Multidose Drug Dispensing and Drug Shortages

A Quantitative Analysis

By

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Masters in pharmacy

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II. Acronyms

MDD - Multidose Drug Dispensing

ASHP - American Society of Health-System Pharmacists

DMP - Direktoratet for Medisinske Produkter (Norwegian Medical Product Agency)

API - Active Pharmaceutical Ingredient

DSB- Direktoratet for samfunnssikkerhet og beredskap (The Norwegian Direktoratet for Civil Protection)

MA - Marketing Authorization

NMD - Norsk Medisinaldepot

PRN - Pro Re Nata (drugs that can be taken as needed)

III. Summary/ Abstract

Objective: The primary objective of this thesis is to explore the impacts of drug shortages on Multidose Drug Dispensing (MDD) system, and assess how MDD practices, particularly those relating to wholesaler prioritization and the system for safety stock, affect drug shortages.

Methods: The study is primarily based on a descriptive quantitative analysis but supported by qualitative data that aimed at detailing the multidose production process.

Results: Among the drugs packed in the MDD system during 2022 and 2023, our study identified Panodil 1gm, Acetylsalisylsyre 75mg, and Calcigran Forte 500mg/400IE as the most frequently packaged drugs. Regarding the impact of drug shortages on MDD, we found that among all drugs packaged within Apotek 1 multidose for 2022 and 2023, over 78% did not experience any shortages. The national drug shortage report reached its peak in 2019 and was at its lowest in 2018, whereas Apotek 1's multidose system reported highest shortages in 2018 and the fewest in 2019. Compared to 2018, Apotek 1's multidose system has demonstrated a significant reduction in shortage reports, with a p-value of less than 0.01 for each consecutive year from 2019 through 2022. This clearly indicates an effective and sustained decrease in shortages over this period. On the other hand, our research on the impact of MDD on drug shortages is inconclusive, showing potential for both positive and negative effects.

Additionally, while foreign-packaged drugs account for only 8% of the total drugs in the MDD system, they represent 25% of the total number of tablets/capsules packed annually due to their larger sizes, enhancing MDD efficiency and reducing the probability of drug wastage. However, their impact on mitigating shortage problems was found to be minimal. This is because in 2022 and 2023, foreign packs could potentially resolve only 6% of drug shortage problems within the MDD.

Our packaging analysis indicates that 44% of drugs in the MDD system are supplied in formats that require deblistering of tablets and capsules. This process potentially increases the likelihood of drug wastage during the repackaging process.

Keywords: Multidose drug dispensing (MDD), drug shortages, foreign packages, safety stock, Apotek 1.

IV. Sammendrag

Mål: Hovedmålet med denne oppgaven er å utforske virkningene av legemiddelmangel på Multidose Drug Dispensing (MDD) systemet, og vurdere hvordan MDD-praksis, spesielt de som er knyttet til grossistprioritering og sikkerhetslager, påvirker legemiddelmangel.

Metode: Studien er primært basert på en beskrivende kvantitativ analyse, men støttet av kvalitative data som tar sikte på å detaljere multidose produksjonsprosessen.

Resultat: Blant legemidlene som ble pakket i MDD-systemet i løpet av 2022 og 2023, er Panodil 1gm, acetylsalisylsyre 75mg og Calcigran Forte 500mg/400IE blant de mest pakkede legemidlene. Når det gjelder virkningen av legemiddelmangel på MDD, fant vår studie at blant alle legemidler pakket i Apotek 1 multidose i 2022 og 2023, opplevde over 78 % ingen mangel. DMP Den nasjonale legemiddelmangelrapporten nådde sitt høydepunkt i 2019 og var på sitt laveste i 2018, mens Apotek 1s multidosesystem rapporterte størst mangel i 2018 og færrest i 2019. Sammenlignet med 2018 har Apotek 1s multidosesystem vist en betydelig reduksjon i mangelrapporter, med en p-verdi på mindre enn 0,01 for hvert påfølgende år fra 2019 til og med 2022. Dette indikerer tydelig en effektiv og vedvarende nedgang i mangelen over denne perioden. På den annen side er vår forskning på virkningen av MDD på legemiddelmangel ikke entydig, og viser potensial for både positive og negative effekter.

I tillegg, mens utenlandspakninger utgjør bare 8 % av de totale legemidlene i MDD-systemet, representerer de 25% av det totale antallet tabletter/kapsler brukt årlig på grunn av deres større størrelser, noe som øker MDD-effektiviteten og reduserer sannsynligheten for legemiddelsvinn. Imidlertid ble innvirkning av utenlandspakninger på å dempe legemiddelmangel funnet å være minimal. Dette er fordi i 2022 og 2023 kan utenlandspakninger potensielt løse bare 6 % av legemiddelmangel innenfor MDD.

Vår analyse av pakningsstørrelser viser at 44 % av legemidler i MDD-systemet leveres i formater som krever deblistering av tabletter og kapsler. Denne prosessen øker potensielt sannsynligheten for legemiddelsvinn under ompakkingsprosessen.

Nøkkelord: Multidose, legemiddelmangel, Apotek1, utenlandspakninger, sikkerhetslager.

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Chapter 1: Introduction

The primary objective of this study is to explore the impacts of drug shortages on Multidose Drug Dispensing (MDD) and vice versa, by assessing how drug shortages influence MDD practices and how MDD practices, in turn, affects drug shortages. In this chapter, we will outline why this study is important.

Drug Shortages and their Consequences: In recent years, the availability of essential medications has become a growing concern worldwide. Various factors contribute to this problem, and this has been exacerbated by the disruption of the supply chain caused by the COVID-19 pandemic. However, reports show that the pandemic has only been directly linked to 7% of the medication shortages, indicating deeper underlying issues (1). Medication shortages have serious consequences, including compromised patient care, the need for less suitable treatments, suboptimal outcomes, and increased costs (2). For example, the American Society of Health-System Pharmacists (ASHP) reported that over 90% of hospitals had to use alternative medications due to shortages (2). This shift, along with the purchase of more expensive substitutes, cost around $209 million in 2013 (2).

Norway, heavily reliant on imported medications with minimal domestic production, faces heightened vulnerability to drug shortages (3). Furthermore, drug shortages can result in delays in medical procedures, medication errors, and eventual harm to patients. Shortages also create significant frustration and stress for everyone involved, including purchasing agents, pharmacists, pharmacy technicians, nurses, physicians, patients and guardians (2). The efforts to cope with shortages impose a significant burden on pharmacy staff, who spend considerable time seeking alternative solutions. This effort results in an annual cost of approximately 64 million Norwegian kroner for Norwegian pharmacies (4).

Multidose System and its Vulnerability to Drug Shortages: MDD is an essential component of Norway´s healthcare system designed to ease medication management for patients. The multidose system involves the automated packaging of drugs into individual pouches tailored for each patient to ensure the right medication is given to the right patient at the right time, reduce medication waste, and optimize nursing efficiency by eliminating the need for manual dose filling (5). The adoption of the MDD system has been steadily increasing,

from 3000 patients using the service in 2002 to almost 100,000 patients in 2022 (5, 6). Majority of MDD users are the elderly who are residing at home care services (7). The elderly population is expected to increase dramatically, indicating further importance of MDD in the coming years. Additionally, there has been a marked increase in the demand for home care services among individuals below 50 years of age (8), which broadens the scope of MDD's relevance beyond just the elderly. Thus, problems related to MDD or any disruption caused by drug shortages is of critical significance to the Norwegian health care system.

One of the reasons MDD users are vulnerable to drug shortages is because patients relying on MDD typically maintain a two-week supply of medications at home, as opposed to three-month supply or longer, depending on the type of prescription, for patients purchasing from normal pharmacies. This limited supply exacerbates the impact of any drug shortages on this vulnerable patient group. Therefore, there is a need for effective solutions to ensure the continuity of care. Evidence suggests that nearly one-fifth of prescription challenges within MDD is attributed to drug shortages requiring pharmacists and prescribing doctors finding alternative solutions (9). Building on this data, this study aims to evaluate the impacts of drug shortages on MDD, and how they mitigate these shortages.

In Norway, the Norwegian Medical Products Agency (DMP) allows the import of foreign medication packages approved in the EU/EEA when no domestic alternatives exist due to drug shortages (10). However, within MDD frameworks, regulatory exemptions have been established that permit importing these foreign packages under any circumstances, giving MDD systems an advantage in managing shortages (11). This practice is detailed in Chapter 2. However, there is a notable research gap regarding the effectiveness of these foreign bulk medications in alleviating shortages within MDD systems. Therefore, this study aims to fill in this gap by examining the role of these foreign packages in mitigating shortage problems within MDD.

In multidose systems, multiple medications are packaged together in a single plastic bag for individual patients. In traditional retail pharmacies, when a specific medication is in shortage, patients have the flexibility to seek alternatives from other pharmacies. This decentralized approach allows for individual adjustments and quick solutions, enabling patients to obtain their required medications with minimal disruption. In contrast, within multidose dispensing

systems, the shortage of even one drug can significantly complicate the entire package. This not only makes the shortage more noticeable but also more demanding to address.

To mitigate these disruptions, multidose suppliers engage in several proactive strategies, including wholesaler's prioritization of MDD suppliers, ensuring they have the necessary stock for production. Additionally, MDD suppliers maintain a safety stock (known as "sikkerhetslager" in Norwegian) to address any disruptions in drug supply. However, the effectiveness of this prioritization and safety stock system remains unexplored. Therefore, this study aims to address this gap by assessing the role of safety stock and prioritization by wholesalers in mitigating drug shortages. Concomitantly, this study will assess the effectiveness of these mitigation strategies and explore whether these practices alleviate or exacerbate drug shortages.

Moreover, it is also crucial to determine which types of medications are most susceptible to shortages, particularly within the MDD framework. Knowledge on the most frequently packaged medications in MDD will allow for more targeted and effective interventions to improve access to these specific drugs. Currently, there is a lack of data on the most frequently packed medications in the MDD system. This study aims to address this gap by identifying which medications are most often packed in MDD, and further analysed their shortage status and mitigation strategies employed by MDD suppliers to address shortages.

Multidose System as a Mitigation Strategy for Drug Wastage: The Norwegian Health Directorate has identified reducing waste as one of the key objectives of implementing MDD system (5). This is mainly because patients not on MDD typically keep up to a three-month supply of medications prescribed on blue prescription forms, and potentially even more for medications on white prescriptions. In contrast, patients using the MDD system, as noted above, generally maintain a two-week supply of medications. However, the effectiveness of MDD in achieving this goal raises several questions. The study aims to address concerns regarding medication wastage within the MDD system, a topic often acknowledged informally within multidose providers but lacking concrete data. Specifically, the process of transferring drugs from their original packaging into MDD machines might introduce potential wastage. While the primary objective was initially to quantify wastage for each medication throughout

the repackaging process, such data was considered confidential, which limited the ability to quantify the wastage.

This notwithstanding, it is important to recognize that the risk of wastage is inherently higher within the MDD system due to the additional steps involved in repackaging drugs compared to retail pharmacies, where medications are dispensed in their original packaging. Although quantifying wastage may not be feasible, the study will explore the types and sizes of packaging used for drugs within the MDD system. This analysis aims to provide insight into the likelihood of wastage based on packaging characteristics.

Chapter 2: Background of the Study

This chapter will begin by outlining the general workings of the pharmaceutical supply chain, followed by a specific examination of the supply chain in Norway. Subsequently, we will delve into a detailed discussion of MDD, including its functioning and the multi-dose production process. Additionally, we will provide background information on operational differences between the two multi-dose suppliers, as this context is crucial for understanding the study's results and discussion.

2.1. Pharmaceutical Supply Chain

Raw materials serve as the foundation for producing active pharmaceutical ingredients (APIs), which are the active substances responsible for the therapeutic effects in patients (10). The production process involves several steps, including the addition of necessary excipients and other additives to create the final pharmaceutical formulations such as tablets, capsules, powders, and injectables. Drug manufacturers have the option to either procure raw materials and manufacture the APIs themselves or purchase pre-made APIs and process them into the final products (10). These are then packaged into appropriate containers like glass bottles and blister packs, labelled, and boxed, ready for shipment.

The packaged pharmaceuticals are transported from the manufacturing site to a central warehouse and then distributed to their destination country. Upon arrival in Norway, they are stored at wholesalers' facilities and later distributed to primary pharmacies and hospital pharmacies across the country using the just-in-time (JIT) delivery principle (10). This delivery principle ensures pharmacies receive medications precisely when they are actually needed. This approach helps minimize inventory levels at each site, effectively managing costs and reducing waste (12). This principle, despite its strategic importance in minimizing waste, also presents challenges during sudden spikes in demand, such as in the case of natural disasters or pandemics, when the need for certain medications increases sharply. Additionally, any disruption in the supply chain can severely impact the availability of medications, especially if there are insufficient stocks on hand to cover the shortfall until normal supplies resume. Drug manufacturing involves several transportation stages, starting with APIs mostly produced in Asia, followed by final assembly in another country, making the process vulnerable to delays

and complications in delivering drugs to Norway (10). The Norwegian Directorate for Civil Protection (DSB) described drug supply chain as shown in the **Figure 1** below.

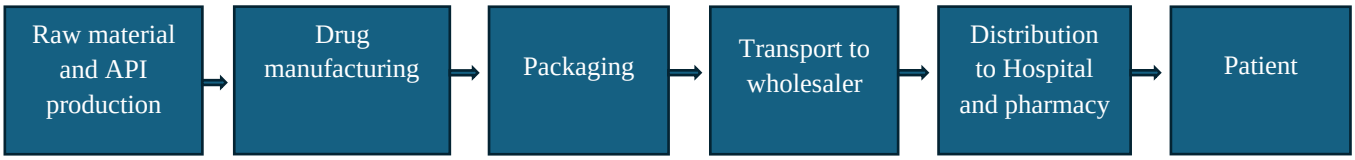

Figure 1 General Overview of Drug Supply Chain (Sourced from DSB with permission)

2.2. Pharmaceutical Supply Chain in Norway

The distribution of drugs in Norway typically flows from manufacturers to wholesalers and then to end-users, facilitating broad access to medicinal products throughout the country. Given Norway's limited local drug production, the country leans heavily on international imports to meet its pharmaceutical needs (10).

The Norwegian Health Directorate classifies the pharmaceutical supply chain into three main categories: production, distribution, and sales and consumption within the country (3)

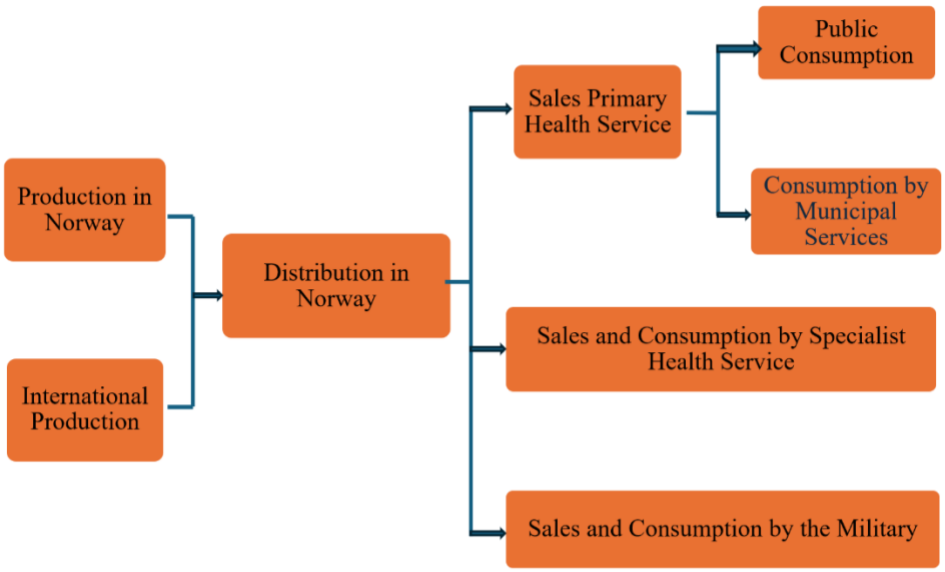

Figure 2 Simplified Drug Supply Chain in Norway (Taken from Norwegian Health Directorate)

Most active ingredients and intermediates that are essential components for drug manufacturing are sourced from countries like China and India, where production costs are lowest (13).

Even pharmaceuticals manufactured within Norway heavily rely on imported raw materials (10). Local production primarily targets export markets, where higher profit margins can be obtained for example, companies like GE Healthcare dedicate their entire production of X-ray contrast agents to exports (14). In Norway, the production of medicines within community and hospital pharmacies, often overseen by entities like Serviceproduksjon AS (SPAS), remains limited (3). This small-scale production typically supplies medications unavailable from commercial manufacturers, although such production has declined in recent years, according to the Norwegian Directorate of Health (3).

Pharmaceuticals produced in Norwegian pharmacies, including hospital settings, are custom-made to meet specific patient needs (3).This production is closely connected to the global market, dependent on the availability of essential raw materials from abroad. Regardless of whether they are produced locally or internationally, pharmaceuticals undergo a distribution process that ensures their availability across the Norwegian healthcare system as shown in Figure 2.

The drug supply chain involves long and complex process, with no single country able to fully control or monitor production and distribution (10). This opacity complicates efforts to mitigate disruptions, delaying the detection of issues within the chain (10). The predominance of active ingredient production in China and India adds to the vulnerability, increasing the risk of shortages if disruptions occur. There is also additional risk associated with relying on long-distance logistics, which depends on reliable information technology systems (10). Cyberattacks and other failures can have serious, immediate effects that could impact patient care worldwide as well as in Norway (10)

It is crucial that a collaborative approach involving all stakeholders in the supply chain, including countries and policymakers, be adopted to address and prevent drug shortages. According to an analysis done by DSB, there is a moderate chance (40-60 %) that Norway will have a severe medicine shortage within the next 50 years (10). They also recommended strategies categorized into probability-reducing and consequence-reducing measures. The former includes initiatives like enhancing international cooperation to secure drug supplies,

maintaining larger stockpiles of essential medicines such as antibiotics and insulin, and imposing requirements for increased stock to improve response times during shortages. The latter focuses on establishing systems to inform patients about shortages to prevent misinformation, implementing national rationing in primary healthcare to curb hoarding, and other similar actions (10).

2.3. Multidose Drug Dispensing System (MDD)

Multidose drug dispensing (MDD) is an organized method of preparing medications where drugs meant to be taken simultaneously are packed into individual pouches (5). Each pouch is distinctly labelled with the medication details, the user's name, and the specified date and time for intake, as illustrated in **Figure 3**. This service, particularly aimed at supporting individuals who need help with dosage and adherence to their medication schedule, is provided by pharmacies (5). Multidose patients receive packages lasting from two - four weeks.

Pharmacies compile a full list of a patient's prescriptions for multidose packaging. Medications unsuitable for multidose packaging such as patches, antibiotics, drops, PRN (Pro Re Nata) drugs and non-oral medications can be supplied in their original containers along with the multidose packs (5). Prescribing medications for multidose packaging can be done either through traditional paper-based means or electronically via e-prescriptions. Regardless of the method used, the multidose packaging system for patients remains the same (5). MDD has been an integral part of the Norwegian health care system since early 2000 (5).

The multidose system is designed to enhance the quality of medication management, especially for patients managing complex regimens. The primary aim is to improve health outcomes by fostering adherence to medication schedules, decreasing the potential for errors, and making healthcare workflows more efficient and reduce medication wastage (5, 15)

Figure 3 Multidose Packaging (sourced from Apotek 1)

In Norway, the management of multidose packaging systems is handled by pharmacies under a contractual agreement with municipalities. While pharmacies also offer MDD to private patients, the majority are served through schemes involving municipalities. Currently there are six authorized multidose provideres: NMD (Norsk Medisinaldepot), Apotek 1 Gruppen, Sykehusapoteket Østfold – Kalnes, Sykehusapoteket Skien, Sykehusapoteket in Trondheim and Sykehusapoteket Ahus-Nordbyhagen (7). However, Apotek 1 and NMD are the two pharmacy chains actively delivering multidose to patients at home care services and those in nursing homes (7). Typically, there is a centralized multidose packaging facility, often co-located with a pharmacy, that manages dispatch and delivery for the entire country. Both NMD and the Apotek 1 operate such centralized facilities (7).

In general, the distribution of medications including in multidose system typically starts with the manufacturers, representatives, or importers who provide the drugs. Wholesalers then buy those medications and distribute them to pharmacies. In Norway, the law requires that these deliveries from wholesaler reach retail pharmacies a well as multidose pharmacies within 24 hours throughout the country (7, 16). However, the supply chain is complex, and many factors can delay the delivery of drugs. One significant and widespread issue affecting this process is drug shortages, which is the subject of this thesis.

2.4. The Multidose Production Process

The multidose system customizes medications by individually packing and labelling products for specific patients. Unlike retail pharmacies, this system takes an additional step: after receiving pharmaceuticals from wholesalers, the medications are customized to suit the unique needs of each patient. This process involves several steps, from receiving the pharmaceutical

items from wholesalers to the dispatch of the final product. The following chart shows the multidose production and dispatch process used by Apotek1 multidose.

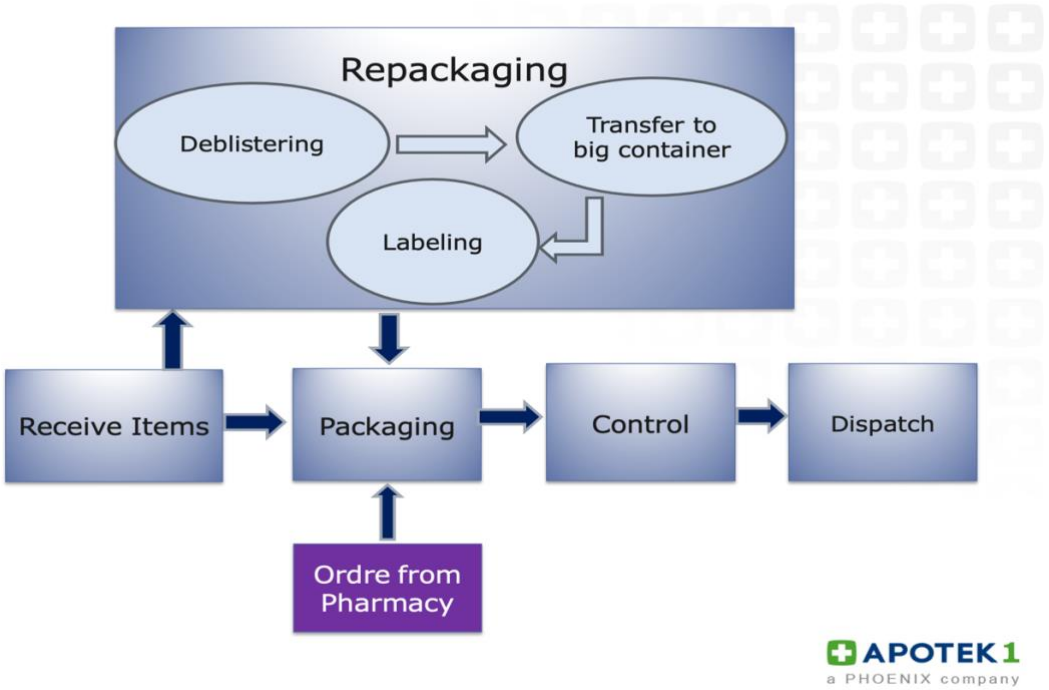

Figure 4 Multidose Process (Sourced from Apotek 1)

Apotek1's multidose production process starts when pharmaceuticals arrive from the wholesaler located at Skårersletta in Lørenskog. Pharmaceuticals arrive in different packaging types and have to be repacked. Repackaging is a detailed and labour-intensive part of the process. It involves transforming medications from their retail packaging into a format that is suitable for the next steps in the multidose system.

During this stage, medications that arrive in blister packs and small quantities are removed from their original packaging. This process is done with the support of deblistering machines and trained technicians. As described by the head of the MDD system for Apotek1, this step is time-consuming and resource-intensive, as each medication unit must be handled individually.

The primary goal of repackaging is to transfer the units into larger boxes so that it will be easier to feed the Cassettes as shown in **Figure 5** and make the subsequent packaging phase easier. The technicians are responsible for ensuring that every tablet or capsule is accounted for during the transfer from the blister packs to the larger boxes.

Figure 5 Cassette Prepared for Multidose Machine (Taken by the Researcher)

Each larger box is labelled with details including the drug name, strength, and batch number. This precise labelling facilitates accurate traceability back to the medication's origin, ensuring safe and correct drug delivery. Compliance with regulations mandates that repackaged medications are correctly labelled to guarantee safe and secure usage (17).

Medications with the same batch number are grouped together. Larger bulk packs containing typically more than 100 units, bypass the repackaging step as their size already supports efficient handling in later stages.

In the deblistering process, there is a risk that tablets or capsules may be damaged or dropped. The technicians are responsible for ensuring that every tablet or capsule is accounted for during the transfer from the blister packs to the larger boxes. After the machine takes the medication out of the blister packs the technician checks each and every strip manually to make sure no medication is left behind, thus minimizing waste. Therefore, drugs that come with blister packs and those that come with small units (few tablets) per container has to go through this extra step increasing the likelihood of drug wastage and increased time and resource during the repackaging process.

In the multidose production process, the step of removing medications from their original packaging inherently increases the risk of wastage, particularly in comparison to the standard dispensing practices in retail pharmacies where medications are provided to customers in sealed packages.

Additionally, when drugs are removed from blister packs and placed in larger containers, labelled manually with drug details, there is a risk of accidental label detachment. In such cases, the entire batch may need to be discarded. Therefore, drugs in blister packs and smaller packaging are especially prone to waste. Compared to boxes with larger quantities, the risk associated with blister packs might be elevated due to the deblistering step, while smaller packs pose a higher risk because they require more frequent transfer into collective containers.

Once repackaged, the pharmaceuticals are transferred to the packaging room. Here, the cassettes are loaded into a production machine equipped with a system called 'Filia'. This system integrates patient-specific information from the pharmacy's order. The machine is programmed with patient-specific details, which is utilized to guide the packaging process into multidose pouches. The packaging of the multidose packs is then carried out in accordance with the orders received from multidose pharmacies.

As the rolls of multidose pouches are created, they undergo a crucial verification step - an automatic and AI-driven photographic visualization check. This system is designed to ensure the accuracy of the packaging process; it captures images of each dose pack and its contents, confirming that the medications match the prescribed drugs for the respective patient. Any packs that do not pass this verification are set aside for further quality control.

These selected packs are then inspected manually by qualified personnel who conduct a thorough review of any discrepancies noted by the machine. This step determines whether the initial fault was due to an actual packing error or simply a misalignment of the tablet or capsule within the pouch. Once confirmed to be accurate, the multidose packs are cleared for dispatch.

The final stage in the process is the dispatch, where the verified and approved multidose pouches are sent out for delivery. The entire process described above ensures that patients receive the correct medications while ensuring efficiency and accuracy within the multidose packaging process.

2.5. Managing Drug Shortages: Operational Variance Among MDD Suppliers

Apotek 1 and NMD are the leading providers of MDD in Norway, each having different arrangements regarding the responsibilities of multidose pharmacies compared to centralized facilities. In the multidose service initiation phase, pharmacies under the NMD system offer their customers the convenience of multidose packaging by becoming multidose dispensing pharmacies. For these pharmacies, the primary task is to ensure that they have an up-to-date medication list from the patient, register them for the service, and establish a service agreement. Once this initial phase is completed, the more complex responsibilities, such as reviewing the medication details for potential interactions and the preparation of the multidose packs, are managed by the centralised facility, Vitusapotek AB28 (also known as VA AB 28). The multidose dispensing pharmacies then receive the prepared multidose rolls from VA AB28 to be delivered to the patients. In contrast, pharmacies within the Apotek 1 chain handle the entire process independently. They are directly responsible for every aspect of the service for their customers. This includes going through the patient's medication list, checking for possible interactions, and ensuring all details are in order before sending the order to the centralised multidose production facility.

The pharmacists both at VA 28 AB and those at Apotek 1 after receiving the multidose orders, they will check for each and every drug packability within MDD. There is thorough list where they check if drugs can be packed in multidose or not, for example effervescent tablets, drugs that are considered dangerous with regard to health safety and environmental reasons and others will be sorted before the order is sent to the multidose production.

The flow of drug related information within the MDD system is complex, involving various stakeholders such as general practitioners, patients, home care services, hospitals, rehabilitation centres, nursing homes, and other relevant parties. Given that patients may be discharged from hospitals with specific medication lists that could subsequently be altered by their general practitioners, ensuring a smooth and accurate information flow is crucial for patients to receive the correct medications promptly. For multidose suppliers, this information flow is especially relevant, as they must pack medications that have been newly updated for the patient. Otherwise, patients may end up taking medications that have not been revised, or it may result

in complete waste of the packed medication if the patient is no longer taking it. The information flow, as outlined by Apotek 1, is depicted in **Figure 6** below. Information flow between different care levels and MDD pharmacies is complex and susceptible to communication errors, particularly in systems that are predominantly paper based. However, the implementation of an electronical shared medication list (ESML) within MDD is reported to significantly enhance communication by increasing access to medication information and reduce discrepancies (18).

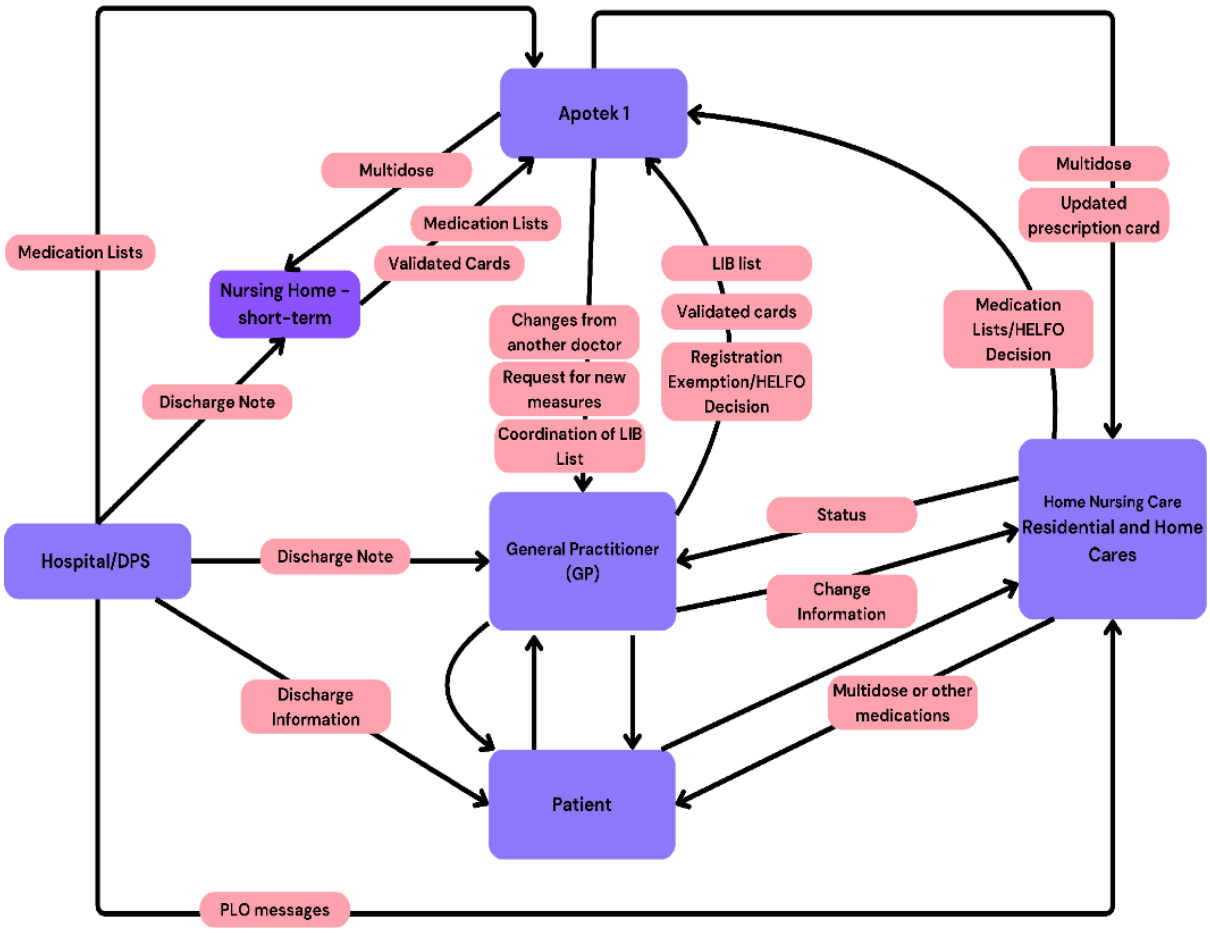

Figure 6 Medication Information Flow within MDD (Sourced from Apotek 1)

In both the NMD and Apotek 1 scenarios, the process for multidose service for private customers begins when a patient visits a local pharmacy and signs up for the service, providing an updated list of their medications for inclusion in multidose packets. For patients in home care services and nursing homes, however, the process is initiated by their doctors who send a valid prescription card to the pharmacy. Both providers have systems in place to ensure that

prescription cards are regularly updated, including a requirement to validate these cards at least once a year. Apotek 1 manages prescription cards for multidose orders using an application called `Nagara´, while NMD uses a system named `Pharmados´.

In the event of drug shortages, a coordinated effort is made across the multidose service spectrum to manage and mitigate the impact on end users. This includes the multidose department, which has dedicated personnel working closely with wholesalers to receive daily updates on drug availability. This proactive communication allows for strategic planning and adaptation to the fluctuating availability of medications. However, the above-mentioned differences can lead to different entities bearing the primary responsibility for manging drug shortages.

In the case of Apotek 1, should a drug become unavailable at the wholesalers, the multidose department swiftly notifies the multidose pharmacy. It then becomes the pharmacists' responsibility to explore alternative solutions, such as substituting with generic equivalents, adjusting medication strength, or, in critical scenarios, discussing with the prescribing doctor to find alternative treatment options.

To this end, Apotek 1 has created a specialized group known as the 'drug shortage group' ('mangel gruppe'), comprising representatives from the multidose department. This team meets weekly to discuss and manage drug shortages. Their primary responsibility is to identify medications nearing stock depletion and assess their stock status in light of shortage reports. This involves checking current inventory levels, consumption rates, and the anticipated duration of shortages to determine if the existing supply can cover the shortfall period or if alternative measures are necessary. The group ensures the pharmacy's medication supply remains uninterrupted by securing additional stock for their safety stock (sikkerhetslager) or considering other viable options. Safety stock levels at Apotek 1 multidose are continuously adjusted based on several factors like the criticality of the medication, the stability of its supply, the number of patients dependent on the drug, and the availability of generic alternatives and shortage notifications. To mitigate shortage notifications within Apotek 1 multidose, additional funds have been allocated to increase the safety stock. This strategy aims to decrease the time and resources spent on communicating with customers and pharmacies about shortage issues.

This structured and anticipatory approach exemplifies the commitment to maintaining a reliable and effective multidose service, emphasizing the importance of adaptability and planning in pharmaceutical care. In Apotek 1, the responsibility for identifying alternative solutions and addressing other drug related issues is distributed among pharmacists providing multidose services. In contrast, at NMD, this responsibility is centralized at VA AB28, which handles these tasks on behalf of all multidose pharmacies.

In the upcoming chapter, we will review existing literatures related to drug shortages and MDD systems, highlighting the current research gaps and outline the contributions of this study towards bridging those gaps.

Chapter 3: Literature Review

In this chapter, we explore the literature related to the MDD system, beginning with its advantages and challenges. We then discuss the broader issues of drug shortages, examining their causes, impacts, and the strategies implemented to mitigate these shortages. Finally, we discuss how drug shortages affect MDD, specifically highlighting Apotek 1's multidose efforts to mitigate these problems.

3.1. Multidose Drug Dispensing (MDD) Advantages

The MDD system in Norway, as of September 2022, facilitates medication management for about 100,000 individuals (19). This system is particularly critical given the projected demographic shift, with the elderly population (those aged 75 and above) expected to nearly double by 2060 (20). Notably, this age group comprises over 80% of MDD users, most of whom utilize home care services, highlighting MDD's crucial role in current and future healthcare provision (21).

The MDD service has witnessed widespread approval since its inception, earning positive reception from patients, healthcare professionals, and caregivers (15). As outlined in chapter 2 section of this thesis, MDD was introduced as a solution aimed at enhancing patient medication adherence, alleviating the workload of health professionals, and reducing medication waste (5).

The implementation of MDD system stands out for its time saving potential, which significantly benefits healthcare professionals in home care settings. It frees up time otherwise spent on manual tasks, such as filling pill organizers (22). Professionals can then dedicate enhanced attention to patient care, thereby improving service quality (15). Moreover, the MDD system is associated with a reduction in medication errors during dispensing and administration, as well as minimizing the waste of unused medications (5).

One of the most pressing challenges in medication management is ensuring patient adherence to their prescribed regimen. The MDD system is considered beneficial in this aspect by promoting adherence. According to a literature review, within the pool of studies analysed, five of them reported an improvement in medication adherence (23).

Research reveals that the MDD system has increased confidence among more than 70% of healthcare professionals in the accuracy of their patients' medication regimens. This confidence is further backed by reports of streamlined medication management routines and a more efficient overview of patients' medications, owing to the system's provision of patient-specific packaging detailing medication types and administration schedules (24).

The advantages of the MDD system are evident in various aspects of healthcare delivery. Not only has it instilled greater confidence in healthcare professionals regarding medication accuracy, but it has also lightened their workloads, led to more precise medication list updates, and yielded other beneficial outcomes (15). The system has also proven instrumental in bridging the gap between general practitioners and home care providers, promoting consistency in medication records and enhancing overall medication management (24). Studies indicates that the incidence of medication administration errors in facilities utilizing the MDD system is lower compared to those who have not adopted the system (6). Studies also report that the introduction of MDD systems contribute to more efficient medication administration processes and improved patient safety (25).

3.2. Multidose Drug Dispensing (MDD) Challenges

It is essential to note that MDD has been introduced to enhance drug handling safety for both patients and healthcare providers. However, studies indicate that patients receiving medications through MDD may face challenges in maintaining their understanding of their prescribed medications and remaining vigilant against medication related adverse effects (26). These challenges arise due to the simultaneous ingestion of multiple medications, making it difficult to attribute specific side effects or adverse reactions to particular medications. Additionally, healthcare providers, such as nurses, may encounter difficulties in identifying drug related issues under this system (26). These factors collectively raise concerns about the potential impact on the overall quality and safety of treatment.

Patients utilizing the MDD system often have a complex medication regimen. A research conducted in Norway examining MDD usage among elderly patients revealed that, on average, each individual was prescribed approximately 10.6 medications (27). A notable proportion of these patients were at risk due to the presence of potentially inappropriate medications (PIMs) and the occurrence of drug-drug interactions (DDIs) (27, 28).

As outlined in Chapter 2 of this thesis, medications dispensed through the MDD system are removed from their original packaging and repacked into plastic bags, often combined with other medications that the patient is scheduled to take concurrently. This repackaging process can obscure the identity of individual medications, potentially hindering healthcare professionals' ability to accurately determine which drugs a patient is actually consuming. Studies support this concern, indicating that patients managing their medication through MDD could struggle to keep track of their prescriptions, posing a risk for adverse medication effects (5, 26). The simultaneous consumption of multiple drugs complicates the ability to pinpoint the causes of specific side effects or reactions to individual medications and impairs the ability of health professionals to provide medical information and observe medication effects (5). These issues collectively signal potential risks to the quality and safety of patient treatment (26).

Although MDD aims to increase safe and accurate patients medication management, there are studies raising significant safety concerns, that the prevalence of suboptimal drug treatment is considerably higher in patients using MDD compared to those without and observed more instances of overtreatment than undertreatment (26). This is particularly alarming given the vulnerability of the patient group relying on MDD. Such patients are more likely to have compromised organ functions, making overtreatment a serious and potentially life-threatening issue.

Another significant challenge associated with the multidose system is communication, as detailed in Chapter 2, Section 2.5 of this paper. The multidose system involves numerous stakeholders, particularly when patients transition between different levels of care. It is crucial to transfer updated treatment information to the patients, their general practitioners, and the multidose pharmacies to ensure the revised medication lists reach the patients. However, a Danish report reveals that only 14% of the modifications made to a patient's multidose regimen at the hospital were communicated to the primary care physicians or pharmacies (25).

3.3. Challenges and Causes of Drug Shortage

Drug shortages worldwide present critical obstacles to healthcare provision, patient health, and economic stability. Drug shortages can delay treatment, worsen patient outcomes, and increase the likelihood of adverse effects. These shortages also financially strain healthcare systems. As

a pharmacist, I have witnessed the distressing impacts of these shortages first-hand. Patients are often left without essential medications, compelling them and their caregivers to visit numerous pharmacies or resort to costlier alternatives, which can lead to frustration, and anger.

A study from a Norwegian Consumer Council survey conducted in December 2021, reported that 91% of prescription medication users in Norway had encountered drug shortages (29). The DSB's risk analysis estimates that drug shortages in Norway, particularly of insulin and certain antibiotics, could lead to direct hospitalization costs of approximately NOK 2.2 billion and indirect economic losses from work absenteeism around NOK 200 million (10).While some may attribute this issue primarily to the COVID-19 pandemic, research indicates that the pandemic accounts for only 7% of these shortages, suggesting that other significant factors are at play that require urgent attention and action (1).

Looking in to the global drug shortage situation, a quantitative study that surveyed transnational drug shortage registers across Europe and the United States, reported a total of 5,132 incidents of drug shortages (30). The distribution of these shortages was as follows: Finland reported 1,522 instances, Spain 814, Sweden 890, Norway 800, and the United States 1,106 (30). This number is disproportionately higher in Norway considering it population size compared to those other countries, highlighting a critical area for further investigation within the context of public health and drug supply chain management.

The mapping study conducted by Apotekforeningen shows that 96.4% of patients promptly received medications prescribed by their doctors at pharmacies, while 3.6% did not (31). In 2023, approximately 197,000 customers visited Norwegian pharmacies daily (32). Given these frequent visits, the 3.6% represents a substantial number of patients experiencing medication shortages. In addition, the reliability of this data heavily depends on the pharmacy staff's consistency in reporting each incident. While the report on patients who received their medications is automatically recorded by existing systems in pharmacies such as Farmapro, without needing staff input, incidents of patients not getting their desired medication must be registered manually. In busy pharmacy settings, staff may swiftly proceed to the next customer, omitting to log shortages, potentially leading to an underreporting of these incidents. Apotekforeningen acknowledges this limitation, highlighting the potential discrepancies in the reported data.

Drug shortages stem from a variety of complex factors, such as production complications, regulatory hurdles, and international politics (10). According to de Vries et al., these can be categorized into 'normal' causes, like those due to external events including pandemics, and 'abnormal' causes related to market demands, manufacturing issues, and distribution challenges (33). The COVID-19 pandemic exposed how vulnerable the pharmaceutical supply chain is to disruptions as it caused sudden shock affecting the entire world (34). Although reports indicate an increasing trend in shortages of generic drugs, the European Medicines Agency (EMA) has stated that 63% of the reported shortages are actually for branded drugs (34, 35). The lengthy and complex drug approval process for alternative medications worsens drug shortages by deterring manufacturers from entering the market, thus delaying timely solutions (36).

When it comes to European countries, Pauwels et al, identify the causes of drug shortages as stemming from production issues, including manufacturing problems, quality defects, and shortages of active pharmaceutical ingredients (35). Economic decisions by manufacturers, such as discontinuing less profitable drugs, also contribute to shortages. Additionally, regulatory policies affecting production and distribution, unexpected spikes in demand, and market dynamics influenced by parallel trade can exacerbate the issue (35).

Regarding Norway, the affordable medication pricing, while beneficial for its citizens, presents a unique challenge. According to a study by Brekke et al. in 2010, Norway's prescription drug prices are among the lowest when compared to ten other European countries (37). This cost-effective strategy, however, may reduce the incentive for manufacturers to prioritize the Norwegian market due to slimmer profit margins.

A notable consequence of this pricing policy is the temptation towards parallel export – the practice of selling drugs intended for the Norwegian market to other countries where they can fetch higher prices (38). This practice not only undermines local supply but also exacerbates drug shortages within the country. Beyond pricing and parallel exports, drug shortages can also stem from various other factors like withdrawal of medicinal products, distribution hurdles and spikes in market demand (38).

Norway's pharmaceutical sector is heavily reliant on international trade, both for finished medications and the raw materials required for domestic production (39). This reliance makes

the country particularly vulnerable to drug shortages, as both the direct import of medications and the acquisition of essential components from abroad are subject to global supply chain fluctuations.

3.4. Mitigation Strategies for Drug Shortage

Although drug shortages were a problem long before the pandemic, the crisis has heightened awareness and underscored the importance of supply chain risk management strategies among governments, academics, and industry experts (34). It has also increased interest in assessing the vulnerability of supply chains, focusing particularly on the preparedness and response capabilities for essential medicines in case of disruptions (34). Furthermore, the causes of drug shortages, as identified in the national reporting systems for essential medicines, oncology drugs, and drugs overall, remain largely unclear with over 63% of causes reported as unknown (35). This lack of transparency in the supply chain system complicates the traceability of disruptions, thereby hindering the ability of countries and stakeholders to develop effective mitigation strategies, since understanding the causes is crucial for addressing the issues. Addressing this issue effectively necessitates a global effort, prioritizing transparency and the development of strategies to mitigate the adverse effects of such shortages on global public health.

A work by Ahlqvist et al. emphasizes the importance of a robust supply chain risk management (SCRM) in the pharmaceutical sector to maintain resilience during both normal and crisis (abnormal) times, such as a pandemic (34). The research highlights that SCRM processes involve identifying, assessing, and mitigating risks to ensure continuity and reliability in product and service delivery. Key strategies include strategic stock piling, to buffer against sudden shortages. Although it is impractical to stockpile all essential medications in Norway to cover every day a drug might be unavailable, such reserves buy the government or responsible body crucial time to source alternative generic manufacturers. Other strategies highlighted are enhancing supply chain flexibility, improving regulatory frameworks to enable faster responses to disruptions, and promoting better coordination and information sharing among governments, manufacturers, and healthcare providers to mitigate shortage issues (34). Ahlqvist et al also point out the importance of adaptive governance, enabling policymakers to effectively shift operational modes in response to crises, thereby sustaining supply chain

operations. The screenshot below presents a summary of the role of policymakers in SCRM as outlined by the researchers.

	Normal	Abnormal
Indirect (Market Based)	• Rotating market share • Lessening of price controls • Volume commitment in contracts • Agreements to allow order quantity adjustments	• Dual/multiple sourcing • Prioritize transport (subsidize/ pay more)
Direct (Command and Control)	• Allow foreign packages* • Increase maximum price* • Establishing emergency stocks (e.g. through directives to suppliers) • Centralizing procurement	• Regulatory flexibility (e.g. for buying or selling)* • Allow foreign packages* • Streamline processes (regulations) • Centralizing procurement • Banning parallel exports
Direct (Joint Risk Management)	• Improve information sharing/ communication • Monitoring consumption and/or availability • Coordination to speed-up checks and approval processes	• Streamline processes (monitoring) • Improve information sharing/ communication • Joint planning/decision-making • Monitoring consumption and/ or availability

Note(s): *Relaxation of command-and-control policies

Figure 7 Policy Makers Role in SCRM in Normal and Abnormal Times (Taken from Ahlqvist et al Paper by Permission from the Author)

Norwegian policy makers have also adopted measures aimed at mitigating some of the impacts of drug shortages. For example, to enhance Norway's preparedness for potential pharmaceutical supply disruptions, the Norwegian Health Directorate has instituted a strategic stockpile known as the national drug preparedness (16). This reserve of essential medicines serves as a national safety net. Additionally, the Health Directorate has forged agreements with pharmaceutical wholesalers that impose export limitations on these critical drugs, thereby prioritizing their availability within Norway to ensure that the population has access to necessary medications in times of scarcity (16, 38). However, the Directorate identified several weaknesses in the national drug preparedness plan, including organizational structures such as the fragmented landscape of preparedness, the lack of integration of the military sector in the plan, very limited local production of pharmaceuticals, and the locations of national preparedness warehouses (3).

In this regard, the LMI (legemiddelindustrien) has also prosed some measures to address drug shortages. One key strategy involves increasing domestic production to reduce reliance on imports (40). Second, it is imperative to safeguard the availability of vital medications, such as narrow-spectrum antibiotics, ensuring they remain consistently accessible within the

Norwegian market. Furthermore, measures to limit parallel export can help maintain the integrity of Norway's drug supply by preventing vital medications from leaving the country despite potential financial incentives elsewhere. These proactive measures collectively aim to mitigate the impact of drug shortages and enhance the resilience of Norway's pharmaceutical infrastructure (40).

3.5. Drug Shortages in MDD System

Drug shortages affects not only retail pharmacies but also suppliers of MDD. Reports indicate that 19% of prescription challenges within MDD are due to drug shortages (9). This issue is particularly critical for patients who depend on MDD services since they typically maintain only a two-week supply of medication. Therefore, ensuring a continuous and uninterrupted supply of medications to MDD users is essential.

Despite this, research on how drug shortages impact MDD systems is limited. As indicated in the above sections, existing research on MDD systems mainly focuses on their safety, efficacy, and acceptance by healthcare professionals and patients. While Josendal, Bergmo, and Granas (9) identify the prescription challenges encountered in MDD, there is a notable lack of research regarding the impact of drug shortages on patients. This includes aspects such as the drugs affected, the number of patients involved, and how MDD specifically addresses these shortage issues. This research aims to fill in this gap by studying the prevalence of drug shortages in MDD, identifying the mitigation strategies and their effectiveness in alleviating drug shortages. The following paragraphs will elaborate on these aims and how this study aims to fill the knowledge gaps in these domains.

Identifying the specific medications impacted by these shortages is crucial for crafting targeted solutions, rather than broad, generalized approaches. A study from Finland has revealed prevalent prescribing patterns within MDD systems, indicating that psychoanaleptics are most frequently prescribed, comprising 85% of drugs, with beta-blockers and dietary supplements following at 64% and 59%, respectively (41). While there is existing information from Apotekforeningen on the top medications used over recent years (42), specific data on those most commonly included in MDD packs is lacking. Our study focuses on filling this gap by examining the specific medications often packed in MDD, and the shortage reports on those

frequently packed medications. The insights help shed light on the potential impact of drug shortage on MDD patients.

In addition, our study will examine the mitigation strategies used in MDD to deal with drug shortages.

In response to the critical need for an uninterrupted supply of medications in MDD systems, various strategies have been implemented to mitigate the risk of shortages. For instance, multidose pharmacies maintain a safety stock, which serves as a contingency against potential supply disruptions. This arrangement requires wholesalers to ensure a specified supply level to MDD suppliers, safeguarding their operations during periods of limited drug availability.

In addition, the Norwegian Directorate of Medicinal Products (DMP) make regulatory exceptions for those suppliers to import. These exemptions permit the dispensing of certain pharmaceuticals without a Norwegian marketing authorization (MA), provided they are part of an MDD system and match a product that is already authorized in a different package size (11). This ensures that foreign medications can be used in Norway under the umbrella of a similar approved drug thereby maintaining the consistency and quality of healthcare services (11). Such regulatory flexibility offers significant benefits to MDD suppliers in tackling the challenges of drug supply within the system. Foreign drug packages, which are not accessible to other retail pharmacies, play a potential role in mitigating shortages.

When MDD suppliers use these foreign packs that lacks a local MA, they associate these unregistered products with an existing item number. Consequently, pricing and reimbursement are managed under these pre-existing item numbers (11). These item number correspond to the legally authorized packaging size of the same medication that does have a Norwegian marketing permit. However, the process can inadvertently skew statistics, registering medicines with MA when in reality, foreign packs are being dispensed. The Directorate of Medicinal Products suggests that if such regulatory exceptions significantly impact drug statistics, they may reconsider these exceptions, potentially exacerbating drug shortages (11). It is, therefore, imperative to assess the role of foreign packs in mitigating these shortages to enable authorities make well-informed decisions and explore alternative solutions to drug statistic issues.

However, the effectiveness of these foreign packages in addressing shortages within the MDD system remains underexplored. This research aims to fill in this gap by studying the role that foreign packs, and safety stocks play in mitigating drug shortages. The analysis on the role of foreign packs and safety stock further aims to shed light on the impact of MDD on drug shortages.

Another effective strategy to combat medication shortages involves rational use of medications and reducing waste. Medication wastage represents a significant global issue. In the United States, it has been reported that a large portion of dispensed medications go unused, particularly those prescribed for pain, antibiotics, and chronic diseases (43). The financial implications are considerable, with estimates suggesting that such wastage could cost the nation billions of dollars annually (43). In Norway, non MDD customers are allowed to purchase medications in quantities sufficient for up to three months for blue prescriptions and even more or white prescriptions. This practice, however, might leads to a significant amount of drug wastage due to reasons like changes in medical regimens, adherence issues, drug interactions, and side effects. A study from Norway reported that within just a four-week period, medications returned for disposal were valued 300,000 Norwegian kroner, with over 50% of those returned drugs are not even opened, indicating a substantial financial and resource wastage (44). My professional experience as a pharmacist has shown me the anxiety patients face over medication availability, often leading to over-purchasing whenever the drugs are available. In Norway where majority of the medications are partly or fully covered by the welfare system, people might not have the incentive to rationalize their purchase. This can lead more waste and exacerbate shortages problems.

By providing medications in limited quantities MDD, have the potential to reduce wastage. This is supported by studies indicating significantly reduced wastage in nursing homes that have implemented the multidose system compared to those without it (25). However, changes in medication regimens account for 85% of medication waste within MDD according to a report (45). Additionally, other Scandinavian reports indicate that 20% of MDD patients change their medication regimen within one month (25). These changes in medication regimen can result in the potential wastage of drugs that are already packed within multidose. Addressing regimen changes within the MDD system can be challenging due to the complexity of drug information flow, as described in **Figure 6**. Consequently, patients may not always

have their drug lists updated, or there may be potential wastage of drugs already packed until the updated multidose pack reaches them.

Although the drugs wasted due to treatment changes may be minimal compared to non-MDD patients, who might have purchased several weeks' supply, the impact is still noteworthy. For example, a study at a residential care facility utilizing MDD reported significant returns: over a four-week study period, 818 medications were returned. This is projected to amount to approximately 2.5 million pills returned annually, with the associated costs estimated at $570,000 USD (45).

Although integrating MDD into the Norwegian healthcare system aims to reduce drug waste, the deblistering and repackaging processes can inadvertently introduce its own form of drug waste. As described in chapter 2 section 2.4 of this study, different packaging sizes and types can affect the likelihood of drug waste. Our study will identify which drug types and sizes are most commonly packed in MDD, providing valuable insights for both MDD suppliers and drug providers. Understanding these patterns can help streamline procurement and packaging strategies, reducing both time and drug waste, and thereby improving the overall effectiveness of the system.

The literature review has highlighted key gaps regarding the most frequently packed drugs in MDD systems, and the implications of drug shortages on MDD systems and their patients. Furthermore, there is a need to explore how strategies within MDD systems, such as wholesale prioritization and safety stock, as well as the system's overall functioning, influence drug shortages in the broader market. Additionally, assessing the types and sizes of drug packaging in MDD systems is essential to evaluate the potential for drug wastage. Therefore, our study aims to address these gaps to enhance the effectiveness of MDD systems overall. In the next chapter, we will detail the main and specific objectives of this study and formulate the research questions we aim to answer.

Chapter 4: Objectives

4.1. Main Objective

The primary objective of this study is to explore the impacts of drug shortages on MDD and how MDD practice in turn affect drug shortages. Specifically, we aim to assess to what extent drug shortages affect the multidose system and assess the effectiveness of mitigation strategies within MDD and explore whether these practices alleviate or exacerbate the extent of drug shortages.

4.2. Specific Objectives

- Study the prevalence of the most frequently packed medications in MDD.
- Identify and analyse the trends in drug shortage reports for medications packed in MDD from 2018 to 2023.
- Asses how drug shortages affect MDD and explore whether these MDD practices alleviate or exacerbate the extent of drug shortages.
- Asses the role of safety stock and foreign packages in mitigating shortage problems in MDD
- Identify the packing type and size of drugs packed in MDD.

4.3. Research Questions

- What are the most frequently packed medications in multidose?
- What are the trends of shortage reports of drugs packed in MDD from 2018-2023?
- What is the impact of drug shortages on MDD and how can MDD practices intern affect drug shortages?
- What is the role of foreign packs, and safety stocks in mitigating drug shortages in MDD?
- What are the specific packing types and bulk sizes drugs packed in MDD?

Chapter 5: Methodology

5.1. Methodology of the Study

This study has predominantly used quantitative descriptive data analysis but is enriched with qualitative insights to enhance understanding on how the MDD system operates. Accordingly, the description of the MDD system in Chapter 2, particularly sections 2.4-2.5, which are not publicly accessible, are described according to the qualitative data received from different experts within Apotek 1 multidose and NMD. Even though the quantitative analysis is based on data received from Apotek 1 Multidose, some qualitative information was also gathered from NMD at the start of this study and additional verifications were made by contacting NMD's service centre to clarify specific operational details of their MDD system. The qualitative information is used to contextualize the quantitative results and discussions in the study.

In the exploration of the multidose system, both quantitative and qualitative research methods hold significant importance due to the diverse range of stakeholders in the supply chain including medication manufacturers, wholesalers, regulatory agencies, retail pharmacies, multidose suppliers, health professionals, and patients. However, a quantitative approach has been chosen to get a baseline information on the types of frequently packed drugs, the prevalence of drug shortages and the extent of their impact on patients to establish a foundational understanding by collecting measurable, numerical data. This method allows for assessing key elements such as frequently packed medication types, shortage profiles, packaging types, mitigation strategies employed by MDD suppliers to resolve shortage notifications.

5.2. Data Collection

In the context of Norway's healthcare system, Apotek 1 and NMD stand out as the two principal suppliers of multidose. Although the original plan was to incorporate data from NMD, access restrictions necessitate focusing solely on Apotek 1 Multidose. Given Apotek 1's substantial market share, the data from this supplier provides a broad view of multidose operations. However, it may not fully represent the entire scope due to operational variations within the

chain, and detailed data on how NMD functions is lacking in this study. However, this data set could be reflective of the larger trends and practices within Norway's multidose supply chain in general.

The study utilized two sets of secondary data. The first set, which we will refer to interchangeably as BI data or DMP data, comprises national shortage notification data provided by BI Norwegian Business School. This dataset includes details of drug shortages reported by DMP from January 2018 to June 2023, and it contains information such as the date of the shortage report, medication name, strength, formulation, item number, ATC code (Anatomical Therapeutic Chemical), manufacturer's name, duration of the shortage, and measures taken to resolve the shortage. The second set comprises data from Apotek 1's multidose system.

Below, we provide an overview of the raw data received from Apotek 1, detailing its format, contents, and how it was utilized in our analysis (the analysis is detailed in **Figure 8** below).

Drug Packaging Data (2022 and 2023): we received two Excel sheets containing comprehensive details of drugs packed in Apotek 1's multidose system, covering the years 2022 and 2023 separately. Each sheet includes information such as item numbers, packaging types, ATC code, foreign packaging status, and the number of tablets packed annually. This is the dat set that was linked to the data form BI to analyse shortage report and other analysis. The analysis was limited to the years 2022 and 2023 because Apotek 1's database only maintains a complete record of drugs packed in the MDD system for the past two years.

Patient Usage Data (as of January 2024): A separate Excel file provided raw data on all item numbers and the corresponding number of patients using these items as of 22nd January 2024. It is important to note that the number of patients varies daily, which impacts the analysis of usage trends.

Safety Stock Data (as of November 2023): Another dataset from Apotek 1 contained in an Excel file details the safety stock of drugs. This list includes all drugs that had safety stocks as of November 2023, a critical factor since safety stock levels are reviewed and adjusted daily based on factors such as shortage status. The data set contains details on the item number, four-week consumption, adjusted amounts due to shortage notifications, and the quantities approved by wholesalers.

Shortage Notifications within MDD (historical data): Additional data was retrieved in another Excel file that includes actual and potential drug shortage notifications registered within Apotek 1's system from 2018-2023 in separate files. This data contains information on shortage notifications, item number, what has been done to reduce potential shortage to actual shortage, number of patients, duration of shortage and drugs with no alternatives available.

Supplementary Information: The historical data on drug shortage notifications provided by Apotek 1, spanning from 2018 to 2023, was found to be incomplete and contained some inconsistencies. To improve the accuracy and depth of our analysis, we supplemented this initial dataset with additional information extracted from Apotek 1's archives. These archives consisted of data originally collected for internal use, including information exchanges, presentations, and email communications. This comprehensive analysis illuminated the actual and potential impacts of drug shortages within MDD and provided valuable insights into both ongoing and historical challenges related to drug shortages.

Data was collected from February to April 2024.

5.3. Data on Variables Collected

5.3.1. Shortage Report

This study analysed all drugs packaged within MDD in 2022 and 2023, using data retrieved from the Apotek 1 multidose database system. We cross-checked each drug with DMP reports to identify shortages and assess their prevalence within the MDD system for those years. Further analysis was done to check whether drugs reported as short had foreign package alternatives available in MDD to evaluate the potential role of foreign packages in mitigating drug shortages within MDD.

Despite DMP reported shortages, MDD may have been less affected due to access to foreign packages, safety stock, and wholesaler prioritization. We have analysed Apotek 1's shortage notifications from 2018 to 2023 to gauge the actual impact on MDD. This analysis included the number of potential shortages, actual shortages, and those requiring physician intervention when no alternatives were available within the MDD. Definitions of 'potential' and 'actual' shortages are provided in the results Chapter.

5.3.2. Safety Stock Within MDD

Safety stock data was received in a separate Excel spreadsheet, which detailed the list of drugs held by Apotek 1 in real-time inventory. This real-time register is essential because both the presence of a drug and the quantity available in Apotek 1's safety stock can fluctuate daily. The spreadsheet included several information like normal consumption rates of each drug, adjusted consumption rates following shortage notifications, and the quantities approved for reserve by the wholesaler. This data was utilized to analyse safety stock level at Apotek 1 and its adjustments to market fluctuations and potential shortages. This analysis aims to understand the role of safety stock in mitigating shortage problems within MDD.

5.3.3. Foreign Bulk Overview

Foreign packages (referred to as 'utenlandspakkninger' in Norwegian), are exclusively accessible to MDD. The analysis of foreign packages examined their proportion among all drugs packed in MDD for 2022 and 2023. It also evaluated the size and type of these packages to determine their impact on improving MDD system efficiency. Drugs packed in MDD that were reported as short in DMP data were checked for available foreign package alternatives within MDD. This was to determine if MDD could utilize these alternatives when a drug was reported short, thereby assessing the role of foreign packages in mitigating shortages within MDD.

5.3.4. Packaging Size and Packaging Type of Drugs in MDD

Drugs packed in MDD vary in packaging size ranging from 10-1000 units per pack. To simplify data analysis, these sizes are categorized into three groups (Small, Medium and Large), as detailed in the results section of this study. Additionally, packaging types are classified into two categories: blister packs (strips) and bulk packaging (those that come in containers or do not require manual extraction of tablets). This classification helps assess the likelihood of resource and time wastage according to the packaging type and size of the drugs.

5.4. Data Analysis

Descriptive statistics, including frequencies and percentages, were utilized to present the results, with data analysis conducted using Microsoft Excel. Further, we performed Chi-

squared test for trends in proportion of drug shortages between the year 2018 and 2023 using the prop.trend.test command in a software called R.

Below is a summary of the essential Excel functions and formulas we used in our data analysis.

1. **YEAR Function**
    - **Excel Formula**: **=YEAR(A2)**
    - **Explanation**: The YEAR function extracts the year from a date. In this formula, "A2" refers to the cell that contains the date from which the year is to be extracted.
2. **IF Function**
    - **Excel Formula**: **=IF(condition, value_if_true, value_if_false)**
    - **Explanation**: The IF function evaluates a condition and returns one value if the condition is true, and another if it is false. In my paper, this function is used for example to sort data based on packaging size
3. **VLOOKUP Function**
    - **Excel Formula**: **=VLOOKUP(lookup_value, table_array, col_index_num, [range_lookup])**
    - **Explanation**: VLOOKUP searches for a specific value in the first column of a table array and returns a value in the same row from the column specified by col_index_num. In my paper, it is used to match data from the "drugs packed in MDD" to the "full notification file from BI" based on the year and the item number.
4. **Subtraction Formula**
    - **Excel Formula**: **=End_Date - Start_Date**
    - **Explanation**: This formula calculates the difference in days between two dates by subtracting the Start_Date from the End_Date. In the context of my research, it is utilized to determine the number of days items have been missing, referred in the data as the "mangel period."

Figure 8 below demonstrates the analysis process, indicating which datasets were used to produce specific results and detailing how data from Apotek 1 was integrated with BI/DMP data for a thorough analysis. The arrows show the flow of analysis from each specific dataset.

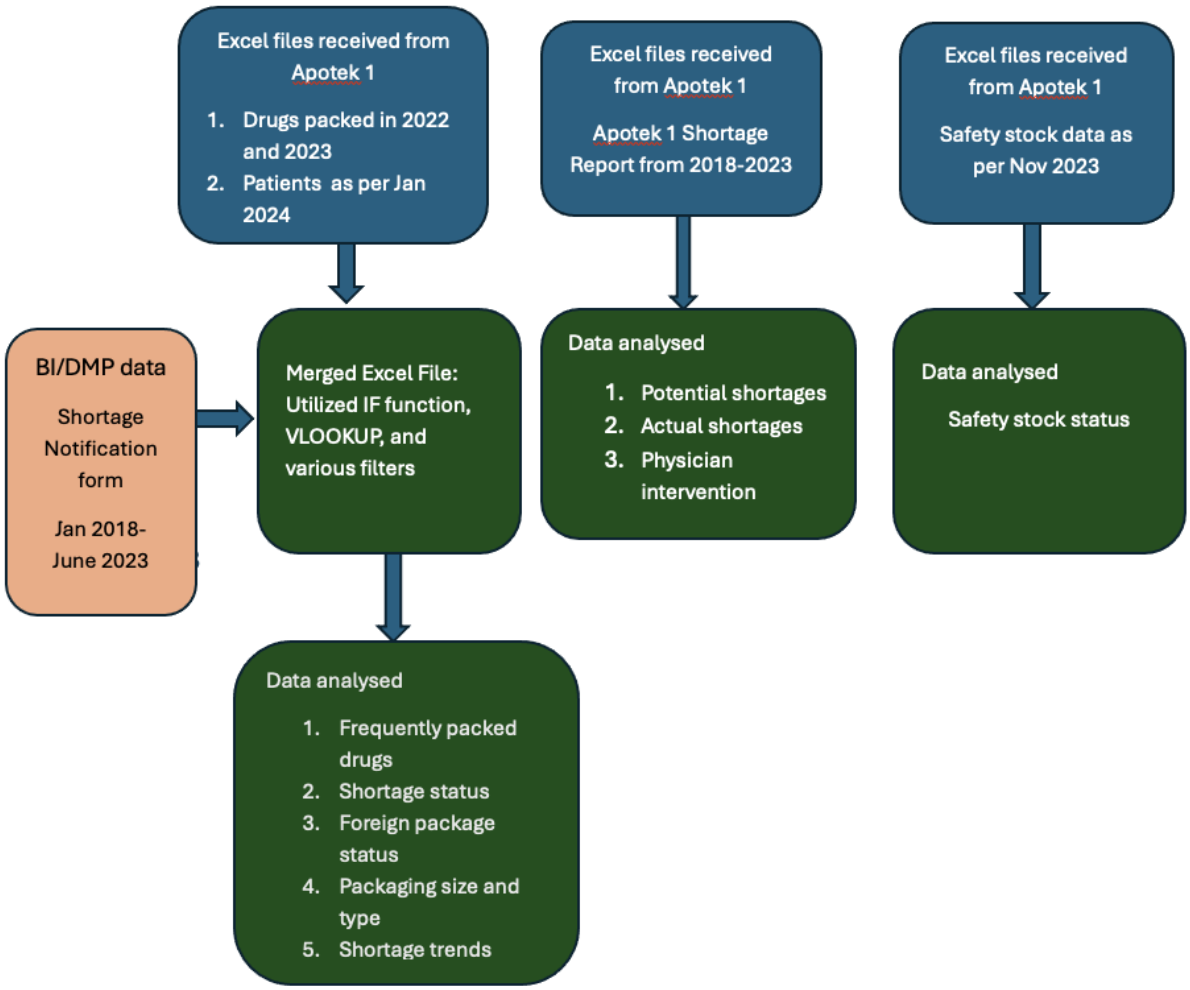

Figure 8 Analysis Process and Results Derived from each Data Set

5.5. Data Validity and Reliability

To ensure the validity and reliability of the data retrieved from BI, we have cross-checked it against publicly available data from the DMP database. The DMP database is particularly reliable as it is a governmental source used nationally to notify report of drug shortages.

To ensure the validity and reliability of the data collected from Apotek 1's multidose system, we utilized a comprehensive verification process. This included cross-referencing shortage reports with multiple reliable sources, such as email exchanges, internal reports, and presentations used within the Apotek 1 MDD system. Furthermore, the data's validity is reinforced by the fact that it was extracted directly from Apotek 1's own databases, which are actively used in their inventory management operations, and they will have the incentive to report it correctly. We also engaged in insightful discussions with key Apotek 1 experts,

including the head of the drug shortage team, the pharmacist responsible for inventory management, and the head of multidose dispensing. These discussions provided additional verification and deeper insights into the data's accuracy.

5.6. Ethical Considerations

This study did not require ethical clearance because it solely involved the analysis of secondary, non-sensitive data related to drug shortages, without any identifiable personal information.

Chapter 6: Results

In this chapter, we detail the results of our study, organized according to the objectives outlined in Chapter 4.

6.1. Most Frequently Packed Medications in MDD

One objective of this study was to identify the drugs most commonly included in MDD. The findings are detailed below.

In 2022, a total of 967 medications were packaged in MDD, a number that saw a modest increase to 1,011 in the subsequent year. The study's findings indicate that Panodil 1gm was the predominant medication packaged in MDD for consecutive years, 2022 and 2023. Looking into the ten most frequently packed medications in 2023, three of those are nutritional supplements. As shown in **Figure 9** and **Figure 10,** 70% of the top 10 drugs packed in MDD were same in both 2022 and 2023 with the exception that Metformin, Atorvastatin and Pantoprazole joining the top 10 category in 2023.

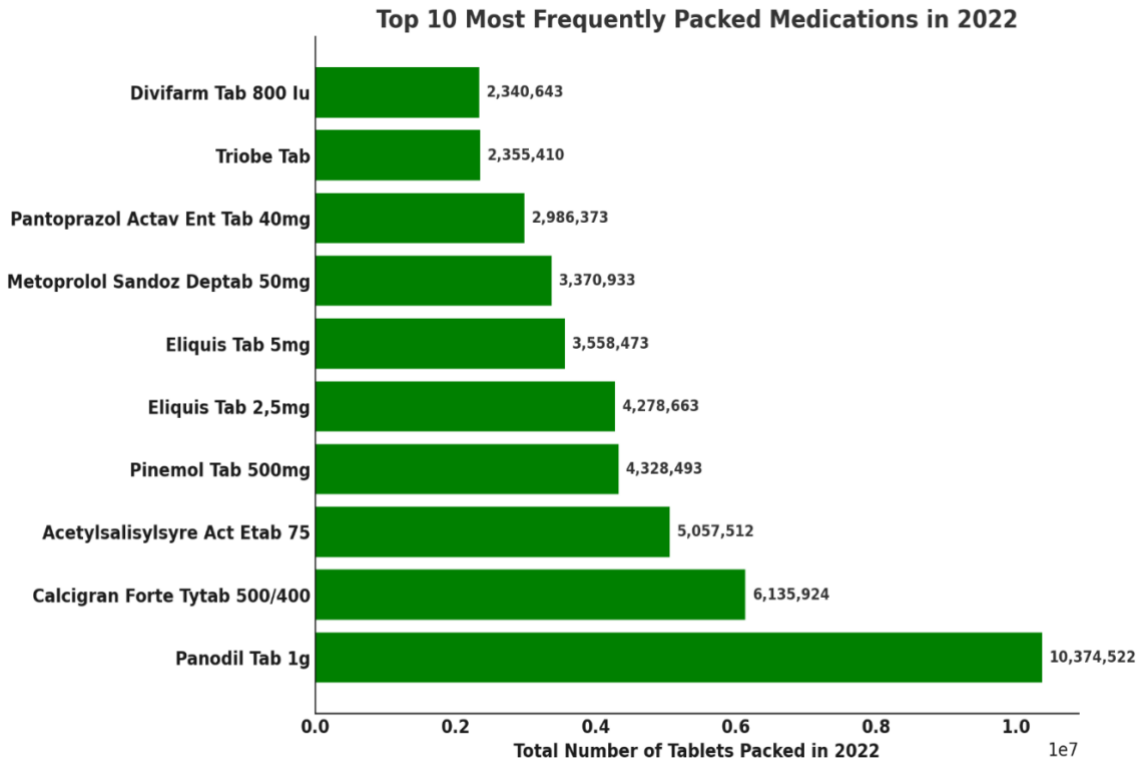

Figure 9 Most Frequently Packed Medications in MDD in 2022

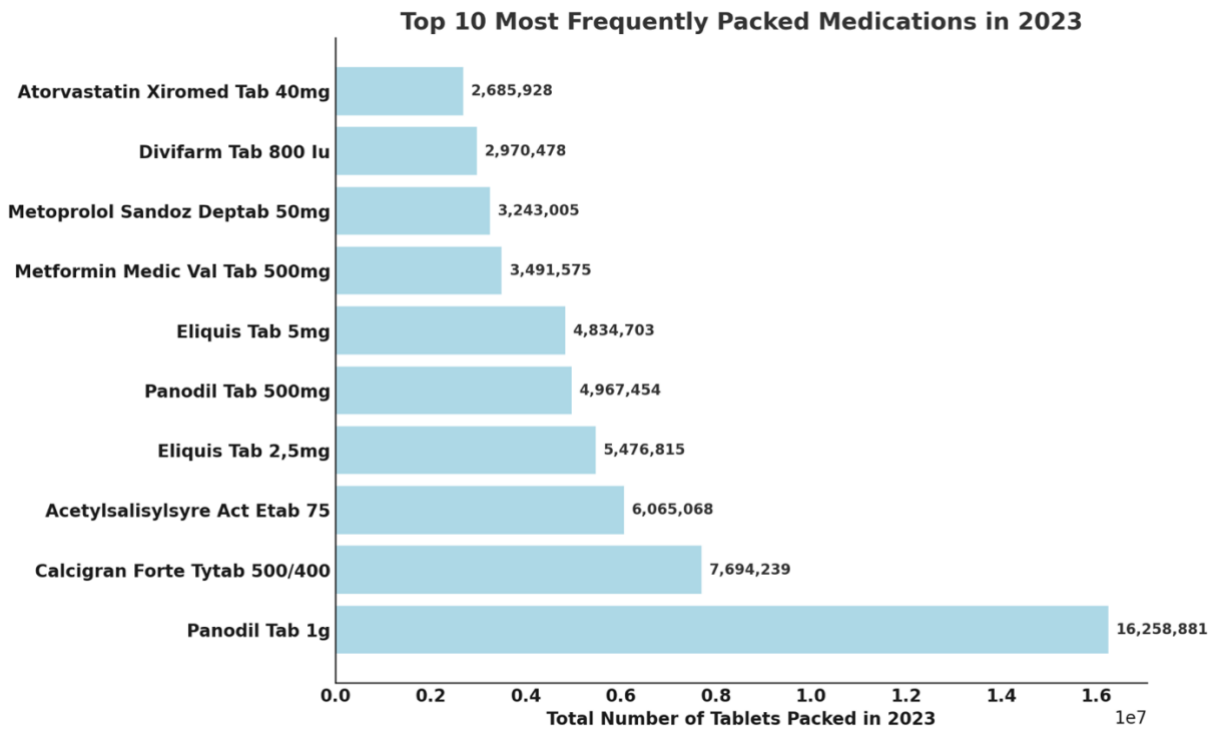

Figure 10 Most Frequently Packed Medications in MDD in 2023

In conclusion, our study has shown that the drugs most frequently packaged in MDD systems during 2022 and 2023 were Panodil 1gm, followed by Calcigran Forte 500mg/400IE, and Acetylsalisylsyre 75mg.

6.2. Medication Usage Trends among MDD Patients

Due to variations in dosing schedules, the frequency of medications packed in MDD quantified by the total number of tablets packed, may not reflect the actual number of patients using these medications. Therefore, it is essential to distinguish between the volume of medication dispensed and the patient utilization rate. For instance, while paracetamol scores highest on the most commonly packed, Acetylsalicylic acid is used by a larger number of patients than paracetamol. This distinction is important in discussions of drug shortages, as understanding the actual patient impact requires examining not just the volume of medication dispensed but also the patient utilization rates.

Figure 11 presents the top 10 medications with the highest number of patients within MDD.

In 2022, the total number of multidose patients increased from 65,000 to 70,000 throughout the year. In 2023, the number of patients varied between 70,000 and 73,000. The distribution

of medication usage among these patients was analysed, and as of January 2024, approximately 22% of MDD users were prescribed Acetylsalysylsyre (15,927 of the 73,000) and similarly 22% (15,784 of the 73000)) were prescribed Panodil 1gm.

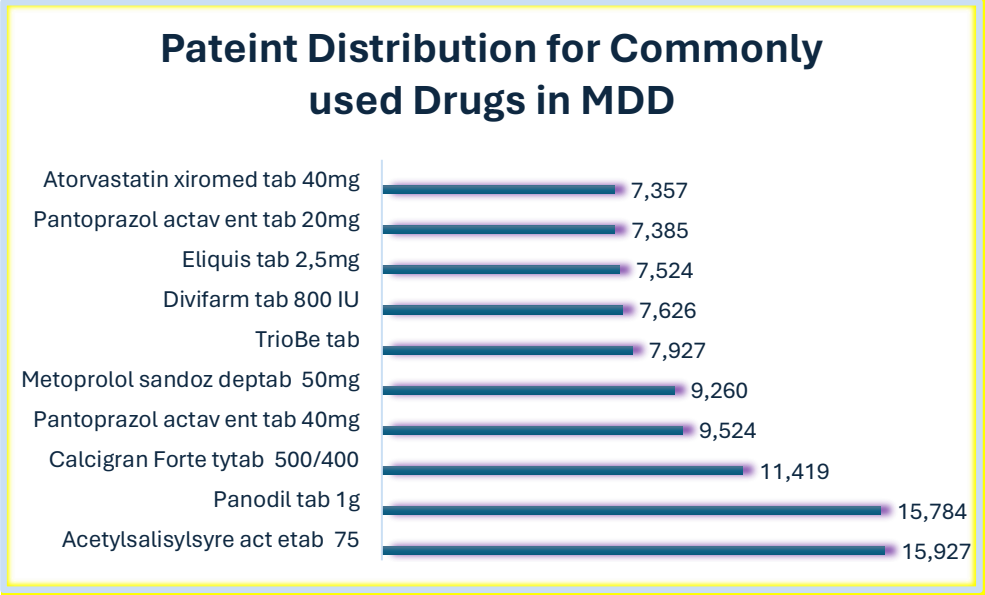

Figure 11 Most Commonly Used Drugs amongst MDD Patients

In conclusion, our analysis reveals that the most commonly utilized drugs amongst MDD patients are Acetylsalicylsyre 75mg and Panodil 1gm with only a slight difference in the number of patients using each. Following closely are the calcium and vitamin D supplement Calcigran Forte 500mg/400IE, and Pantoprazole 40mg.

6.3. Shortage Reports of Drugs Packed in MDD

Another objective of this study was to analyse drug shortage reports involving medications packaged in MDD and assess the trends from 2018 to 2023. Below are the findings,

In the years 2022 and 2023, a total of 967 and 1,010 drugs were packed in MDD respectively. The investigation into whether these drugs experienced shortages during the same period is summarized in **Table 1**. Over 78% of these medications were consistently available without any market shortages reported during this time. Looking into the top 10 most frequently packed medications within MDD, except for the drug Triobe (a vitamin B supplement) none of them were reported short in both years.

Year	Drugs packed in MDD	Reports of market shortage (2022-2023)	% short
2022	967	217	22 %
2023	1010	216	21 %

Table 1 Drugs Packed in MDD and Reports of Market Shortages (2022-2023)

We have looked into shortage reports of drugs over the past six years (2018-2023) both in case of all drugs reported short nationwide and specifically those reported short within MDD (actual shortages experienced). The result of our study identifies an interesting shortage report trend where that national drug shortage report peaked highest in 2019, and lowest in 2018, while the opposite was true in Apotek1 Multidose system where shortage report was highest in 2018 and lowest in 2019.

Table 2 (Row 2) shows how often wholesalers reported having enough stock to handle drug shortages. The data demonstrates a positive trend: over time, wholesalers are increasingly able to mitigate shortages with their available inventory.

Year	2018	2019	2020	2021	2022	2023
Drugs reported short by DMP	915	1558	1247	1029	1293	721*
Wholesalers had enough in their stock**	38	17	234	305	317	140*
Potential shortage in MDD	NA	NA	NA	50	70	87
Actual shortages in MDD	77	21	43	28	31	53
Needed physician intervention	32	8	22	11	21	33

Table 2 Drug Shortage Trends as Reported by DMP and Apotek 1 Multidose

* The data over shortage report in 2023 only contains until June 2023. Shortages happening from June 2023 until the end of 2023 are not reported.

** Indicates the number of drugs for which wholesalers reported sufficient stock to cover the shortage period.

N/A: there is no data on those years as the system of reporting potential shortage was not in place. The system for safety stock, which is a key differentiator between actual and potential shortages, was implemented in April 2019 and was not fully operational until 2021. Our study shows that as per November 2023, 57% of drugs in MDD had safety stock levels ranging from 4-19 weeks of supply. Of the medications that maintained a safety stock during this period, 50 were reported short within MDD. In 78% of these cases (39 out of 50), where drug shortages were reported, MDD managed to secure a safety stock exceeding their usual consumption.

The terms 'Potential shortage' and 'Actual shortage' are defined as follows:

- Potential shortage: Occurs when the safety stock cannot fulfil the demand, and intervention is required. To reduce this figure to 'Actual shortage', generic alternatives are considered.
- Actual shortage: Takes place when no generic alternatives are available, leading to a change in the strength of medication or the use of unregistered drugs (uregistrert) upon approval from the DMP. The last raw in **Table 2** above indicates the number of drugs

that necessitated a treatment change due to the absence of suitable alternatives within MDD.

Looking into the shortages reported by Apotek 1 multidose, if we take 2018 as our reference year, we observed a statistically significant reduction in drug shortages for the subsequent years - 2019, 2020, 2021 and 2022 with a p-value less that 0,01.

Figure 12 below shows the trend over the years and p value.

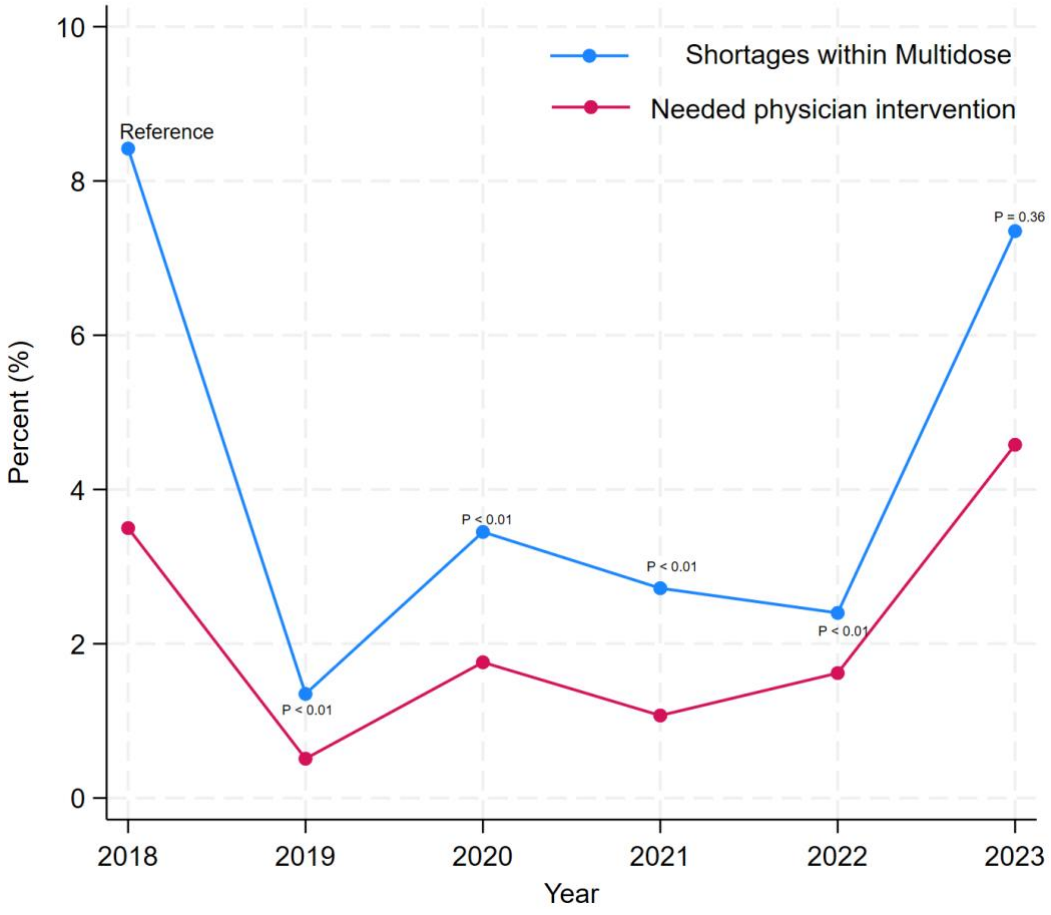

Figure 12 Shortage Trends as Reported within Apotek 1 Multidose

6.4. Impacts of Drug Shortages on MDD Patients

We have analysed the shortage reported by DMP and looked into the number of MDD patients who could potentially be affected by the problem. Among the drugs reported short, Triobe followed by Zopiclone 7.5mg and Sobril 10mg were identified as having the most significant impact on patient groups. A further analysis was done to see how many days in the course of

2022 and 2023 were those drugs not available in the market. Notably, Zopiclone 7.5mg was unavailable for the longest period, with a shortage lasting 366 days. **Table 3** below summarizes the top 10 drugs reported short, highlighting those with the highest number of patients impacted.

Drugs reported short	Shortage duration in days	Number of patients affected
TrioBe	39	7927
Zopiclone Actavis 7,5 mg	366	4407
Sobril 10 mg	40	4192
Escitalopram Actavis 10 mg	65	3707
Behepan 1 mg	8	3571
Kalcipos-Vitamin D 500 mg/800 IE	215	3569
Allopurinol Sandoz 100 mg	84	3124
Levaxin 75 mikrog	73	2960
Prednisolon Alternova 5 mg	210	2630
Zopiclone Actavis 5 mg	200	2421

Table 3 Overview of Drug Shortage, Shortage Duration and Number of Patients Affected

Despite a high number of drugs reported as short over recent years, Apotek 1's multidose system has largely succeeded in mitigating these shortages. This success is attributed to their prioritization by wholesalers and the effective use of their safety stock, as indicated in Section 6.3. Nonetheless, there have been instances where alternative solutions were not feasible.

The data presented in **Table 2** illustrates that the incidence of requiring physician consultation for alternative treatment options remained below 33 drugs each year over the six-year period, with the lowest occurrence in 2019 (8 drugs) and the highest in 2023 (33 drugs).

The most significant patient impact within this period occurred in 2023, when approximately 1,700 patients using Magnesium 120mg faced a lack of treatment alternatives. Particularly

notable was the clinical impact on patients prescribed Rivotril 0.5mg and Lasix 30mg, who, due to the absence of alternatives, required their physicians to seek other treatment options.

Table 4 below summarizes the drugs that led to the highest number of patients being affected by shortage.

2021		2022		2023	
Physician intervention needed	**Patients affected**	**Physician intervention needed**	**Patients affected**	**Physician intervention needed**	**Patients affected**
Minifom kps 200mg	248	Rivotril 0,5mg	630	Magnesium tygg 120mg	1700
Flux sugetab 0,75mg	219	Neo-mercazole	315	Lasix ret dpkaps 30mg	624
Tramagetic Ret Depottab 100mg	110	Rivotril 2mg	163	Rivotril 0,5	548
Bendroza 1,25/573 mg	95	Dolcontin dp 5mg	124	Monoket OD depotkaps 25mg	312
Magnesium Diasporal 150mg	63	Cortison 25mg	90	Rocaltrol 2care4 kaps 0,25mcg	280
Kodein 25 mg	36	Tramagetic ret 100mg	89	Lixiana tab 30mg	265
Apresolin 25 mg	34	Tramagetic OD 150mg	75	Normorix Mite tab	233
Xanor 0,5mg	31	Magnesium Diasporal 150mg	72	Lixiana Tab 60mg	229
Pramipexole 0,7mg	13	Kodein 25mg	45	Imdur 30	85

Table 4 MDD Drugs Lacking Alternative Solutions, Requiring Physician Intervention in 2021, 2022, and 2023

6.5. Role of Foreign Packs in Mitigating Drug Shortages in MDD

Another aim of this study was to examine the impacts of foreign packages in MDD system. Our study shows that in 2022, 8% of the medications packed in MDD were sourced from foreign packages. In 2023, the proportion of foreign-packaged medications in MDD rose

marginally to 9%. However, the role of foreign-packaged drugs to mitigating shortages seems limited. Specifically, our analysis revealed that in 2022 and 2023, out of all the MDD drugs reported short, only 13 could potentially have their shortages resolved by substituting them with foreign-packaged versions. This represents only 6% of all the MDD drugs reported short.

Table 5 below outlines which drug shortages could potentially be addressed by sourcing foreign packages, along with the anticipated impact on patients. Triobe, a vitamin supplement is most likely to affect a large number of patients in the event of a shortage.

Drugs Reported short with foreign packaging alternative	Number of tablets packed in 2022	Number of patients using the drug
Oxycodone Actavis Caps 10mg	135 113	198
Prednisolone Altern Tab 5mg	432 289	2630
Mianserin Mylan Tab 10mg	181 055	396
Reltebon Depot Depottab 20mg	182 067	262
Hydroxyzine Orifarm Tab 25mg	179 388	323
Lyrica Kaps 75mg	472 938	725
Escitalopram Actavis Tab 10mg	1 170 269	3707
Triobe Tab	2 355 410	7927
Hydroxyzine Orifarm Tab 10mg	209 829	314
Quetiapin Sandoz Tab 100mg	322 150	727
Allopurinol Sandoz Tab 100mg	552 134	3124
Mianserin Mylan Tab 30mg	285 633	587
Reltebon Depot Depottab 40mg	52 411	85

Table 5 Drugs Reported Short with Foreign Packaging Alternatives.

In conclusion our study indicates that the role of foreign packs in mitigating shortage problems within MDD is minimal.

6.6. Packaging Size and Packaging Type of Drugs Packed in MDD

This study also aimed to assess the packaging type and size of drug packed within MDD, focusing on the physical form and volume of the packages. We have investigated whether drugs arrive in blister packs or containers, and we also assess the size of the packaging, which denotes the number of units per container or box.

For the sake of a simplified presentation of data, we have categorized packaging sizes into three groups: 'small' for packages containing 50 units or fewer, 'medium' for those with 51 to 100 units, and 'large' for packages with more than 101 units.

Our analysis indicates that most drugs packed in MDD are categorized as medium-sized based on the quantity per package. **Figure 13** below provides a breakdown of the total number of drug products packed within each size category for 2022 and 2023.

In 2022, the range of tablets per package varied from as few as 10 to as many as 750. In 2023, this range extended further, with the smallest packaging still at 10 tablets, and the largest containing up to 1000 tablets.

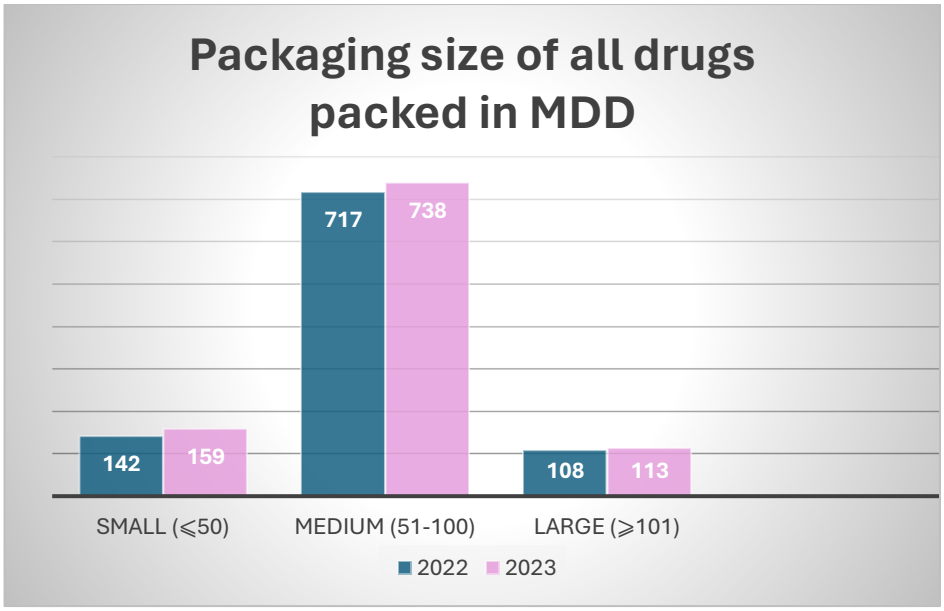

Figure 13 Packaging Size of all Drugs Packed in MDD

The packaging sizes of foreign-sourced medications present notable variation. None of the foreign packs comes in small pack while largest was 1000 units per pack. **Figure 14** shows packaging sizes of all foreign packs packed in MDD for the year 2022 and 2023. Foreign-packaged drugs make up only 8% of the total drug count. Yet, they account for 25% of all tablets or capsules dispensed annually through MDD.

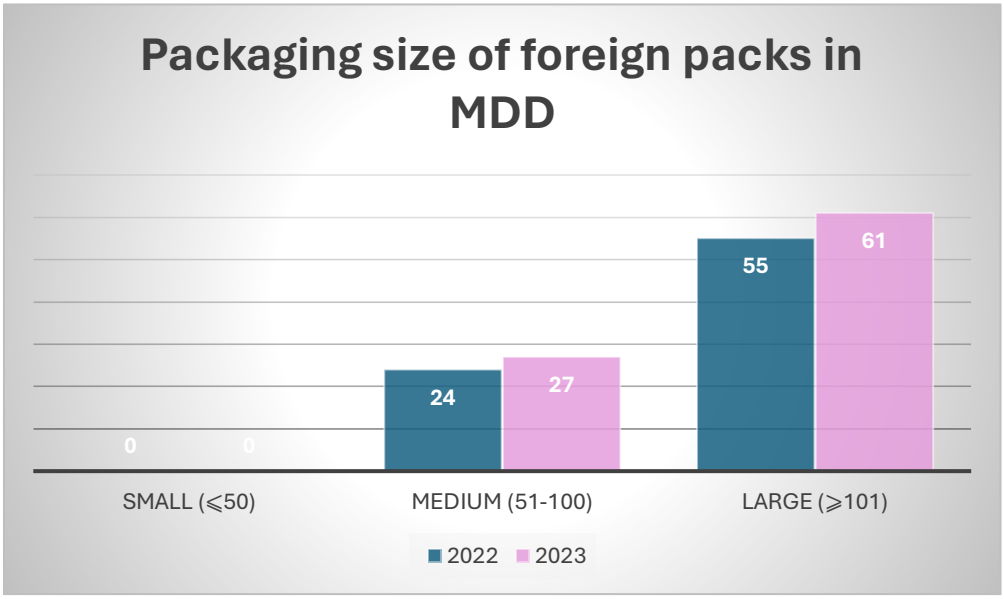

Figure 14 Packaging Size of Foreign Packs in MDD

Regarding the types of drug packaging used in MDD, our analysis distinguishes between drugs packaged in bulk containers and those in blister packs. Our findings reveal that within MDD, 44% of the drugs are packed in blister packaging, requiring manual extraction or deblistering. Conversely, 56% of the drugs are supplied in bulk containers, where tablets are readily accessible and do not require deblistering.

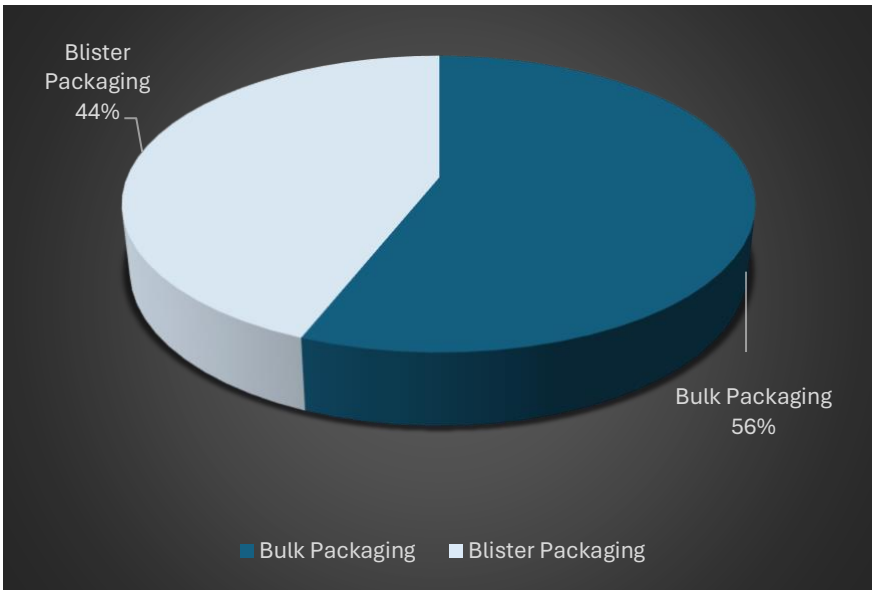

Figure 15 Packaging Type of Drugs Packed in MDD

In conclusion, a significant portion of MDD drugs are supplied in blister packs, necessitating the manual removal of tablets or capsules for processing. Additionally, a notable fraction of drugs from 2022 and 2023 are supplied in smaller packages, requiring transfer to larger containers prior to the commencement of the multidose packaging process. In contrast, all foreign-packed drugs arrive in packages containing over 100 units, which enhances production efficiency as they do not require repackaging and can be directly filled into the cassettes.

Chapter 7: Discussion

7.1. Drugs Packed in MDD

This study aimed to investigate the most frequently packed drugs in MDD. The findings reveal that although Panodil 1gm has the highest total number of tablets packed in MDD, Acetylsalisylsyre 75mg is used by the majority of MDD patients. The difference in usage between these drugs is slight and may be attributed to their dosing schedules: Panodil could be administered in multiple doses throughout the day, while Acetylsalicylic acid is typically taken just once daily.

Our research shows that Panodil (paracetamol) and Acetylsalisylsyre are the most commonly used drugs among MDD patients. This finding is consistent with a Norwegian study that shows the widespread use of cardiovascular and nervous system medications, specifically antithrombotic and non-opioid analgesics (27). Notably, our analysis further specifies that within the nervous system category, paracetamol is predominantly used. Although paracetamol is considered safe and effective for pain relief, liver toxicity is often reported to be a concern (46). Its prevalent use among the elderly could raise concerns due to potential compromised liver function, potential drug interactions, polypharmacy, and other comorbid conditions. Therefore, it is crucial to monitor its use, especially since paracetamol can be taken as needed rather than on a fixed schedule. This highlights the importance of careful medication management in this vulnerable patient group.

According to the Norwegian prescription database, the drugs with the highest number of users in Norway in 2020 included Paracetamol, Atorvastatin, and Acetylsalicylic acid, reflecting a similar usage trend among MDD patients (47). This observation suggests that the most commonly prescribed medications are consistent both within the general population and among those receiving medications through MDD systems.

However, the findings of this study concerning the most frequently used medications within MDD significantly diverge from a Finnish report, which noted 85% usage of psychoanaleptics, followed by 64% for beta-blockers, and 59% for dietary supplements within their treatment schemes. Notably, our results did not include psychoanaleptic drugs among the top 10 most frequently used medications. This discrepancy could stem from differences in disease

prevalence or diagnosis patterns between the two countries. Furthermore, the Finnish report highlights that 89% of their study participants had cardiovascular diseases, followed by significant occurrences of Alzheimer's and severe mental disorders. These conditions might explain the higher usage rates of those drugs in Finland. Additionally, the limited sample size of 208 in their study may not adequately represent broader medication use patterns.

The presence of Metformin among the top 10 most frequently packed medications in MDD for 2023, which was not the case in 2022, could suggest a growing number of patients with diabetes. This observation aligns with a Norwegian study indicating a rising prevalence of diabetes within the elderly population receiving home care services (48). Our results should not be considered conclusive regarding an upward trend given the limited scope of data across multiple years. Nonetheless, this data could serve as a foundation for further research, adding valuable insights to existing studies and aiding in future analyses.

However, more recent data from Apotekforeningen for 2023 highlights that Atorvastatin is the most used prescription medication, followed by Acetylsalicylic acid and Candesartan (42). In our study, Atorvastatin ranks 10th in terms of the number of patients using this medication. This discrepancy might be attributed to the demographic differences where MDD patients are typically older. While the general population data include younger individuals who might use Atorvastatin as a preventative measure against cardiovascular diseases, the elderly MDD patients are likely already diagnosed and treated for such conditions, potentially reducing the preventative use of this medication in this group.

In our analysis of the medication usage within the MDD system for the years 2022 and 2023, we found that the types of medications dispensed remained largely unchanged. This stability can be attributed to the demographic characteristics of the MDD users, who are predominantly elderly individuals. These older adults commonly require medications to manage prevalent conditions in their age group. The Norwegian Public Health Institute notes that among patients aged 70 and older, the most frequently used medications are those targeting common elderly health issues such as cardiovascular diseases, antithrombotic, and cholesterol-lowering agents (49). This pattern reflects the specific health needs of this age group, underlining the consistency in medication usage observed in our data.

Calcigran Forte is also reported to be the most commonly used among MDD patients and this might underscore the prevalence of osteoporosis in the elderly population. Osteoporosis is a condition characterized by a significant decrease in bone mass and density, leading to weakened bones and a higher risk of fractures (50). It predominantly affects older adults, becoming more severe after age 70 as fracture risks and fall likelihood escalate (50).

The Norwegian Public Health Institute highlights Oslo's high incidence of fractures, ranking among the highest globally (50). This aligns with the widespread use of Calcigran Forte in MDD, underscoring its crucial role in managing osteoporosis and fracture prevention in Norway's aging population. According to Felleskatalogen, Calcigran Forte can be indicated for both prevention and additional treatment of osteoporosis.

While aging is a known risk factor for osteoporosis, certain medications like Pantoprazole, a proton pump inhibitor, can exacerbate this risk (50). Reports suggest that long-term use of Pantoprazole is associated with a significantly higher risk of osteoporosis-related fractures (51). Our study identified Pantoprazole, in both 20mg and 40mg doses, as among the most commonly prescribed medications in our patient group. Although our data does not conclusively establish whether patients take both Pantoprazole and Calcigran Forte, further research could explore the potential risk of Pantoprazole-induced osteoporosis among MDD patients.

Given the associated increase in osteoporosis risk, this finding alone might not be enough to prompt the search for alternative solutions. However, it could serve as a valuable discussion point, encouraging healthcare professionals to reflect on the data when considering treatment options. Furthermore, conducting a thorough analysis of the necessity and impact of these medications could help prevent unnecessary drug use among this vulnerable patient group. By optimizing prescription practices, we can not only reduce drugs related problems within this patient group but also medications are more effectively allocated to those who genuinely need them, potentially reducing drug shortages and improving access for all patients.

7.2. Impacts of Drug Shortages on MDD

Although drug shortages have been prevalent in recent years, our analysis reveals that Multidose system appears largely unaffected. In 2022 and 2023, 78% of the drugs distributed

through MDD systems did not face any shortages. One of the reason often mentioned as a cause of drug shortage is high demand (52). Contrary to that, our findings suggest that the drugs with the highest usage and those most frequently packed in MDD did not experience shortages over the past six years. For instance, the top five medications commonly packaged in MDD systems remained consistently available from 2018 to 2023. A possible explanation for this trend could be the nature of the medications utilized within these systems. Predominantly, these medications are aimed at treating chronic conditions, which hold strategic importance for pharmaceutical companies because the consistent demand ensures a steady profit. This will intern motivate manufacturers to prioritize the production and supply of chronic disease medications over those for acute conditions. As a result, there will be a strong incentive for pharmaceutical companies to ensure a stable supply of these drugs. Supporting this claim, reports indicate that global spending on medicines was estimated to reach $1.4 trillion by 2020, with a significant portion (85%) concentrated on non-communicable (chronic) diseases (53). This indicates a substantial market size and potential profitability for pharmaceutical companies focusing on these areas.

Relatedly, the production and supply chain for chronic medications are often robust, given the predictable and ongoing need for these treatments. Companies invest in efficient manufacturing processes, build up safety stock, and establish reliable distribution networks to prevent shortages. They are also more inclined to navigate regulatory complexities, market dynamics, and supply chain challenges to maintain an uninterrupted supply of these essential medications.

There might be additional reasons that could broadly explain why the majority of drugs packaged in MDD are not reported as short in supply. The medications typically included in MDD are either tablets or capsules, which generally have a longer shelf life (54). This extended shelf life allows medications to be manufactured and stored in bulk, which acts as a buffer during periods of heightened demand or production delays. Wholesalers, manufacturers, pharmacies, hospitals, and healthcare providers can maintain larger inventories without the concern of expiration, ensuring that existing stock either in the market or held by manufacturers can suffice until any temporary shortages are resolved.

This notwithstanding, a report by the American Society of Health-System Pharmacists (ASHP) on drug shortages from 2001 to 2023 indicates that injectable drugs have been reported to

experience more shortages than other formulation types (55). But this is not consistent across all countries. For example, a transnational registry report reveals that the US reports more shortages of injectable preparations than European countries, where tablet formulations, including in Norway, Sweden, and Finland, are more frequently reported as short (30). This contrasts with our data, which shows that despite all drugs packed in MDD being tablets and capsules, there are few reports of shortages. This discrepancy could be attributed to differences in distribution and stockpiling practices, market demand, and prioritization. Additionally, the high number of shortage reports for antimicrobial tablets, which are not packed in MDD, may also explain this variance.

In Norway, pharmaceutical companies are required to report any temporary or permanent disruptions in their supply to wholesalers and DMP at least two months before the disruption is expected to occur (56). Although 20% of drugs packed in MDD systems are reported as short in these notifications, it does not necessarily imply that MDD suppliers have experienced actual shortage of this scale. Thanks to their prioritization by wholesalers, and safety stock piling, MDD suppliers have significantly mitigated these shortages, as detailed in **Table 2**.

As shown in **Figure 11**, using 2018 as the reference year, there is a statistically significant reduction in shortages within the MDD system in the following years, with the exception of 2023. This anomaly could be attributed to the incomplete data for 2023, as noted in the methodology section of this thesis. Specifically, the DMP data only includes shortage reports up until June 2023, the data might show significant reduction in 2023 if we had the full year report of shortage in 2023. A reasonable explanation for the decrease in shortage report within MDD after 2019 could be the implementation of a safety stock system in April 2019, which has shown increasing effectiveness over time. As noted in Section 6.3, our study shows that as per November 2023, 57% of drugs in MDD had safety stock levels ranging from 4-19 weeks.

Prior to the implementation of safety stock, 2018 experienced the highest potential for shortages, clearly demonstrating how important safety stock has become in mitigating supply issues within MDD. This finding is in line with studies that underscore the importance of maintaining emergency stock as a key mitigation strategy for combating drug shortages (34).

One might argue that the prioritization of MDD by wholesalers significantly contributed to mitigating shortages, which is a valid point. However, an analysis of the data reveals that the

number of drugs where wholesalers had sufficient stock to cover reported shortages is relatively low as shown in **Table 2**. This indicates that while wholesaler prioritization does play a role, it is not the sole factor in preventing shortages. Safety stock levels are also crucial in this respect.

The drug shortage team at Apotek 1 is taking proactive steps to address potential supply issues effectively. By working closely with wholesalers to fine-tune and maintain safety stock levels, they ensure readiness to prevent any interruptions in patient treatment. This approach underscores their commitment to managing the drug supply within the MDD system effectively. Additionally, our data analysis revealed that Apotek 1 multidose consistently increased its safety stock levels in response to reported shortages, ensuring that the stock is sufficient to cover the anticipated duration of each shortage. This strategy has been crucial in mitigating the impact of supply disruptions on patient care.

Another possible explanation as to why MDD systems may report fewer shortages compared to DMP might be their ability to use foreign-packaged drugs as alternatives. Our study found that among the drugs listed as short by DMP, 13 had foreign packaging options available exclusively to MDD systems. Importantly, none of these 13 drugs were among those lacking alternative treatments or requiring physician intervention. This suggests that MDD may have effectively managed these particular shortages by sourcing from these foreign-packaged alternatives instead.

7.3. Impact of MDD on Drug Shortage

Determining whether MDD system alleviates or exacerbates drug shortages in the country requires a nuanced analysis and robust, quantifiable data. Our study has explored various aspects of MDD's impact on drug shortages, showing both positive and negative effects. In the following paragraphs, we will discuss these aspects in more detail and offer possible explanations for why MDD could have mixed impacts on drug shortage.

Among the medications dispensed through MDD systems, 88 have available foreign alternative packages. The MDD department utilizes these alternatives, allowing the original items with marketing authorization to remain accessible in the market. This approach effectively mitigates drug shortages by substituting market shares of certain medications with these foreign-packaged alternatives. Consequently, patients receiving these medications through MDD are

less impacted by market shortages, highlighting a positive contribution of MDD systems to addressing drug availability issues.

Additionally, MDD makes a positive contribution to mitigating drug shortages for non-MDD patients by effectively managing its drug sourcing. Specifically, when shortages occur for medications that are also available to MDD in foreign-packaged forms, MDD utilizes these alternatives rather than tapping into the domestic market supply. This practice ensures that domestically authorized versions of these drugs remain available to the broader market, thereby alleviating potential shortages. This strategic use of foreign-packaged alternatives by MDD helps maintain a stable supply of critical medications in the domestic market.

Another indication supporting the argument that the MDD system can positively impact drug availability during shortages is evident in our findings. Although foreign packs constitute only 8% of the total types of drugs in the system, they represented 25% of the total volume of drugs packaged in 2023. This suggests that the drugs most frequently packed within MDD are sourced from foreign packs (in 2022, 16 of the top 50 most frequently packaged medications were foreign packed, increasing to 20 in 2023) which does not impact the supply of these medications in the domestic market. This allows the rest of the market to maintain the supply without depletion due to MDD’s sourcing strategies.

Another explanation for MDD's impact on drug shortages is the comparative limited medication supply provided to patients in this system versus non-MDD patients. Patients in the MDD system typically receive a 2- or 4-week supply of medication, which may help reduce waste. For instance, if a patient needs to change medications due to side effects or other reasons, the MDD system can quickly adapt and include the new medication in the next delivery. In contrast, non-MDD patients who may purchase larger quantities of medication could be left with excess if their treatment plan changes, leading to potential waste. Therefore, the MDD approach could indirectly contribute to lessening drug shortages by minimizing the quantity of unused medications.

In terms of the potential negative impacts, our data reveals a significant dependence on general market sources for MDD supplies, with only 8% of drugs used in the MDD system sourced from foreign packages. This indicates that 92% of the medications packed within MDD are procured from the same sources that supply the general population. The reliance on standard

sources means that the majority of the MDD's demands are met through the same supply channels that serve the broader national market. This could potentially raise concerns about market strain from allocating a significant portion of drugs to MDD either by being prioritized by wholesalers or their practice of having safety stock.

MDD suppliers do have criterion to determine which drugs can be included in their safety stock. These criteria include how critical the medication is, its recent market stability, the number of people who use it, and whether generic alternatives exist. If a drug not initially listed in the safety stock becomes problematic in terms of availability, MDD can decide to add that medication to the safety stock list. Therefore, their safety stock levels are continuously adjusted in response to market conditions and drug availability.

Approximately as per November 2023, 57% of drugs in MDD had safety stock levels ranging from 4-19 weeks. This reserve is strategically managed to ensure availability during shortages, reflecting a secured buffer for emergencies. MDD uniquely adjusts its safety stock levels in response to shortage notifications, increasing reserves as needed.

When analysing the drugs for which the multidose department requested wholesalers to secure quantities beyond immediate need, particularly those reported as being in short supply, it was found that wholesalers generally succeeded in obtaining the amounts requested by Apotek 1 Multidose. In some case, MDD actually managed to secure a safety stock exceeding their usual levels with regard to drugs reported short by DMP (see Section 6.3).

This approach differs from typical market practices, where sales are often rationalized during shortages to broaden accessibility. For example, during the COVID-19 pandemic, restrictions were placed on certain medications like paracetamol and dexamethasone to prevent stockpiling and ensure availability for those in need. Although this approach to increase safety stock after shortage reports might be justifiable from the perspective of MDD providers, it could potentially disadvantage non-MDD patients by limiting their access to essential medications.

Experts in the field suggest that maintaining emergency stock is a recommended mitigation strategy for combating drug shortages (34). Meanwhile, another study categorizes mitigation strategies as either reactive or proactive (57). Reactive strategies are implemented after a problem has occurred, while proactive strategies are taken in anticipation of potential problems to prevent them. While maintaining safety stock in MDD is typically viewed as proactive,

adjusting safety stock levels in response to shortages could be seen as reactive. This approach, as indicated in the second study, can lead to relational issues such as behavioural uncertainty, which complicates relationships and coordination efforts.

Therefore, it is our recommendation that effective coordination and communication among all supply chain stakeholders are essential to align safety stock strategies with broader market demands, ensuring that the accumulation for one segment does not detrimentally impact overall drug availability.

This notwithstanding, the potential negative impacts of MDD on drug shortage should be understood in light of the results presented in Section 7.2 above. Despite the advantages provided to MDD, and even though more than 90% of drug sources are shared with the general market, 78% of the drugs included in MDD were consistently available. Furthermore, the top five medications most frequently packed in MDD systems, despite high demand, experienced no shortages from 2018 to 2023. This suggests that the MDD system's practices of maintaining safety stocks and receiving prioritization from wholesalers do not seem to adversely affect the overall medication supply. Our findings support the conclusion that the high demand managed through MDD does not substantially impact market availability.

7.4. Role of Foreign Packs in Mitigating Drug Shortages in MDD

Another objective of this study was to examine the impact of foreign-packaged drugs in the MDD system. Our findings reveal that only 8% of the drugs packaged in MDD are foreign packages. Initially, we hypothesized that the ability of multi-dose suppliers to access these special packages without needing marketing authorization might play a crucial role in addressing drug shortages. However, our data suggests that the impact may not be as significant.

We analysed MDD-listed drugs reported as short in supply to see if they have foreign-packaged alternatives. The results showed that only 13 medications, representing about 6% of the drug shortages, have alternative foreign packaging available. This indicates that only a small fraction of drug shortages could potentially be alleviated by these special packages. It is important to

note that these shortage reports are based on data from the DMP, which might not fully reflect the actual situation faced by MDD suppliers.

Despite the possibility that 6% of drug shortage problems could be resolved by these packages, it is also crucial to consider the impact of these shortages on specific patients. Our study indicates that the number of patients who might be affected by these shortages is relatively low. The most significant impact could be on patients taking Triobe (vitamin B supplement) prescribed for 7927. However, the absence of this drug is not critical as it is unlikely to cause death or exacerbate diseases, given that there are many over-the-counter alternatives that could serve as replacements in worst-case scenario.

Moreover, it is important to recognize the advantages of foreign-packaged drugs within the MDD system. If a shortage exists in drugs that have a domestic marketing authorization, MDD can rely on these foreign variants to mitigate the issue. This ensures that MDD remains well-supplied without affecting the availability of these drugs for non-MDD patients. Essentially, by utilizing these foreign alternatives, the MDD system does not tap into the domestic stock, thereby preserving uninterrupted access for others and helping alleviate potential drug shortages.

7.5. Packaging Types and Size of Drugs Packed in MDD

As noted in Chapter 2 regarding the operational workflow of MDD, all drugs must be removed from their original packaging for machine repackaging into individual pouches. This necessity aligns with a preference for suppliers that offer packaging conducive to this process ideally, those providing larger box sizes to streamline handling and machine feeding. Despite the clear inclination of MDD providers for these larger sizes, fulfilling this preference is not always feasible, thus warranting an investigation into the packaging types utilized in MDD.

The results of our data indicated only 11% of those drugs packed in MDD come in large size. This finding indicates that while there may be a strong preference for larger packaging sizes, the department often does not procure them. This discrepancy could be due to the reluctance of drug suppliers to undergo the extensive marketing authorization process for larger package sizes, which might only appeal to a niche segment like MDD, constituting a smaller portion of the overall market.

Furthermore, our examination of foreign-packaged drugs, to which MDD has special access, shows that the majority come in sizes exceeding 200 units. This preference might suggest that MDD's procurement of foreign packs is driven by the aim to minimize unpacking time and cost rather than as a strategy to address drug shortages.

Despite regulatory exemptions by DMP that allow the import of foreign packages for MDD systems, and their convenience in the repackaging process due to larger sizes, only 8% of drugs used in MDD are from foreign packs. This low usage is primarily due to the higher purchasing costs of these packages compared to those with a Norwegian marketing authorization. According to DMP, foreign packages are 3-7 times more expensive than those with Norwegian authorization (58). This economic impact not only affects multidose providers but also the Norwegian welfare system, which covers the costs for these drugs under the blue prescription scheme (58). The DMP reported that the use of foreign packages in response to shortages costs the Norwegian welfare system over one hundred million kroner in 2023 (58).

Although this study was unable to quantify wastage due to the inability to obtain data, medications in blister packs, such as acetylsalicylic acid, necessitate manual extraction of tablets, leading to a potential for wastage. As indicated by the head of the MDD department at Apotek 1, this added step of deblistering, essential for multidose packaging, increases the risk that tablets or capsules may be damaged or dropped during the transfer. To the extent this is valid, foreign packs, which currently come in larger packaging sizes, might reduce potential waste from deblistering. This anecdotal observation highlights the need for manufacturers to consider alternative packaging, like boxes, for more efficient use in multidose dispensing systems. Despite these concerns, the resilience of the supply chain has ensured the uninterrupted availability of these essential medications, demonstrating its capability to overcome potential wastage issues.

7.6. Further Research

This study identifies multiple avenues for further research to enhance the effectiveness and efficiency of Norway's MDD system. Future investigations could include evaluating the potential of implementing a safety stock systems used in MDD for broader application in retail pharmacies, which might help manage drug shortages independently of national preparedness programs. Additionally, exploring the resource and time expenditures in the MDD repackaging

process and assessing the cost-effectiveness of procuring foreign packages that facilitate this process could provide insights into improving operational efficiencies. Another critical area involves quantifying wastage within MDD to assess its impact on drug shortages and determine the significance of the concerns identified in this study. Moreover, examining the strategies of stockpiling and prioritization by wholesalers could reveal if such practices contribute to market shortages and affect patients not covered by MDD. Finally, understanding the reasons and challenges faced by manufacturers in providing packaging convenient for MDD processes, such as the use of bulk packages, could lead to more tailored solutions that align with the needs of the MDD system. Our study noted the prevalent use of Calcigran Forte and Pantoprazole among the top 10 drugs. While we haven't directly linked PPIs to osteoporosis, literature suggests a possible association. Considering Oslo's high fracture rates, further investigation into PPI-induced osteoporosis within MDD patients is warranted.

7.7. Limitation of the Study

The study presented here has several limitations that should be noted. Firstly, our ability to quantify wastage was constrained due to data limitations. Additionally, we did not include data from other multidose providers, such as NMD, which may limit the generalizability of our results. However, as Apotek 1 is the largest provider of multidose services, the findings of this study could provide meaningful insights into multidose services more broadly.

A further limitation concerns the data on drug shortages for the year 2023. The dataset only included reports up until June 2023, which complicates the assessment and comparison of shortage reports for the entire year. Moreover, the study was only able to access a complete assortment list of drugs packaged within the MDD system for the years 2022 and 2023. This limitation arises because Apotek 1's database can only retrieve assortment data from the past two years.

Lastly, while wholesaler prioritization has clearly been beneficial, our study could not quantify the extent to which this practice alone has helped mitigate shortages, nor could we precisely measure how often safety stock was a decisive factor in preventing shortages on a case-by-case bases. This indicates a need for further research to isolate and more distinctly evaluate the impact of these variables.

Conclusion

This study explored the MDD system, uncovering insights into its operations and impact on drug shortages. We identified panodil 1gm, Acetylsalisylsyre 75mg and Calcigran Forte 500mg/400IE as the most frequently packed drugs in MDD. Despite reported shortages by the DMP the impact on MDD appears minimal, highlighting the system's effective strategies for managing shortages through collaborative efforts across various actors.

Our findings indicate that prioritization by wholesalers and the strategic use of safety stocks have significantly mitigated shortage issues within the MDD system over the years. Furthermore, foreign packages play some, albeit minimal role, in addressing drug shortages. Despite this, foreign packages offer other advantages to the MDD system because of their bigger packing sizes, potentially saving resources (minimizing wastage) and time that would otherwise be spent deblistering medications from their original packaging.

A significant portion of MDD drugs are supplied in blister packs, necessitating the manual removal of tablets or capsules for processing. Additionally, a notable fraction of drugs from 2022 and 2023 are supplied in smaller packages, requiring transfer to larger containers prior to the commencement of the multidose packaging process. This process of deblistering potentially increases the likelihood of drug wastage during the repackaging process.

While our research provides a nuanced understanding of MDD's impact on drug shortages, highlighting both the positive and negative impacts it might have, it stops short of conclusively determining whether the positive outcomes outweigh the negatives. However, it offers valuable insights into various aspects of MDD's operations and their broader implications, suggesting that the benefits likely play a substantial role in stabilizing drug supply in challenging times.

Author’s Contribution

The research area was initially introduced by my main supervisor during the "Masters Torg" session of my master's course (the project description is attached as an appendix). This area is part of a larger project (MIA) run by BI Norwegian Business School, which is funded by the Research Council of Norway, the Helsevel programme. I have further developed and pursued this specific aspect of the study. Below, I detail my contributions as the author in this study.

- Conducted a thorough review of relevant literature in the field, identified research gaps, set research objectives, and formulated research questions to address the aim.
- Organized and systematically integrated data provided by BI and Apotek 1.
- Designed and executed the methodology in collaboration with my supervisors.
- Performed data analysis and presented the results.
- Interpreted and discussed the results in the context of existing literature.
- Concluded the study and highlighted potential avenues for future research.

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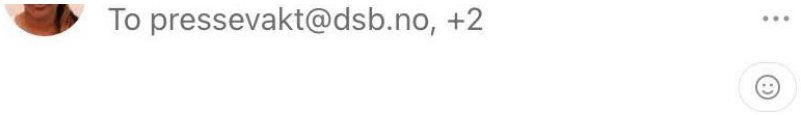
Appendix

1. Permission for using figures from DSB:

This appendix shows the exchange of emails between the researcher and the Direktoratet for samfunnssikkerhet og beredskap (DSB) regarding the request for permission to use figures from their report. It includes the initial inquiry from the researcher and the response from DSB.



Hei,

Mitt navn er Selam, og jeg er masterstudent i farmasi ved Oslomet. Jeg hadde nylig en telefonsamtale med en av deres kolleger som anbefalte meg å sende en e-post angående dette. Jeg skriver en masteroppgave som primært handler om legemiddelmangel. Jeg har kommet over en rapport publisert av dere med tittelen "Risikoanalyse av legemiddelmangel: Krisescenarioer 2018 – analyser av alvorlige hendelser som kan ramme Norge."

Ved Oslomet er det strenge krav ikke bare til å kreditere kilder, men også til å innhente tillatelse for å bruke materiale som figurer fra publikasjoner. Jeg ønsker derfor å spørre om jeg kan få tillatelse til å bruke noen av figurene som er i rapporten i min oppgave. Jeg skal selvfølgelig sørge for å korrekt sitere rapporten.

Takk

Mvh, Selam

JO

Johansen, Ole Tom

To You

24 Apr

You don't often get email from ole.johansen@dsb.no. Learn why this is important

Hei

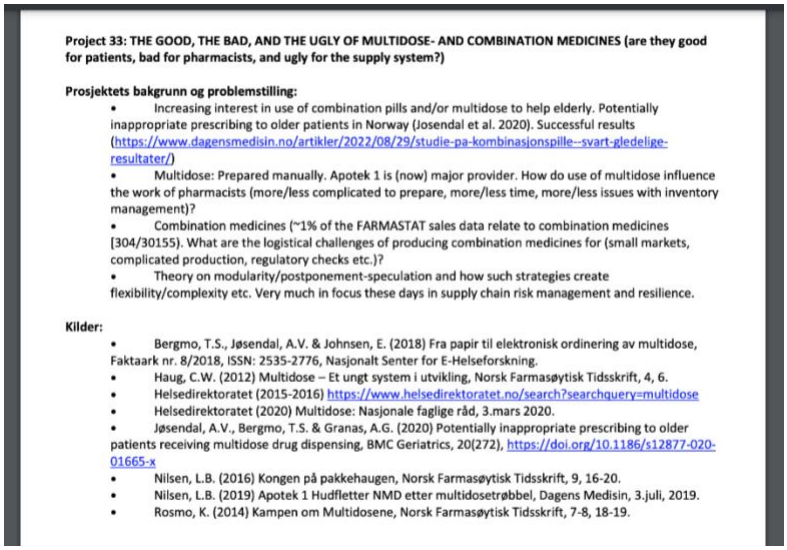
Det er i orden at du siterer tekst og gjengir figurer fra "Risikoanalyse av legemiddelmangel: Krisescenarioer 2018" så lenge du oppgir kilde DSB (vis ikke annet er oppgitt som kilde i publikasjonen).

https://www.dsb.no/rapporter-og-evalueringer/risikoanalyse-av-legemiddelmangel/

Fotoene i publikasjonen kan ikke gjenbrukes siden disse kun er tillat for bruk i denne publikasjonen. Eventuell ny bruk av foto her må avtales med- og honoreres til billedbyrå (opphavsperson).

Mvh
Ole Tom Johansen
Publikasjonsredaktør DSB

2. Project Description when Presented at the "Master Torg"



Project 33: THE GOOD, THE BAD, AND THE UGLY OF MULTIDOSE- AND COMBINATION MEDICINES (are they good for patients, bad for pharmacists, and ugly for the supply system?)

Prosjektets bakgrunn og problemstilling:

- Increasing interest in use of combination pills and/or multidose to help elderly. Potentially inappropriate prescribing to older patients in Norway (Josendal et al. 2020). Successful results (https://www.dagensmedisin.no/artikler/2022/08/29/studie-pa-kombinasjonspille--svart-gledelige-resultater/)
- Multidose: Prepared manually. Apotek 1 is (now) major provider. How do use of multidose influence the work of pharmacists (more/less complicated to prepare, more/less time, more/less issues with inventory management)?
- Combination medicines (~1% of the FARMASTAT sales data relate to combination medicines [304/30155). What are the logistical challenges of producing combination medicines for (small markets, complicated production, regulatory checks etc.)?
- Theory on modularity/postponement-speculation and how such strategies create flexibility/complexity etc. Very much in focus these days in supply chain risk management and resilience.

Kilder:

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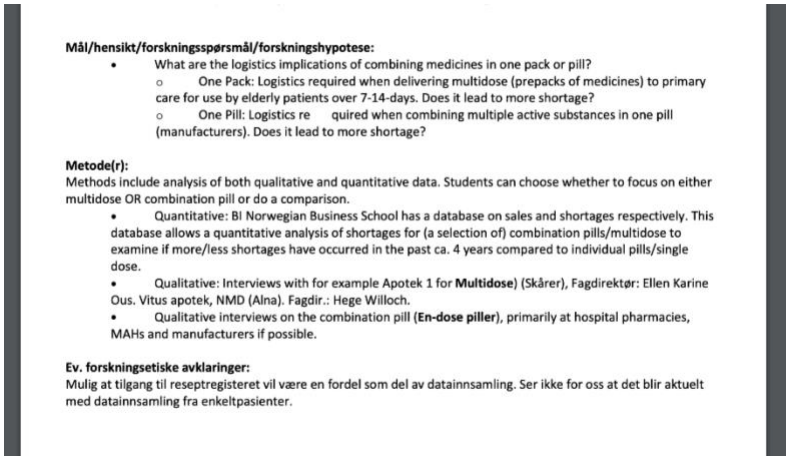

Mål/hensikt/forskningsspørsmål/forskningshypotese:

- What are the logistics implications of combining medicines in one pack or pill?
  - One Pack: Logistics required when delivering multidose (prepacks of medicines) to primary care for use by elderly patients over 7-14-days. Does it lead to more shortage?
  - One Pill: Logistics re quired when combining multiple active substances in one pill (manufacturers). Does it lead to more shortage?

Metode(r):

Methods include analysis of both qualitative and quantitative data. Students can choose whether to focus on either multidose OR combination pill or do a comparison.

- Quantitative: BI Norwegian Business School has a database on sales and shortages respectively. This database allows a quantitative analysis of shortages for (a selection of) combination pills/multidose to examine if more/less shortages have occurred in the past ca. 4 years compared to individual pills/single dose.
- Qualitative: Interviews with for example Apotek 1 for **Multidose**) (Skårer), Fagdirektør: Ellen Karine Ous. Vitus apotek, NMD (Alna). Fagdir.: Hege Willoch.
- Qualitative interviews on the combination pill (**En-dose piller**), primarily at hospital pharmacies, MAHs and manufacturers if possible.

Ev. forskningsetiske avklaringer:

Mulig at tilgang til reseptregisteret vil være en fordel som del av datainnsamling. Ser ikke for oss at det blir aktuelt med datainnsamling fra enkeltpasienter.