication management chain and their needs would improve the workflow of the nurses and pharmacists involved.

**Keywords:** e-prescribing; multidose drug dispensing; community care; interviews; nurses; pharmacists; work; workflow; collaboration



**Citation:** Josendal, A.V.; Bergmo, T.S. From Paper to E-Prescribing of Multidose Drug Dispensing: A Qualitative Study of Workflow in a Community Care Setting. *Pharmacy* **2021**, *9*, 41. <https://doi.org/10.3390/pharmacy9010041>

Academic Editor: Jeff Taylor

Received: 28 January 2021

Accepted: 12 February 2021

Published: 16 February 2021

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## 1. Introduction

Electronic prescribing (e-prescribing) can improve physicians' workflow, increase pharmacy efficiency, and improve patient safety [1–6]. In recent years, the use of e-prescribing has increased significantly in Europe, especially in the Nordic countries, Estonia, and the Netherlands [7]. It is also widely used in the United States, Australia, and Canada [8]. E-prescribing improves the eligibility and clarity of prescriptions [4–6], reduces prescribing errors [4], improves coordination, and ensures the privacy and security of personal health information [9]. However, it can also create new errors, such as incorrect dosage instructions, missing information, incorrect product (medicine or strength), and wrong quantity or duration of therapy [1,8,10,11].

In Norway, e-prescribing was implemented in primary care in 2013, and today, over 90% of prescriptions are sent electronically (27 million per year) [12]. The prescriptions are sent directly from the prescribers to a central database called the Prescription Mediator, which stores the prescription until it is dispensed, a physician deletes it, or the prescription expires (usually one year from the date of prescribing). All pharmacies have access to the Prescription Mediator, and the patient can collect the prescriptions from any pharmacy in the country. The only prescriptions still on paper are for individuals receiving prepacked multidose dispensed drugs (MDD).

MDD is an adherence aid used by one-third of patients receiving home care services in Norway [13]. Here, medicines are machine-dispensed in unit-of-use disposable bags, one unit for each dose occasion [13,14]. The MDD system is used in the Nordic countries and the Netherlands [15]. Compared to patients with ordinary prescribing, patients with MDD have fewer serious drug–drug interactions in their medication lists [16,17] and higher medication adherence [18,19] but are also more prone to medication errors in care-level transitions and inappropriate prescribing [17,20–22].

In the current paper-based system, the general practitioner (GP) prints out a list of the patient’s medication treatment and faxes it to the pharmacy. This printed list is the MDD prescription and is valid for one year [23]. The pharmacy staff manually transfer the medicines information from the paper prescription into the electronic MDD system at the pharmacy. They then order MDD from the manufacturer, who packs the medicines and sends them to the home care services, along with a paper copy of the prescription list. The nurses manually enter the medicines information from this list into their own electronic record system [23]. In addition to being very time-consuming, all these manual steps in the medicine management process increase the risk of medication errors [8]. Concerns have also been voiced about duplicate prescriptions when GPs prescribe an electronic prescription in addition to the paper prescription list [24].

There is now an ongoing effort in Norway to implement e-prescribing for MDD. Here, the paper medication list is replaced by individual e-prescriptions for each medication, which are stored in the existing Prescription Mediator [25]. From the implementation of e-prescriptions, we know that technical standards, system design, and training are important foundations to realise the full potential of e-prescribing [1] but also that these systems can create new workarounds because of inconsistent use, computer systems, and network limitations [1,9]. No studies have analysed the transition from paper to e-prescribing of MDD. However, the e-prescribing of MDD has the potential to improve the work and workflow for the staff involved. Going from paper and fax to electronic transmission of prescriptions should reduce manual entry work, which, in turn, should reduce prescription errors [8,26]. Moreover, e-prescribing can minimise interruptions from phone and fax communications, improving work efficiency [27–29].

The first pilot test of e-prescribing of MDD began in 2016, the second in 2018. At the time of writing the current paper, 26 GP offices, 2 pharmacies, and 4 home care districts in the southern part of Norway use the system. The current study is part of a larger case study exploring how the e-prescribing of MDD affects patient safety and the health professionals’ work, experienced benefits, risks, and challenges. We have previously investigated how e-prescribing affects the GPs involved; the participants found the new system to be less time-consuming than paper and fax, hence improving workflow and efficiency [23]. This current study investigates how the e-prescribing system affects the work and workload for the home care nurses and pharmacists involved.

## 2. Materials and Methods

### 2.1. Research Design

We used a qualitative research design to explore how the work and workload of nurses and pharmacists in a primary care setting are affected by e-prescribing of MDD. We used a pragmatic process evaluation approach [30] taking advantage of the real-world setting to identify core experiences from the implementation process. The focus was on how the health professionals experienced the change during the early phase of disseminating the e-prescribing system.

We used a theme-centred interview guide with open-ended questions. The interviews were semi-structured, and the order of topics and questions varied, depending on the informants’ responses. How the e-prescribing affected their work before, during, and after the start-up, experienced benefits, risks, and challenges and how they perceived the impact on patient safety were topics for the interviews. We emphasised that both positive and negative experiences were of interest. In the current paper, we focused on how the new



system affected work and workload for the nurses and pharmacists involved in the MDD process (Table 1).

**Table 1.** Excerpt from the interview guide relevant for this study.

<b>Aspects of E-Prescribing of MDD Affecting Work and Workload</b>	
<ul style="list-style-type: none"> <li>• How does e-prescribing change the way you work?</li> <li>• How does e-prescribing change the communication and collaboration with the GPs, home care nurses, or pharmacists?</li> <li>• How do you think the new system affects patient safety?</li> </ul>	

*2.2. Recruitment and Setting*

The national health authorities are responsible for implementing the e-prescribing system, but the process has been slower than expected due to technical difficulties. We took a pragmatic approach to recruitment, aiming to recruit all professionals involved in the implementation. The recruitment started in 2016 and is still ongoing. In this study, we focused on the pharmacists and the home care nurses. We consecutively sent e-mail invitations to designated contact persons at each site, asking them to forward the invitations to relevant health personnel. The invitations briefly described the project and main themes of the interviews. One reminder was sent to the non-responders. We sent invitations for follow-up interviews 10 months to 2 years after start-up.

A total of 26 nurses and 8 pharmacists accepted our invitation to be interviewed (see Table 2). We conducted 12 in person interviews; 7 group interviews with up to 6 participants at a time, and 3 individual interviews with one pharmacist working in homecare and two nurses/nurse managers. The choice of individual or group interviews was based on practical and time-saving reasons for those interviewed. We considered that groups would provide sufficient depth to the information we wanted to collect, and in addition, the informants could stimulate each other to provide experiences and views. Differences in views and experiences were as interesting as uniform opinions among the informants. We also sent invitations to participate in follow-up phone interviews. Only one community pharmacist in the home care service and two pharmacists at one of the pharmacies accepted and were interviewed a second time.

**Table 2.** Interview details.

No	Participants	Number of Participants (n)	Setting	Second Interview
1	Pharmacist	3	Pharmacy 1	
2	Nurse	6	Home service 1	
3	Nurse	6	Home service 2	
4	Nurse	5	Home service 3	
5	Pharmacist	1	Home service 4	Yes n = 1
6	Nurse	2	Home service 4	
7	Pharmacist	4	Pharmacy 2	Yes n = 2
8	Nurse	1	Home service 5	
9	Nurse	5	Home service 6	
10	Nurse manager	1	Home service 6	

*2.3. Data Collection*

Two researchers completed the group interviews, which took place at the participants' workplace. Phone interviews were conducted for practical reasons, and were completed by one researcher. The interviews lasted 30–45 min and were recorded on tape and transcribed

by a professional agency. We stored audio recordings separate from the anonymised transcribed data material.

#### 2.4. Data Analysis

Both authors (a pharmacist and a registered nurse) read, discussed, and structured the transcribed material and participated in the analysis of the data. The systematic text condensation (STC) method described by Malterud [31] was used to conduct a thematic analysis of the meaning and content of the data across cases. STC is based on principles of Giorgi's psychological phenomenological analysis [32] and includes a descriptive approach presenting the experience as expressed by the participants themselves [31]. The procedure consisted of the following steps:

1. Reading of the material several times to obtain an overall impression (from chaos to themes);
2. The identifying and sorting meaning units representing different aspects of the research question, and perform coding and sub-coding for these (from themes to codes);
3. Condensation and summarising the content in the coded groups (from code to meaning); and
4. Developing descriptions reflecting the participants' important experiences (from condensation to descriptions and concepts).

The transcripts were coded to maintain the content using NVivo 12 software. We created nodes that were arranged in a coding tree with three recurring themes: local workflow changes, change in collaboration and communication pattern, and increased access to information. To achieve trustworthiness, the researchers engaged in an ongoing process of discussion and reflection throughout the process of analysis. We focused on changes in workflow that persisted after the initial start-up and have not included challenges and problems directly related to the transition. We used the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist to ensure the structure and style of this manuscript.

#### 2.5. Ethics

The Data Protection Officer at the University Hospital of North Norway approved the project (Project No. 02003). All participants voluntarily accepted to be interviewed. The participants received both written and oral information about the study; they were informed about the reason for conducting the research, the researchers' roles, credentials, and experiences; about anonymity; and that they could withdraw from the study at any time. The data was handled according to local security requirements. To ensure anonymity of the home-care service pharmacist and the nurse manager in the interviews, we only included the setting when presenting quotes.

### 3. Results

The results section presents the findings from the analysing process described above. Changes in the workflow were categorised into three major themes:

1. Local workflow changes;
2. Change in collaboration and communication patterns; and
3. Increased access to information.

#### 3.1. Local Workflow Changes

For the pharmacists, one of the biggest advantages of the new system was the direct transfer of prescriptions into the pharmacy dispensing programme. This eliminated the first step in the paper-based workflow: sorting incoming faxes. Because the e-prescriptions were ordered by date, the pharmacist always knew which prescription was the current one, and the prescription-check could be moved from close to the order deadline to about two days prior to the deadline. This gave the pharmacist more time to do necessary clarifications with the GP. A third advantage with the electronic transfer was that any supplementary

documentation that used to be on paper (e.g., applications for compassionate use) was now also electronic.

However, the pharmacists said that correcting prescriptions was more difficult and time-consuming. In one of the interviews, the e-prescribing system was described as limiting the pharmacist's ability to perform professional judgements and their ability to correct obvious errors made by the GPs:

*"We are more vulnerable if the GP makes a mistake on the e-prescriptions ( . . . ) on a regular paper list we can make the change ourselves and ask the GP to sign it afterwards, and when we have received a signature, the problem is solved ( . . . ), but now (with e-prescribing) we must have a completely new e-prescription (if the medicines are to be dispensed)" Pharmacy 2*

Specifically, the pharmacists reported having to manually change the item number a lot more frequently. For each active substance, there are only a few item numbers that are dispensable as MDD. In the paper-based system, the pharmacist chose this item number when entering the prescription into the dispensing program. Now, the item number is transferred automatically from the electronic prescriptions. The nurses reported some patients who did not get their regular medications dispensed as MDD because the item number on the e-prescriptions was not dispensable as MDD. This was a particular problem in the first few months. When the pharmacy staff became aware of this problem, they created new routines to check for MDD-dispensable item numbers of the same medicine and manually change the prescriptions.

Because of missing medicines, some home care nurses had started to double-check the MDD deliveries. They reported that the extra checking led to staffing problems; they went from one to four nurses on delivery days after e-prescribing was introduced. Some emphasised that all the double-checking increased their responsibility for the patients' drug treatment. They further said that these new routines increased patient safety compared with the old system:

*"Before (e-dose), it was not necessary to check if, for example, the prescriptions needed a renewal – we did not have to check if there were any medications missing on the prescription list. Before it was it was the norm that all medicines were included, but now we have to check all the time that ok, the medicine is missing. Why is it missing?" Home service 4*

However, some nurses also experienced that e-prescribing led to faster changes of the MDD bags, which meant fewer manual corrections of the bags. They suspected that this was both because the process of transferring prescriptions was faster and also because the GPs sent the updates during the consultations rather than waiting until the end of the day:

*"It is our experience that if they do it electronically, then it is much easier, because then we know that it arrives quite quickly. With those who do not have e-prescribing, it may be that they have not sent that fax, or the fax has not arrived and then they have to send it by post. So, the (paper) process takes a lot more time" Home service 1*

### 3.2. Change in Collaboration and Communication Patterns

One of the built-in changes with the new system was electronic messaging between the pharmacy staff and the GPs. The pharmacists said that the GPs replied faster and that there were fewer misunderstandings when communication was electronic compared to fax. In addition, they said the messages could be sent and replied to at more convenient times so that they did not disrupt the GP in the middle of a patient consultation:

*"We get answers (from the GPs) quickly. We do not have to fax, call and all that, it saves quite a lot of time. In addition, we get answers to what we actually asked about to a much greater extent." Pharmacy 1*

Despite these improvements, the pharmacists agreed that communicating with the GPs took more time overall. This was because they did more clarifications, especially regarding

the renewal of prescriptions. The former paper prescription list was valid for a one-year supply of medicines, needing only an annual renewal. With the new system, each medicine had an individual e-prescription. Although one pharmacist expressed relief over not having to renew the prescription list by fax anymore, all the informants agreed that individual e-prescriptions were more time-consuming. First, it led to more inquiries about renewals; second, when a prescription was renewed, it needed to be checked by a pharmacist. One pharmacist explained that this was especially problematic because the GPs frequently prescribed very small quantities, even though the patients used them regularly:

*“ . . . we have to contact the GP much more frequently and say: you have prescribed medications for ten days, a multi-dose roll is for 14 days, and we need more tablets.”*  
Pharmacy 2

Prescription renewals were also one of the main workload concerns of the nurses. Whenever a prescription was updated, both the GPs and pharmacy staff sent messages to the home care nurses. These messages had to be checked to see if there was an actual change in the medication treatment. Because the number of messages had increased, so had the nurses' workload. The nurses also considered information about renewals that were irrelevant and voiced concerns that the increased number of messages without useful information made them overlook the relevant information:

*“We get a lot of information that we do not really need, which only creates a lot of work (for us). I think this can cause dangerous situations in relation to whether we are able to administer the medicines that we are obliged to.”* Home service 4

Both the pharmacists and many of the home care nurses also said that the renewal of prescriptions had led to many unnecessary phone calls between the two because the home care nurses did not have access to the Prescription Mediator, where the e-prescriptions were stored. One nurse said that:

*“ . . . we call the pharmacy and ask what prescriptions are there, and we also have to call the GPs a lot to check what they have included . . . . Before, we had it (the prescription list) physically in our hands, and there was no doubt which prescriptions were valid.”*  
Home service 2

### 3.3. Increased Access to Information

Storing all e-prescriptions in the same database had several implications for our informants. The pharmacists were notified of all changes in the patient's medicines treatment, even when the prescriptions were not dispensed in MDD. Though this resulted in them doing more prescription checks, they also noted that this change seemed to improve patient safety:

*“The disadvantage is that (...) all transactions in the Prescription Mediator are flagged as a change for us. On paper multidose, this course of antibiotics would never have been noticed because it was not reported to us. So, the safety is much better with electronic multidose because you will notice all changes. But the workload increases. It increases a lot.”* Pharmacy 1

Storing MDD prescriptions and ordinary prescriptions in the same place also implied that the pharmacists had direct access to prescriptions from doctors other than the GP. This was particularly beneficial after hospital visits. In the paper-based system, the e-prescription could not be used to dispense MDD, and the pharmacists would wait for the GP to fax an updated prescription list. In the new system, they had a valid prescription to dispense right away. However, when the GPs updated the prescription list after a hospital visit, this could also cause new problems because the hospital doctors and GPs had different prescribing privileges. The GP and hospital doctor could also prescribe the same medication to the same patient or the GP could renew prescriptions without withdrawing the old ones. This led to outdated and duplicate prescriptions in the Prescription Mediator, and the

pharmacists used more time to identify which prescription was the correct one. In one of the interviews, the pharmacists described one such situation:

*“P1: They (the GP) had not renewed the prescriptions, they had just prescribed new ones, and the old ones remained. P2: Three prescriptions on one medication and three on another, you know. P1. Maybe both from a specialist and from the GP, and another one from the GP...( . . . ) P3: Yes, for many patients the Prescription Mediator is full of clutter.” Pharmacy 1*

A last implication of using a common database for e-prescriptions was that regular community pharmacists now had access to the MDD prescriptions. This increased the pharmacist’s workload because the patients or their caretaker could collect the prescriptions. When it was time to order MDD, there were no valid prescriptions, and they had to contact the home care service and the GP to get new ones. In addition, both the home care nurses and the pharmacists expressed concerns that patients might misuse the system and collect addictive medications at their local pharmacy in addition to getting them in MDD.

However, in one of the pharmacist interviews, it was also stated that this might actually improve patient safety. With the paper-based system, the GPs sometimes unintentionally prescribed a medication both as an e-prescription and as a paper-based MDD prescription, which could lead to the patient taking a double dose. With the electronic system, this was no longer possible:

*“The good thing about the addictive medications is that we definitely catch it (now), we cannot dispense multidose if there is no valid prescription (...) We can see that it had been taken out, so in that sense it gives us better control, but it is very inconvenient for us.” Pharmacy 2*

#### 4. Discussion

The current study shows that e-prescribing of MDD affects the work of pharmacists and home care nurses. First, it changed the workflow locally at both the pharmacy and home care services. Second, the system changed the collaboration patterns between the different personnel involved. Third, it increased access to the medicines information for health personnel who were not directly involved. Despite many of the steps in the medication management being more time-efficient, the frequency of which they were performed increased, and the overall impression from both the nurses and pharmacists was an increased workload. However, most agreed that the additional work also increased patient safety.

Most of the experiences from the informants—both positive and negative—seem to stem from the fact that the prescribing of MDD and ordinary prescriptions is now closely integrated. More integrated systems mean that the prescriptions and communication pathways are more standardised, information is transferred more quickly between the actors, and access to medicines information is changed. This is similar to the GPs’ experiences, who also described the system as having an in-built safety mechanism, but could be more time consuming because they needed to incorporate prescriptions from other physicians [23,33]. Though the design and interface of the computer systems have been shown to influence workflow [3], and was an important issue for the GPs [33], this was not brought up by the informants in our study.

The most prominent change in terms of workload for both the pharmacists and nurses was the increased frequency of prescription renewals. This is an effect of going from one complete prescription list with one expiry date to individual standardised e-prescriptions of separate dates and quantities. Previous studies have shown that prescribing the wrong quantity of a medicine is among the most common errors in e-prescribing [10,11,34]. However, the GPs involved in the electronic prescribing of MDD also received insufficient training before the transition [23] and this challenge might thus improve with time as the GPs realise the importance of prescribing the correct amounts in the new system.



E-prescriptions have been shown to require more frequent contact with GPs than paper-based prescriptions [35,36]. This might be a result of an increased number of errors but could also be because the standardised prescriptions leave less room for interpretation, thus making corrections more difficult [6,37]. This means that the pharmacist might have to contact the GP to correct errors they would normally correct themselves. In the interviews, both the pharmacists and nurses expressed that they were now more dependent on the GPs and more vulnerable to the GPs' mistakes.

The fact that the pharmacists find correcting errors more time-consuming might also be because their local workflow had changed. In the paper-based MDD system, the pharmacist corrected many errors while entering the prescription into the dispensing programme. However, because this transfer step was now eliminated, correcting prescriptions became a procedure outside the normal workflow, thus feeling more time-consuming. In fact, it would seem that the standard workflow was improved within the pharmacy in the new system. The pharmacists worked continuously with the changes as they arrived rather than waiting until the deadline, resulting in a more even workload throughout the day. In addition, the standardised prescriptions, together with the automatic transfer, eliminated many of the manual steps in the prescription handling at the pharmacy. When the pharmacists expressed an increased workload in the new system, this seems to be because of a higher number of deviations from the standard workflow and possibly more time-consuming corrections.

For the nurses, faster transfer of the prescriptions and changed access to prescription information seemed to affect the local workflow the most. Because the prescriptions were transferred faster, the nurses found that the medicines were dispensed in MDD quicker, which resulted in fewer manual corrections of the MDD bags. However, the changed collaboration and communication pattern meant that prescriptions were now stored in the Prescription Mediator, which they did not have access to. This increased the need to contact the GP or pharmacy to ask about the patients' medication use. This need should be reduced when the nurses get access to updated medication lists, a process that is now underway as part of a national e-health strategy [38].

Some home service units also added an extra control step to check the content of the MDD bags, and this increased their workload further. They went from one to four nurses on MDD delivery days. Though this error was corrected after a few months, the nurses continued to double check the bags. This also increased the feeling of being more responsible for the patients' drug treatment. E-prescribing has previously been linked to increased workload and responsibilities for the nurses involved [39]. This can negatively affect the patients if the nurses are reallocated from other areas involved in direct patient care. Home care services have expanded in recent years but not the staffing levels, and this can affect nurses' job satisfaction, create adverse event incidents, and lower patient satisfaction [40,41].

The pharmacists also described an increased responsibility and patient safety. They performed an extended prescription check compared to the paper-based system, and identified potential misuse of narcotics, which would not have been possible previously. Additionally, the system prevented the GP from prescribing an e-prescription and an MDD prescription for the same medication, which had been a challenge with the paper-based system. Common to all these improvements is that they stem from having prescriptions for MDD users and non-MDD users in the same database.

Using the national database also means that the health personnel not directly involved in handling the MDD got access to the MDD prescriptions. This is particularly useful for clinicians, where a lack of access to an up-to-date medication list can cause medication errors [42]. Such errors are especially common during care transitions and occur more frequently for MDD users [21,22]. That hospital doctors can make changes in the MDD bags directly can also reduce discrepancies and errors in the medication lists during care-level transitions.

However, this could also cause misunderstandings and result in potentially dangerous situations for the patients, i.e., patients taking double doses if the old prescriptions are not withdrawn when new ones are issued. Because all physicians could make changes to the MDD prescript, the GPs involved in the e-prescribing system also expressed uncertainty about the status and validity of the current medication list [33]. Ultimately, when more actors can influence prescribing and dispensing, the system becomes more complex. In turn, this increases the uncertainty about what the other actors could and should do, resulting in an increased need for communication between the actors involved.

Communication and collaboration between health personnel is, however, essential for safe medication management, but establishing new routines and collaboration patterns takes time. Because most of our interviews were held only a few months after start-up, these new routines would not yet be fully incorporated. It would thus be difficult to see if there are any long-term benefits of closer collaboration, and this might explain why our informants' views on increased contact were mostly negative. Future research should focus on collaboration and how this affects the quality of prescribing, drug use pattern, and other aspects of patient safety.

#### *Strengths and Limitations*

This is an exploratory study with a pragmatic approach to recruiting participants. We invited everyone involved in testing the electronic MDD system and included those who accepted our invitation. We interviewed 34 nurses and pharmacists across several sites, and we believe that we have captured the most important experiences of those who have started using the system. However, only two pharmacies from the same pharmacy chain participated. We know that the MDD work practices vary between pharmacies [13] and the experiences of future pharmacists who start using this system might thus differ from what we have found here. We plan to continue to collect data and include more pharmacies as they begin using e-prescribing for the MDD users.

#### **5. Conclusions**

Our study shows that the e-prescribing system for MDD led to a greater integration between systems, both within the existing MDD system and across care levels. The increased integration has several benefits in terms of faster information exchange and easier access to more complete information about the patients, increasing patient safety. However, the structured prescriptions also meant that it was more difficult for the nurses and pharmacists to correct mistakes. This, in turn, resulted in more frequent contact between the actors involved and increased their workload. In addition, increased integration implies that those not a part of the current MDD system, such as hospital doctors and community pharmacists, could influence the prescribing and dispensing of MDD. A greater understanding of the roles and responsibilities of the other actors in the medication management chain and their needs could improve many of the challenges that the nurses and pharmacists in the present study experienced.

**Author Contributions:** Conceptualization, A.V.J. and T.S.B.; methodology, A.V.J. and T.S.B.; formal analysis, A.V.J. and T.S.B.; investigation, T.S.B.; data curation, A.V.J., T.S.B.; writing—original draft preparation, A.V.J. and T.S.B.; writing—review and editing, A.V.J. and T.S.B. All authors have read and agreed to the published version of the manuscript.

**Funding:** This study was internally funded by the Norwegian Centre for E-health Research.

**Institutional Review Board Statement:** 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. 02003).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data presented in this study are available upon reasonable request from the corresponding author. The data are not publicly available due to ethical reasons.

**Acknowledgments:** The authors would like to thank Elin Johnsen for developing the interview-guide and conducting interviews and Monika Knudsen Gullslett for helping with interviews. We would also like to thank all of the participants in this study sharing their experiences.

**Conflicts of Interest:** Authors declare no conflict of interest.

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