Use of Non-Steroidal Anti-Inflammatory Drugs among elderly patients in selected Norwegian Nursing Homes

Master thesis in Pharmacy

Senay Abraha Beyene

December 2021

Centre for Pharmacy and
Department of Global Public Health and Primary Care

ACKNOWLEDGEMENT

First and foremost, I would like to thank my supervisors Lone Holst, and Hilde Erdal, for guiding me through this project. Writing this thesis under the COVID-19 pandemic was very challenging. But you ladies have invested a lot of your time finding me the alternative task to submit my thesis at the right time. The valuable guidance, suggestions, and instructions that I have received from both of you have served as the major contributor to the project's completion. Thank you again for giving me the golden opportunity to do such a wonderful project.

Then I would like to thank Reidun Kjome and Amani Thomas for creating such an exciting project. Even though the project doesn't go well as we planned, I still used your project's title as a base to accomplish my thesis.

My gratitude goes to my father, Abraha Beyene, my mother, Mebrat Ghezai, my sisters Sefanit Abraha and Yohana Abraha, and my brother Eyob Abraha. I'm proud to have such a lovely family. You have always helped me to get through all the hardships of life. I'm forever great full to God for blessing me with such a beautiful family. Thank you so much for your love and affection. You have always helped me to fight against all odds in my life. Thank you for being there with me always, and thank you for always being by my side.

I want to thank all my friends and colleagues for encouraging me to continue and never give up on my study.

Last but not least, I would like to thank my classmates Berhane Fire, Tsegazeab Tekle, and Luwam Gebrehiwet. It wouldn't be easy to have such a long study without you guys.

Senay Abraha Beyene
Bergen, December 2021

ABSTRACT

Background: Non-Steroidal Anti-inflammatory Drugs (NSAIDs) are among the most widely used medicines in managing pain, fever, blood clotting, and inflammatory conditions. However, concerns have been raised that NSAIDs may be associated with an increased risk of adverse effects in the elderly. The present study aims to describe the use of NSAIDs among elderly patients in a selected Norwegian nursing home population.

Material and method: A study was conducted based on data from the COSMOS study (2013-2016). The data included information extracted from questionnaires and physical examinations in 544 participants recruited from 67 nursing home long-term-care wards in eight different Norwegian municipalities. Medication data was used to describe the use of oral NSAIDs among Nursing home patients and binomial logistic regression analysis was conducted to investigate associations between use of cardiovascular medicines and proton pump inhibitors and regular use of oral NSAIDs.

Results: Overall, 2.2% of the study population used oral NSAIDs regularly. Including on-demand (PRN) use, a total of 8% of the study population used oral NSAIDs. The most common oral NSAIDs used were ibuprofen and diclofenac. We found no significant association between regular use of oral NSAIDs and either cardiovascular medicines, neither proton pump inhibitors.

Conclusions: During the study, 8 % of the study population used oral NSAIDs regularly or PRN. The majority of the participants used oral NSAIDs PRN, but around 2% of the entire study population were prescribed regular oral NSAIDs for different indications. Regular oral NSAID-users were taking different cardiovascular medicine or proton pump inhibitors during the study. However, no difference in prevalence of use of regular CV medicines or PPIs was found between regular oral NSAID-users and the study population not using regular oral NSAIDs.

Key words: NSAIDs, ibuprofen, diclofenac, coxibs, regularly used NSAIDs, on-demand used NSAIDs (PRN), indications for NSAID use, elderly/older adults, nursing home (NH) patients, Norway, COSMOS study, Norwegian prescription database, medication list, adverse effects, drug interactions, CV-medicines, CV-complications, GI- disturbance, PPIs.

LIST OF ABBREVIATIONS

AA	Arachidonic acid
ACEI	Angiotensin-converting-enzyme inhibitor
ARB	Angiotensin Receptor Blockers
ASA	Acetylsalicylic Acid
ATC	Anatomical Therapeutic Chemical Classification
BID	Twice a day
CI	Confidence interval
COX	Cyclooxygenase
COX-1	Cyclooxygenase-1
COX-2	Cyclooxygenase-2
CVD	Cardiovascular disease
DDD	Defined daily dose
GI	Gastrointestinal
HR	Hazard ratio
HWs	Hospital wards
INHU	Intermediate care nursing home unit
MI	Myocardial infarction
NORGEP	Norwegian general practice
NH	Nursing Homes
NSAIDS	Non-Steroidal Anti-Inflammatory Drugs
tNSAIDS	traditional Non-Steroidal Anti-Inflammatory Drugs
OR	Odds Ratio
OTC	Over the counter
PGH_2	Prostaglandin H2
PGE_2	Prostaglandin E2
PGI_2	Prostaglandin I2
PLA_2	Phospholipase A2
PPI	Proton pump inhibitors
PRN	Pro Re Nata /On-demand
RAAS	Renin-Angiotensin-Aldosterone System
SSB	Statistics Norway
TXA_2	Thromboxane A2

Table of Contents

GLOSSARY ..... *II*

1. INTRODUCTION *1*

1. 1 The history of inflammation and NSAIDs: from discovery to development 1

1. 2 Modern explanation of inflammation and NSAIDs 1

1.2.1 what is inflammation 1

1. 2. 2 What are NSAIDs 2

1. 2. 3 Mechanism of action 2

1. 2. 4 Therapeutic actions 3

1. 3 Different types of NSAIDS 3

1. 3. 1 Commonly used NSAIDs in Norway 4

1. 3. 2 NSAIDs which are withdrawn from the market 6

1. 4 Common adverse effects of NSAIDs 6

1.4.1 Cardiovascular side effects 6

1.4.2 Gastrointestinal disturbances 10

1.4.3 Adverse renal effects 11

1.4.4 Skin reactions 12

1.4.5 Other adverse effects 12

1. 5 Common drug interactions 12

1.6 Elderly population and Nursing homes in Norway 13

1.6.1 An overview of the challenges facing the elderly due to aging 14

1.6.2 Use of NSAIDs in the elderly population in Norway 15

1.7 An overview of NSAID-use among the elderly according to gender 17

1.8 The importance of the study 18

1.9 Aim and study questions 19

1.9.1 Aim 19

1.9.2 Study questions 19

2. METHODS *20*

2.1 The COSMOS study 20

2.1.1 Study design 20

2.1.2 Inclusion and exclusion criteria 20

2.1.3 Participant recruitment 20

2.2 Data material used in this thesis 22

2.2.1 Data security 22

2.2.2 Medication list 22

2.2.3 Statistical analysis 23

2.3 Ethical approval 23

3. RESULTS *24*

3.1 Characteristics of study population 24

3.2 Use of oral NSAIDs in the study population 25

3.3 Indications for oral NSAIDs use during the study 27

3.4 Concomitant use of NSAIDs and CV-medicines or PPIs **27**
3.4.1 Use of medicines for cardiovascular diseases by patients taking regular oral NSAID 27
3.4.2 Use of proton pump inhibitors (PPIs) among oral NSAID-users 29
3.5 Deaths among oral NSAID-users during the study period **30**
4. DISCUSSION ***31***
4.1 Method discussion **31**
4.1.1 Study population 31
4.1.2 Data collection 31
4.1.3 Medication list 32
4.1.4 Statistical methods 33
4.2 Discussion of the results **33**
4.2.1 Baseline characteristics of the study population 33
4.2.2 Prevalence and type of oral NSAIDs in the study population 34
4.2.3 Characteristics of oral NSAID users 35
4.2.4 Indications for NSAID use during the study 35
4.2.5 Use of medicines for cardiovascular diseases by patients taking regular oral NSAID 36
4.2.6 Use of Proton pump inhibitor by patients taking oral NSAID 37
4.2.7 Future studies 38
5. Conclusion ***39***
6. REFERENCE LISTS ..... ***III***
7. APPENDICES ..... ***IV***
7.1 Appendix 1 Questionnaire from the COSMOS study ..... **IV**

GLOSSARY

Anatomical Therapeutic Chemical (ATC) is a classification system which is used to classify the active substances of drugs based on the system or organ they work on and on their therapeutic, pharmacological, and chemical properties, by which the World Health Organization Collaborating Centre for Drug Statistics Methodology (WHOCC) controls. It has fourteen main anatomical/pharmacological groups (1st level), further divided into pharmacological or therapeutic groups (2nd level), chemical, pharmacological or therapeutic subgroups (3rd and 4th levels), and the 5th level is the chemical substance. In order to identify pharmacological subgroups, the 2nd, 3rd, and 4th levels are often used [1].

COX-1 enzyme is responsible for protecting the gastric mucosa (the stomach's lining) from the acid that the stomach naturally produces. COX-1 enzyme also plays a significant role in platelet aggregation to form clots.

COX-2 is an enzyme which is responsible for inflammation and fever.

Defined Daily Dose (DDD) is a quantitative unit defined as the assumed average maintenance dose of a drug per day, indicating adults' main indication. There is only one DDD is assigned per ATC code and route of administration. It doesn't consider individual patients' characteristics such as age, weight, type, and severity of the disease.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are members of a drug class that reduces pain, decreases fever, prevents blood clots, and decreases inflammation. They work by inhibiting the activity of cyclooxygenase (COX) enzymes.

Selective NSAIDs are drugs that only target on specific COX enzyme.

Non-Selective NSAIDs are drugs that inhibit both types of the COX enzymes.

Nursing Homes (NH) is a health institution that provides patients with round-the-clock accommodation, treatment, and care that does not have to take place in a hospital, but which nevertheless requires more health professional effort than is practically possible or justifiable to provide in the patient's own home.

PRN (Pro Re Nata / on-demand) medicine that you take it as you need it

1. INTRODUCTION

1. 1 The history of inflammation and NSAIDs: from discovery to development

Inflammatory diseases are among the most common significant challenges that have caused and still causing the loss of hundreds of lives [2]. Inflammation is one of the earliest recognized diseases, in which its name derived from the Latin word ‘‘inflammare’’ meaning to set on fire [3]. Cornelius Celsus, a Roman encyclopedist was the first person who has described inflammation by the four cardinal signs, namely ‘‘pain (dolor), redness (rubor), warmth (calor), and swelling (tumor)’’.

Willow bark has been used for centuries by the great ancient, civilized societies for the treatment of fever, pain, and inflammation. In 1828 professor Johann Büchner isolated a yellow substance from the tannins of willow bark and named it ‘‘salicin’’ (a Latin word meaning willow), who then used it to treat rheumatism [4]. The study on inflammation and NSAIDs has been continued and developed from time to time and came up to a scientific definition which is based on experimental investigation and clinical studies.

1. 2 Modern explanation of inflammation and NSAIDs

1.2.1 what is inflammation

Inflammation is part of the body's defense mechanism which gets triggered when the body is attacked by viruses, bacteria, and other harmful substances. It aims is to bring defense cells to the area of concern and inactivate and/or destroy invaders. The body releases inflammatory mediators into the bloodstream increasing the blood flow to the area of infection or injury, causing redness and warmth in that body part. These help the immune system to recognize and remove harmful and foreign substances and begin the healing process [5]. Inflammatory mediators are subdivided into two groups: cell-derived, and plasma protein derived mediators. Cell-derived mediators include histamine, serotonin, prostaglandins, cytokines, chemokines, and Nitric oxide which are produced locally by cells. Whereas plasma-protein derived mediators include complement- and kinin- systems (e.g. Bradykinin) which are produced in the liver. Inflammation can be either acute lasting from hours to days, or chronic that lasts

from months to years [2]. Inflammation is clinically denoted by suffix-itis, such as dermatitis inflammation of the skin or arteritis inflammation of the joint.

1. 2. 2 What are NSAIDs

Non-Steroidal Anti-inflammatory Drugs (NSAIDs) are among the most widely used medicines in the management of pain, fever, and decreasing inflammatory conditions [6]. NSAIDs are well known for the treatment of joint diseases, and they are available in the market in different formulations including tablets, capsules, gels, and injections. These drugs work by inhibiting the inflammatory mediators in our body that are responsible for inflammation, similarly to corticosteroids, thereby named “non-steroidals” meaning drugs that act like cortisones without being steroids. Nowadays there are several types of NSAIDs sold by prescription and over the counter for the treatment of minor pains.

1. 2. 3 Mechanism of action

NSAIDs primarily inhibit the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) enzymes, which are responsible for the production of prostaglandins and thromboxane [6]. Prostaglandin is a hormone-like compound which controls different body processes such as blood clotting, inflammation, and blood flow. COX-1 enzyme, which is found in most tissues and in blood platelets, is responsible for the production of prostanoids that mainly regulate homeostatic activities in the body such as in the regulation of gastric acid secretion and in the activation of platelets. COX-2 enzyme on the other hand is responsible for the production of prostaglandins during inflammation stimuli, such as an infection or injury [7]. Both COX-1 and COX-2 produce prostaglandins that promote pain, fever, and inflammation, but there are two features that are unique to COX-1 namely that it produces Thromboxane A2 (TXA_2) and produces prostaglandins that protect the stomach from gastric acids. Most prostaglandins act locally as a vasodilator in the walls of blood vessels, resulting in a decrease in blood pressure by increasing the rate of blood flow. On the other hand, thromboxanes constricts blood vessels, which raises the blood pressure. TXA_2 is located within the platelets and works as a procoagulant, whereas Prostaglandin I_2 (PGI_2) is located in endothelium and acts as an anticoagulant [8].

1. 2. 4 Therapeutic actions

NSAIDs generally have three major therapeutic actions:

- *Analgesic effects*: when our body is in pain, it causes activation of COX-enzymes and production of prostaglandins. NSAIDs inhibit COX enzymes, thereby decreasing the production of prostaglandins (PGs), which are either responsible for activating nociceptors to inflammatory mediators, or responsible for vasodilation on the cerebral vasculature. This blockage gives the body relief from pain and headache [6].

- *Antipyretic effects*: inflammations and pyrotoxins from bacterial infections can result in a high body temperature (fever). NSAIDs give the body relief from fever by inhibiting the production of PGs in the hypothalamus which is responsible for the elevation of body temperature set point.

- *Anti-inflammatory effects***:** NSAIDs doesn't have any direct effect on the underlying chronic disease itself. But they suppress the signs and symptoms of inflammation by blocking the production of vasodilator PGs, resulting in reduction in blood flow [6, 8].

1. 3 Different types of NSAIDS

Based on their mechanism of action, NSAIDS are categorized in to three subgroups [9]:

- Those which only inhibit COX-1 enzyme (selective COX-1 inhibitors),
- Those which only inhibits COX-2 (selective COX 2 inhibitors) and
- Those which inhibits both COX-1 and COX-2 enzymes non-selectively.

Table 1. 1 List of Common NSAIDs according to their affinity of binding COX enzymes.

More COX-1 selective

Generic	**Brand**
Ketoprofen	Orudis
Acetylsalicylic acid	Aspirin

Relatively non-selective

Generic	**Brand**
Naproxen	Naproxen, Napren, Proxan
Ibuprofen	Ibux, Ibumetin, Ibuprox, Advil

Less than 50-fold COX-2 selective

Generic	**Brand**
Diclofenac	Cataflam, Voltaren, Voltarol, Ignorin
Celecoxib	Celebrex, Celebra

More than 50-fold COX-2 selective

Generic	**Brand**
Rofecoxib	Vioxx
Etoricoxib	Arcoxia

COX-2 enzymes can be induced with more than 50 fold range or less than 50 fold range, by a variety of inflammatory mediators and stimuli such as injury, hypoxia, synaptic excitation and etc. [10]. In the in vitro assay systems, the inhibition of COX-1 and COX-2 is expressed in terms of the IC50 of an agent. That is the concentration required to inhibit COX activity by 50%. Ratios for COX-2/COX-1 have been calculated in order to determine the differential inhibition rate of the different isoforms. For instance, a low COX-2/COX-1 ratio indicates that the isoform is relatively selective for COX-2 [11].

1. 3. 1 Commonly used NSAIDs in Norway

Ibuprofen

Ibuprofen is used during headache, back pain, arthritis, menstrual cramps in order to reduce or treat pain, inflammation, and fever. This medicine is sold in pharmacies, shops and at petrol stations. It comes in different forms such as gels, tablets, injections, and syrups.

Naproxen

Naproxen is used to treat pain and inflammation caused by arthritis, tendinitis, gout, or menstrual cramps. Naproxen is sold only in pharmacies and they are available on prescription and OTC. Naproxen comes either as a regular tablet or enteric-coated form.

Diclofenac

Diclofenac is used to treat mild to moderate pain and aches, as well as problems with muscles, joints, and bones, including osteoarthritis and rheumatoid arthritis, and postoperative pains. Diclofenac comes in different pharmaceutical formulations such as tablets, capsules, and suppositories, which are available on prescription only, and gels are available OTC. In addition, diclofenac comes as injection or eye drops, but it is only given in hospitals [12]. Some examples of this drug are Voltaren, Cataflam, and Voltarol, and they are sold only in pharmacies.

Celecoxib

Celecoxib explicitly inhibits the COX-2 enzyme and treats arthritis, acute pain, menstrual pain, and discomfort. Celecoxib is available on prescription only, in a capsule form.

Etoricoxib

Etoricoxib inhibits COX-2 enzymes selectively, and currently used in the treatment of various indications such as acute pain, osteoarthritis, rheumatoid arthritis, and gouty arthritis. Etoricoxib is available on prescription only, in a regular tablet form.

High-dose acetylsalicylic Acid (ASA)

High-dose acetylsalicylic acid is used to treat pain, and reduce inflammation and fever [13]. High-dose ASA is defined as ASA-doses ranging from 350mg and above [14]. ASA 500mg is available by prescription and OTC. It is only sold in pharmacies, and it is only available as a regular tablet form. The sales of ASA as an analgesic are very low. It was much more common earlier, but because of its serious side effects, other analgesics have been promoted as the drugs of choice [15].

1. 3. 2 NSAIDs which are withdrawn from the market

Rofecoxib

Rofecoxib selectively inhibits Cox-2 enzymes. It has been used to treat mild to moderate pain, migraine, osteoarthritis, menstrual pain, and rheumatoid arthritis. Rofecoxib was officially withdrawn from the market in 2004 right after different studies have shown its high risk for CV complications [16]. The 3-year clinical trial called APPROVe (Adenomatous Polyp Prevention of Vioxx) included 2586 eligible patients with a history of colorectal adenomas [17]. Randomly selected 1287 patients have received rofecoxib with a mean duration of treatment 2.4 years, whereas 1299 received placebo with a mean duration of treatment 2.6 years. The study was terminated two months before the intended time due to high numbers of adverse effects in the group taking rofecoxib. The risk for having thrombotic events among rofecoxib groups was twice as high (RR of 1.92 (95% CI 1.19-3.11)) compared to placebo groups.

1. 4 Common adverse effects of NSAIDs

1.4.1 Cardiovascular side effects

NSAIDs are associated with an increased risk of cardiovascular (CV) events especially of COX-2 selective NSAIDs [6]. Some of the common CV adverse effects are: thrombotic events, increased blood pressure, congestive heart failure, myocardial infarction, stroke, and palpitations, and the risk seems to occur early in treatment, and increase with the duration of use.

Drug-induced hypertension is commonly associated with patients taking non-selective NSAIDs, in both treated and untreated secondary hypertension (that occurs because of another disorder). Both COX-1 and COX-2 enzymes are expressed in renal and vascular tissue, inducing cytoprotective vasodilation in the kidney. Inhibition of these enzymes results in renal vasoconstriction which in turn increases fluid and sodium retention in the body. These effects can contribute to an increase in blood pressure, and thereby increasing the risk of CV complications. There has been reported an increase of 5 mm Hg in the systolic blood

pressure among patients taking NSAIDs concomitantly to antihypertensive drugs [18], mitigating the beneficial effects of antihypertensive medicines. Thrombotic events are also associated with the use of selective COX-2 NSAIDs. COX-2- enzymes are responsible for reducing platelet aggregation in the bloodstream. Inhibition of these enzymes increases in platelet aggregation and thereby increasing the risk of thrombotic events which in return results in myocardial infarction, heart failure, and stroke [6].

Recently different clinical studies have been conducted to evaluate the safety of NSAIDs with regards to CV events, and results have shown cardiac problems as a class effect, with a widely varying risk between individual NSAIDs [19]. In a Danish nationwide cohort study which included 1 370 832 users of diclofenac, 3 878 454 users of ibuprofen, 291 490 users of naproxen, 764 781 users of paracetamol, and 1 303 209 non NSAID-users, the adverse effects increased by 50% among users of diclofenac versus non-users, 30 % compared to naproxen-users, and 20% compared to ibuprofen users. The study showed an increased rate of heart failure, atrial fibrillation, and myocardial infarction among diclofenac users compared to non NSAID-users [20].

A further meta-analysis included 138 randomized trials with a total of 145 373 participants taking selective COX-2 inhibitors (rofecoxib, celecoxib, etoricoxib, lumiracoxib, and valdecoxib) versus placebo or versus a traditional NSAID (such as naproxen and ibuprofen) or both showed a 42% relative increase in the incidence of cardiovascular events among patients using selective COX-2 inhibitors [21]. Among 121 placebo-controlled trials who were exposed to a selective COX-2 inhibitor, a total of 216 vascular events were registered during 18 490-person years, compared to 112 vascular events during 12 639-person years. Besides the study compared selective COX-2 inhibitors versus traditional NSAIDs (tNSAID), and resulted in no significant difference in cardiovascular incidence between participants assigned to a selective COX 2 inhibitor (340 vascular events during 33 260-person years) and a traditional NSAID (211 vascular events during 23 325-person years). Participants who used diclofenac had 1.63 (95% CI 1.12 to 2.37) times the rate of having cardiovascular events compared with the placebo groups, followed by ibuprofen 1.51 (0.96 to 2.37), and selective COX-2 inhibitor 1.42 (1.13 to 1.78). The relative risk of causing serious cardiovascular events shown by diclofenac is equivalent to or possibly even higher than that of rofecoxib, which was withdrawn from the market in 2004 [16].

A meta-analysis conducted by Trelle S et al (2011) included thirty-one randomized control trials comparing patients who use different types of NSAIDs with placebo. A total of 116 429 patients were assigned to naproxen, rofecoxib, etoricoxib, lumiracoxib, or placebo, and followed up over 115 000 patient-years. As a result, patients who used rofecoxib had two times the rate of having a myocardial infarction (rate ratio 2.12, 95% CI 1.26 to 3.56) compared to placebo, followed by lumiracoxib (2.00, 0.71 to 6.21). Besides, participants who used ibuprofen had 3 times the risk of having stroke compared with the placebo groups with a rate ratio of (3.36, 1.00 to 11.6), followed by diclofenac (2.86, 1.09 to 8.36). Furthermore, Diclofenac and Etoricoxib were associated with the highest incidence of CV death resulting in (4.07, 1.23 to 15.7) and (3.98, 1.48 to 12.7) respectively [22]. A systemic review and a meta-analysis of randomized double-blind clinical trials of celecoxib (2006), included 4 422 patients in four placebo-controlled trials comparing celecoxib with placebo in the primary meta-analysis, whereas in the secondary meta-analysis a total of six studies were analyzed such as placebo with controlled trials among 12 780 patients who were using NSAIDs [23]. In the primary meta-analysis, the odds of having myocardial infarction with celecoxib treatment were twice as high compared to placebo groups, OR 2.26 (95% confidence interval 1.0 to 5.1), and in the secondary meta-analysis, the odds of having myocardial infarction were twice as high with celecoxib treatment compared to placebo groups OR 1.88 (95% CI 1.15 to 3.08). Aldington s et al. (2005) performed a systematic review and meta-analysis of placebo-controlled randomized double-blind clinical trials to evaluate the risk of CV thrombotic events on patients taking etoricoxib for at least 6 weeks. The project included five studies with a total of 2 919 participants resulting, an increase in the odds of having thrombotic events among patients taking etoricoxib compared to placebo groups with an odds ratio of 1.49 (95% CI 0.42-5.31) [24]. Later in 2007, Scott P A et al. compared different randomized controlled trials and systematically reviewed evidence from different observational studies. The aim was to compare the risk of myocardial infarction (MI) among patients taking selective COX-2 inhibiting drugs and traditional NSAIDs. The study showed a small overall risk of MI with a standard dose of tNSAIDs and selective COX-2 inhibiting drugs rather than rofecoxib [25].

1.4.1.1 Does the risk depend on the dose, duration of treatment, and other factors?

Different studies were performed to investigate the risk of NSAID use according to dose [23, 26-29], and have shown a dose-effect relationship in most NSAIDs except for naproxen. McGettigan & Henry [28] identified in 9 of 12 studies an increased risk of CV events within the first 30 days of use of rofecoxib, celecoxib, diclofenac, and ibuprofen, whereas 3 studies reported an increased risk within 14 days of use. The CV risk was seen with low doses of etoricoxib, celecoxib, rofecoxib, and diclofenac, and elevated with higher doses. The risk for ibuprofen was only seen with higher doses. Besides, studies have shown that ibuprofen has a low risk of CV complications when used in low doses (less than 1 200mg/day) [26, 28]. In contrast, studies by McGettingan & Henry [28], and N Bhala et al. [30] have shown that naproxen carries a lower risk of cardiovascular events in comparison to other non-steroidal anti-inflammatory drugs, and was risk-neutral at all doses.

A further study from 2008 [27] compared 6 randomized placebo-controlled trials with a total of 7950 patients taking celecoxib. The study categorized the patients into 3 dose regimens and followed them up for 3 years. Patients were administered celecoxib 400 mg once a day (OD), 200 mg twice a day (BID), or 400 mg BID. This resulted in a lower risk of CV events for the 400-mg-QD dose hazard ratio 1.1 (95% CI 0.6 to 2.0), intermediate for the 200-mg-BID dose hazard ratio 1.8 (95% CI 1.1 to 3.1), and highest for the 400-mg-BID dose hazard ratio 3.1 (95% CI 1.5 to 6.1), indicating in an increase in CV events with an increase in the dose regimen.

Olsen A et al. (2011) in a Danish nationwide cohort study assessed the correlation between the duration of NSAIDs treatment and CV risk among patients with prior myocardial infarction (previously had a heart attack). The study included a total of 83 677 patients who were using ibuprofen (23.2%), naproxen (2.2%), diclofenac (13.4%), rofecoxib (4.7%), or celecoxib (4.8%), showed an increased risk of death after 7-14 days of use for rofecoxib, 14-30 days of use for celecoxib, after seven days for ibuprofen, and for diclofenac the risk of death increased from the start of the treatment, whereas naproxen didn`t show any increased risk of death during the entire study period. During the observational period a total of 29 234 deaths were registered which is 35% of the population [31].

1.4.2 Gastrointestinal disturbances

Gastrointestinal (GI) disturbances are one of the most common unwanted effects of NSAIDs. The reason is believed to be the inhibition of the gastric COX-1 enzyme, which is normally responsible for the production of PG that protects the gastric mucosa, by inhibiting acid secretion [6]. Some of the most common adverse effects are nausea, vomiting, dyspepsia, constipation, diarrhea, gastric bleeding, and ulceration. Patients who have other predisposing risk factors such as advanced age, smoking, or a history of peptic ulcers should use NSAIDs cautiously [32].

A meta-analysis of observational studies and randomized trial (2013) which was aimed to study vascular and upper GI effects of NSAIDs included 280 trials of NSAIDs versus placebo (124 513 participants, 68 342 person-years) and 474 trials of one NSAID versus another NSAID (229 296 participants, 165 456 person-years). Among these 184 trials compared coxib versus tNSAID, and 113 trials compared coxib versus tNSAIDs (diclofenac in 33 trials, 61 572 participants, 90 644 person-years; ibuprofen in 22 trials, 22 225 participants, 11 668 person-years; naproxen in 48 trials, 48 706 participants, 31 631 person-years; and another tNSAID in 14 trials, 6192 participants, 928 person-years). The study resulted in an increased upper GI complication (such as bleeding, perforation, and obstruction) among patients taking celecoxib, diclofenac, ibuprofen, and naproxen in comparison with placebo. But among these upper GI complications, there were only 2% were registered as being fatal [30].

GI problems often come with COX- 1 selective- and non-selective- NSAIDs. But it can be seen also with COX-2 selective NSAIDs at a lower rate. An Observational cohort study was conducted in Ontario, Canada to compare the relative risk of upper GI bleeding among elderly patients taking selective COX-2 inhibitors and non-selective NSAIDs [33]. The study included over 40 000 elderly patients from the age of 66. Non-selective NSAIDs were given to 5 391 patients, diclofenac misoprostol (n=5087), rofecoxib (n=14 583), celecoxib (n=18 908), and 100 000 randomly selected elders which were not exposed to NSAIDs. The reason for including the randomly selected non-NSAIDs users was to estimate the baseline risk of upper GI bleeding not related to NSAIDs. During the study, 187 hospitalizations for upper GI bleeding were observed, and the rate of upper GI bleeding was four times higher for users of non-selective NSAIDs (adj. Rate ratio 4.0 (95% CI 2.3 to 6.9) compared to placebo

groups, followed by diclofenac plus misoprostol 3.0 (1.7 to 5.6), and rofecoxib 1.9 (1.3 to 2.8), but not celecoxib, since1.0 (0.7 to 1.6) the result was similar to that in the control group not using NSAIDs [33].

Table 1. 2 Prevalence of upper GI bleeding among elderly patients using different NSAIDs from 17 April 2000 to 31 March 2001, in Ontario, Canada.

	Control group (n=100 000)	Non-selective NSAIDs (n=5 391)	Diclofenac + misoprostol (n=5 087)	Rofecoxib (n=14 583)	Celecoxib (n=18 908)
No of admissions for upper GI bleeding	82	17	13	43	32
Mean (SD) days of follow up	138.7 (77.4)	91.7 (68.3)	97.8 (71.2)	146.9 (89.6)	170.3 (97.0)
Risk ratio (95% CI)	1.0 (reference)	4.0 (2.3 to 6.9)	3.0 (1.7 to 5.5)	1.9 (1.3 to 2.8)	1.0 (0.7 to 1.6)

1.4.3 Adverse renal effects

NSAIDs can cause both acute renal failure (ARF) and chronic renal failure (CRF) by suppressing the production of PG, resulting in a reduction in renal blood flow [34]. In both cases, the glomerular filtration rate (GFR) is reduced, causing the accumulation of waste products in the body. NSAIDs do not give a significant risk in patients having a normal kidney function. But with the elderly and patients with heart, liver, or kidney disease, NSAIDs can further impact the renal blood flow and lead to an aggravated ischemic injury [35]. However, NSAIDs -induced ARF is more likely to be seen with patients having a history of predisposed diseases such as heart disease, hypertension, and diabetes than with patients having a normal kidney function [36]. Other common adverse effects are peripheral edema due to NSAID-induced sodium retention, and hyperkalemia due to the blockage of the Renin-Angiotensin-Aldosterone System (RAAS). In 2009, Harirforoosh S. et al estimated that 1-5% of NSAIDs users may develop renal adverse effects such as ARF and CRF in their lifetime [37].

1.4.4 Skin reactions

Itching and skin rashes are other common unwanted effects of NSAIDs. The severity of the rash could vary from mild to more serious. The mechanism of skin rashes is still unclear, but some of the common skin reactions are morbilliform rash, urticaria, angioedema, intolerance, or hypersensitivity to nonselective NSAIDs, salicylates in urticaria pigmentosa (including ASA), and true allergic reaction [38].

1.4.5 Other adverse effects

Bronchospasm and asthma are also other common adverse effects of NSAIDs, especially with ASA [39]. Common early symptoms in association with this are malaise, sneezing, rhinorrhea, nasal obstruction, and often a productive cough. These early signs and symptoms can be followed by conjunctival irritation, rhinorrhea, flushing of the head and neck, and even circulatory collapse and respiratory arrest [40].

1. 5 Common drug interactions

Drug interactions between NSAIDs and other medicines such as CV medicines, corticosteroids, and selective serotonin reuptake inhibitors are major concerns in several clinical settings [41]. Drug interactions are commonly seen in patients taking more than one medicine, along with certain beverages, food, or OTC medicines or herbs. It is important to check for drug-drug interactions before taking OTC medicines /herbs in order; to reduce the risk for toxicity and side-effects, to prevent worsening of previous medical conditions, and to prevent prescribed medicines from being affected. Different studies have shown that NSAIDs are involved frequently in drug to drug interactions causing an increase in hospitalization and unnecessary health costs [42]. Some of the commonly used medicines that are affected by NSAIDs are further explained in table 1.4.

Table 1. 3 List of commonly used drugs which interact with NSAIDs [43].

Medications	**Interactions with NSAIDs**
Beta blockers	Increases in blood pressure by attenuating antihypertensive effects
Calcium antagonists	Increases in blood pressure by attenuating antihypertensive effects
Antiplatelets	Increased risk of GI bleeding
Angiotensin-converting-enzyme inhibitor (ACEI) and Angiotensin Receptor Blockers (ARB)	Increases in blood pressure by attenuating antihypertensive effects
Corticosteroids	Increased risk of GI bleeding
Digitalis glycosides	Increased serum digoxin level
Diuretics	Increases in blood pressure by attenuating antihypertensive effects
Methotrexate	NSAIDs reduce renal excretion of methotrexate, causing methotrexate toxicity
Selective serotonin reuptake inhibitors (SSRIs)	Increased risk of GI bleeding
Warfarin and other anticoagulants	Increased risk of GI bleeding

1.6 Elderly population and Nursing homes in Norway

According to Statistics Norway (SSB), the total population of Norway per January 2021 was 5 472 234 [44]. The life expectancy of the country is 82.9 years combining for both sexes, in which 84.7 years for females and 81.2 years for males. The Norwegian government provides the elderly population facilities such as Nursing homes, home care services, and other care services in order to make their life easier. So, what is a nursing home?

According to the Norwegian directorate of health, nursing homes are defined as follows: "A nursing home is a health institution that provides patients with round-the-clock accommodation, treatment, and care that does not have to take place in a hospital, but which nevertheless requires more health professional effort than is practically possible or justifiable to provide in the patient's own home." Nursing homes are part of the municipal health service, and people are admitted to nursing homes if they cannot continue living at home due to illness or normal aging. For some, the stay in a nursing home will be for a limited time, which could be due to injury or transient illness, and for some, it is a livelong.

On an everyday basis, they are assisted by nurses, and unskilled assistants. In 2017, there were about 42 000 people age 67 years and older who were registered as residents of institutions, in which 30 845 of these had long-term stays, and among those over the age of 80, 12.9 percent lived in nursing homes [45]. In 2019 SSB reported that 30.0% of inhabitants 80 years and over, use home-based services [46].

A report published by Statista Research Department (2020) which is an online portal data provider in Hamburg, showed that the number of elderly populations in Norway was 440 000 between the age of 70 and 79 years, and 230 000 from the age of 80 years and above [47]. When we calculate this number roughly, in 2020 there were a total of 670 000 elderly people between the age of 70 and above, which is around 12 % of the total population.

1.6.1 An overview of the challenges facing the elderly due to aging

Age-related physical changes are gradually seen in elderly people over time. These include stiffening of the blood vessels, weakening of bones and muscles, decrease in motility of the GI system, frailty, and many diseases at the same time. Due to the above factors, they are forced to take different medicines at the same time (polypharmacy) to ease the different age-related diseases, they are facing, such as high blood pressure, muscle and joints pain, heart diseases, and others. In a Norwegian report from 2017, the proportion of people over the age of 65 was approx. 17% of the whole population, consuming 40-50% of all prescription drugs [48]. Besides the reasons for 10% of hospitalizations among elderly people were non-compliance, side-effects, and drug interactions [49, 50]. Non-compliance is common among the elderly due to several factors such as polypharmacy due to many diseases, reduced tolerance to side effects, poor information, and misunderstood due to reduced vision and hearing, and cognitive impairment. In addition, this group of people typically face side effects from the medicines they`re taking such as dry mouth, drop in orthostatic blood pressure, kidney failure, increased blood pressure, and gastrointestinal discomfort.

1.6.2 Use of NSAIDs in the elderly population in Norway

Table 1. 4 A summary of NSAIDs Consumption (ATC M01) in the Norwegian home living elderly above the age of 65 in 2015 and 2020 based on data from the Norwegian Prescription Database [51].

ATC	ATC level name	Norwegian prescription database (Users per 1000 inhabitants)	
		2015	2020
M01AB05	diclofenac	297	191
M01AB55	diclofenac, misoprostol	45	30
M01AE01	ibuprofen	213	171
M01AE02	naproxen	123	91
M01AE52	naproxen and esomeprazole	156	246
M01AH01	celecoxib	29	32
M01AH05	etoricoxib	119	127

Table 1.2 showed an overview of users of NSAIDs in the ATC group M01 per 1000 inhabitants among Norwegian home living elderly above the age of 65. The number of NSAID-users per 1000 inhabitants gets decreased for most of the NSAIDs in 2020 compared to 2015. Table 1.2 does not show specifically the use of NSAIDS among elderly patients in NHs. However, it gives us an overview of how large the consumption of NSAIDs among the elderly in-home living is, compared to our study population.

Different studies have shown an increase in the use prescribed medicines among the elderly in NHs due to multimorbidity [52]. As a result, the elderly was highly exposed to inappropriate medicine combinations. In a Norwegian observational study which was instructed by the municipality of Bergen, a total of 400 community-dwelling people from the age of 70 and above who had been admitted to an intermediate care nursing home unit (INHU) or hospital wards (HWs) were included [53]. The study aimed to identify the inappropriate prescribing pattern among elderly patients in Norway by direct follow-up from admission to discharge. Patients who were consecutively admitted to emergency hospitals from August 2007 to June 2008, were randomly assigned to an INHU (n=200) and to HWs (n=200). In the study, the population gets reduced to 290 patients due to consent withdrawal, unavailable medication lists and others, and among this 157 were assigned in the INHU, and 133 in HWs. All the medication lists were screened for each patient for drug-drug interactions on the Norwegian interaction database and evaluated based on Norwegian general practice (NORGEP) criteria.

The table below shows some of the inappropriate medicine combinations which were identified during the study [53].

Table 1. 5 Inappropriate medicine combinations in percent which were identified within the assigned population in the INHU and HWs, from admission to discharge.

NORGEP criteria	**INHU admission (n=157) %**	**INHU discharge (n=157) %**	**HW admission (n=133) %**	**HW discharge (n=133) %**	**All patients admission (n=290) %**	**All patients discharge (n=290) %**
NSAID/Coxib + ACE inhibitor/ARB	2,5	5,1	1,5	1,5	2,1	3,4
NSAID+ diuretic	1,3	3,2	0	2,3	0,7	2,8
NSAID + glucocorticoid	0	1,3	0	1,5	0	1,4
NSAID+ SSRI	0	3,2	0	0,8	0	2,1
NSAID + Warfarin	0,6	0,6	0	0	0,3	0,3

Notes: ACE Angiotensin-Converting Enzyme. **SSRI** selective serotonin reuptake inhibitors. **ARB** Angiotensin II receptor blocker. **INHU** Intermediate care Nursing Home Unit. **HN** Hospital wards

In the study, 21 single drugs and 15 drug combinations were found inappropriate for elderly patients according to the NORGEP criteria [54] regardless of their medical condition. Besides, the mean (SD) number of drugs used was increased from 6.0 (3.3) per patient on admission to 9.3 (3.8) on discharge. The number of regularly taken medications has increased from 5.6 (3.2) to 7.3 (3.3), and drugs used "as required" from 0.4 (0.8) to 2.0 (1.6). This means that the percent of inappropriate medications has increased from 24% on admission (20% men, 26% women) to 35% on discharge. Furthermore, the study has reported a total increase in the prevalence of use of NSAIDs (in the ATC group M01) from admission to discharge, increasing from 4.1% on admission to 9.7% on discharge [53].

Brekke M et al. (2009) assessed the level of prescribing a potentially harmful drugs for elderly patients by the Norwegian general practitioners (GPs). Prescription data for patients ≥70 years for one year were analyzed from the 454 GPs who had participated in the study. A total of 86 000 patients received one or more prescriptions whereas 18.4% of the patients (66% females and 34% males) received pharmacologically inappropriate prescriptions which are close to 22 000. Among these NSAIDs were prescribed for 7% of the elderly patients in a

harmful combination with a serotonin reuptake inhibitor, a diuretic, warfarin, or an angiotensin-converting enzyme inhibitor. A total of 752 elderly patients have received NSAID+ACE inhibitor or Angiotensin II receptor blocker (A2-blocker) as well as a diuretic whereas 184 elderly have received NSAID+ACE inhibitor or A2-blocker as well as SSRI [55].

1.7 An overview of NSAID-use among the elderly according to gender

Table 1. 6 A data of commonly prescribed NSAIDs (ATC M01) among home living elderly according to gender in Norway in 2020, based on data from the Norwegian Prescription Database [51].

Users/1000 inhabitants	Diclofenac	Diclofenac + misoprostol	Etoricoxib	Celecoxib	Ibuprofen	Naproxen	Ketoprofen
Women	195	37	136	38	201	87	6
Men	186	23	115	24	136	96	5

Table 1.6 described gender difference in the use of NSAIDs among home living elderly in Norway, showing that different NSAIDs were more commonly used by women compared to men in 2020. A further Canadian observational cohort study from 2000-2001 in Ontario which was intended to compare the rate of upper GI bleeding among elderly patients taking non-selective NSAIDs and selective COX 2 inhibitors showed that women were significantly higher users of both NSAIDs groups than men [33]. The study included a total of 43 960 elderly patients aged ⩾66 years taking non-selective NSAIDs, diclofenac plus misoprostol, rofecoxib, or celecoxib, in which 66% of those users were women. Besides, a greater proportion of celecoxib and rofecoxib usage was seen among women than in other groups of NSAIDs.

Table 1. 7 characteristics of elderly patients in Ontario who used different NSAIDs from 17 April 2000 to 31 March 2001

	Non-selective NSAIDs	Diclofenac + misoprostol	Rofecoxib	Celecoxib
No of patients (% women)	5 391 (59)	5 087 (62)	14 583 (72)	18 908 (70)
Mean (SD) age (years)	75.5 (7,0)	76.6 (7.1)	76.5 (6.9)	76.5 (6.8)
Residence in long term care facility (%)	398 (7)	503 (10)	652 (4)	810 (4)

1.8 The importance of the study

This study will describe the use of NSAIDs in a population of elderly nursing home residents. The knowledge of prevalence and concomitant treatment can indicate if the use of NSAIDs in this population is appropriate or if there are potential improvements.

1.9 Aim and study questions

1.9.1 Aim

The study aims to describe the use of oral NSAIDs among elderly patients at Norwegian nursing homes and explore associations between regular use of oral NSAIDs and use of cardiovascular medicines and/or proton pump inhibitors.

1.9.2 Study questions

- How prevalent is regular or PRN use of oral NSAIDs in nursing home patient?
- Which oral NSAIDs are most commonly used in nursing homes?
- What are the indications for the use of oral NSAIDs in nursing home residents?
- How frequent is use of cardiovascular medicines in nursing home residents using regular oral NSAIDs compared to non-regular NSAID-users?
- How frequent is the use of proton pump inhibitors among regular oral NSAID-users compared to non-regular NSAID-users in a nursing home population?

2. METHODS

2.1 The COSMOS study

2.1.1 Study design

In this sub-study, data collected by the COSMOS study (2013-2016) is used to achieve the study's aim. COSMOS means "COmmunication, Systematic assessment and treatment of pain, Medication review, Organization of activities, and Safety," Its primary aim was to improve the mental health and nursing home (NH) patients' quality of life based on their needs. The secondary aims of the COSMOS study were to reduce unnecessary medications and hospital admissions, improve pain assessment and pain treatment, and increase cost-effectiveness [56, 57]. A questionnaire was designed at the beginning of the COSMOS study, and it has been used at baseline, four months and nine months (refer to appendix 1).
Data were collected at baseline, four months, and nine months to check if there were any changes in the outcome measures. Data were extracted from medical records by reviewing medical examinations, laboratory tests, and prescribed medicines of every individual.

2.1.2 Inclusion and exclusion criteria

NH patients aged 65 and older with and without dementia were eligible for inclusion, and patients with schizophrenia or life expectancy ≤6 months were excluded from the study.

2.1.3 Participant recruitment

The study population included five hundred forty-five patients aged 65 and above who were recruited from 67 nursing home long-term-care wards and 8 Norwegian municipalities (**Figure 2.1**). These were Bergen, Bærum, Sarpsborg, Sund, Fjell, Øygarden, Askøy, and Kvam. The locations were chosen to include large and small, wealthy and less prosperous municipalities and ensure a representative sample of the nursing home population in Norway.

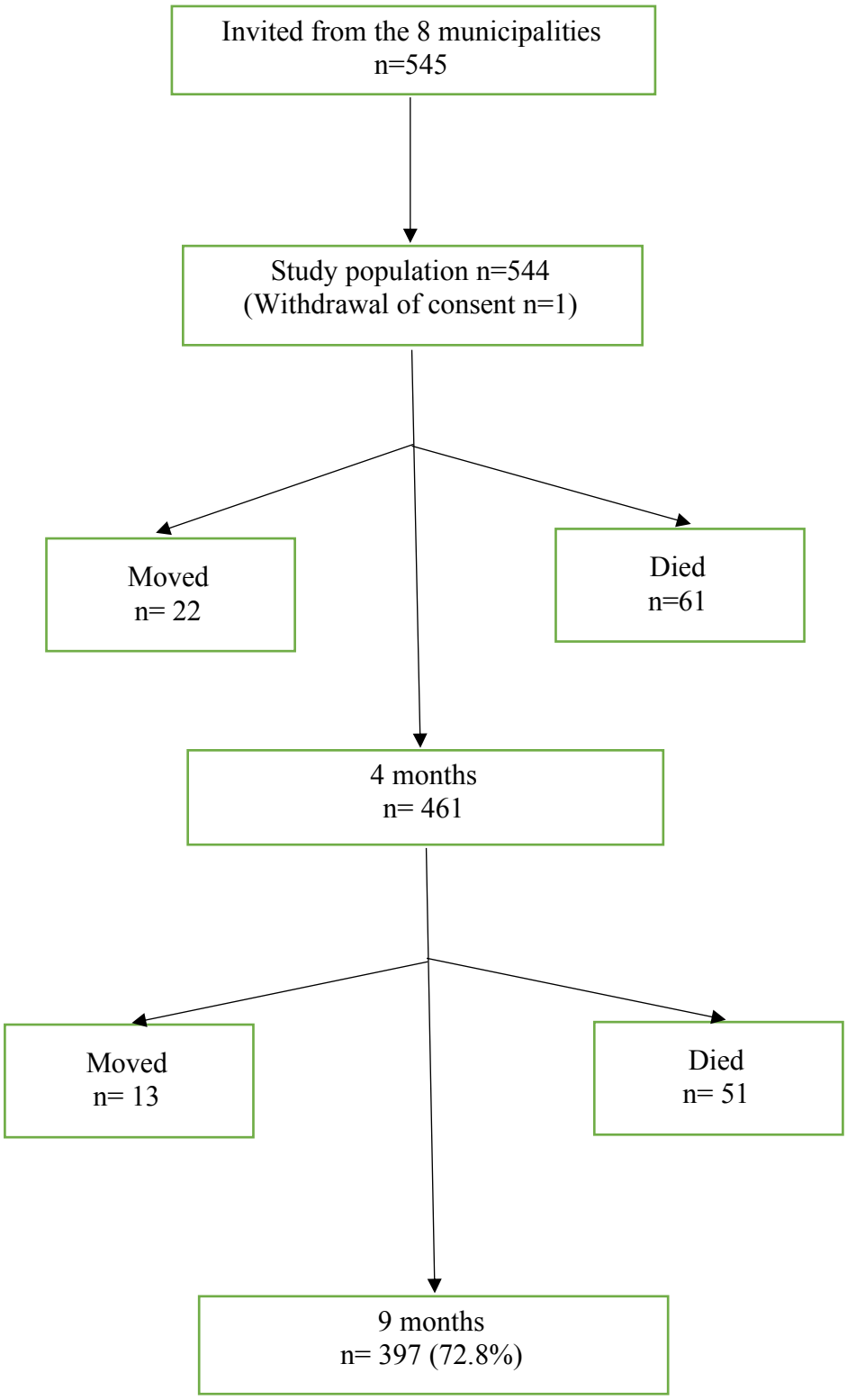


Figure 2.1 Flow chart of participants in the COSMOS study.

2.2 Data material used in this thesis

This thesis utilizes data from the COSMOS study of 544 NH patients. The data material will be used to conduct the prevalence, pattern, and associated factors of regular oral NSAID use in this population, independently of the COSMOS intervention. We are using the participants' medication history as a base to perform this study, and the procedures that were performed in this thesis will be described in detail in the following sections.

2.2.1 Data security

Data was stored on SAFE, a secure server at the university of Bergen. All data analysis for this sub-study was performed in SAFE.

2.2.2 Medication list

Most of the study population had a written list of prescribed medication which includes information about prescribed medicines, drug doses, administration form, and if the medicines were used regularly or as needed (PRN) (see appendix 1). The total number of prescribed drugs was counted and divided into three categories. Polypharmacy was defined as concomitant use of ≥ 5 regularly used drugs [58], and the other two categories were set at 0 and 1 - 4 medicines.

During the present sub-study, use of NSAIDs, cardiovascular medicines, and proton pump inhibitors (PPIs) were analyzed. The list of NSAIDs, CV-medicines, and PPIs were referred from Felleskatalogen https://www.felleskatalogen.no/medisin/, which shows an overview of all medicines marketed in Norway. NSAIDs were defined as all substances that were classified within the Anatomical Therapeutic Chemical (ATC) classification system as ATC groups M01A (anti-inflammatory and anti-rheumatic preparations, non-steroid) and M02A (topical products for musculoskeletal pain). Moreover, we defined CV-medicines as ATC groups B01 (Antithrombotic), C01 (Cardiac therapy), C02 (Antihypertensives), C03 (Diuretics), C07 (Beta-blockers), C08 (Calcium channel blockers), C09 (Agents acting on the renin-angiotensin system), C10 (Lipid modifying agents). In addition, we defined PPI as ATC group A02BC (Drugs for peptic ulcer and gastro-oesophageal reflux disease (GERD)).

Furthermore, NSAIDs use was classified as “regularly” or “on-demand” (PRN), and “oral” or “topical”. Oral NSAIDs use is defined as having one or more oral prescriptions of regular or PRN NSAID at any point during the study. Since our aim with this study is to find out the use of oral NSAID among elderly patients with CV medicine, we were mainly interested in using regular oral (systemic) NSAIDs by the elderly, especially in combination with regular CV medicines or proton pump inhibitors. Therefore, only use of one or more oral NSAID regularly during the study were used during the statistical analysis (excluding PRN prescriptions because the frequency of use is unknown). CV medicine use is defined as having one or more CV-medicine prescriptions regularly at any point during the study. Finally, PPI use is defined as having one or more prescriptions of regular scheduled PPI at any point during the study.

2.2.3 Statistical analysis

In the present study, different statistical methods were used. The Person $\chi 2$ –test is used to find out if there was a significant difference between subgroups within demographic variables. The demographic variables which were tested were age, sex, BMI, and number of total medications. Binomial logistic regression analysis was conducted to test if there were an association between the use of regular oral NSAIDs and regular CV medicines or regular PPIs. In addition to crude estimates, adjusted OR was calculated adjusted for age and sex.

All the statistical analyses were performed using statistical software Stata 16.1 (StataCorp, Texas, USA). Whereas ORs were presented with 95 % confidence intervals (CIs), and a p-value <0.05 was considered statistically significant.

2.3 Ethical approval

The COSMOS study was approved by the Regional Committee for Medical and Health Research Ethics in West Norway (REK Vest) on January 24, 2014, and it was registered with a reference number 2013/1765.

3. RESULTS

3.1 Characteristics of study population

A total of 544 patients were included in this study, of which 143 (26.3%) were male, and 401 (73.7%) were female. The mean age of the study population at inclusion was 87 (95% CI 86.074-87.332) years, with a range of 66 to 104. Further characteristics of the study population are summarized in table 3.1.

Table 3.1 The demographic of the study population, *N=544*

Characteristics	**Total, n (% of COSMOS study population)**
Gender	
Men	143 (26.3)
Women	401 (73.7)
Age (years) [a]	
66-84	178 (32.7)
85-90	178 (32.7)
>90	188 (34.5)
Body mass index (kg/m^2) [b]	
Underweight <20	96 (17.6)
Normal 20-25.9	248 (45.6)
Overweight level 1 26-29.9	84 (15.4)
Overweight level 2 ≥30	116 (21.3)
Number of regular medications	
0 medicines	2 (0.4)
1≤ 4 medicines	32 (5.9)
≥ 5 medicines	510 (93.8)
Oral NSAID-users regularly or PRN	
Men	12 (8)
Women	33 (8)

a, b: measured at baseline

3.2 Use of oral NSAIDs in the study population

A total of 45 of the 544 participants in this study used different regular or PRN oral NSAIDs at any point during the study. Figure 3.1 shows a flow chart of regular or PRN oral NSAID-users at baseline, four months, and nine months.

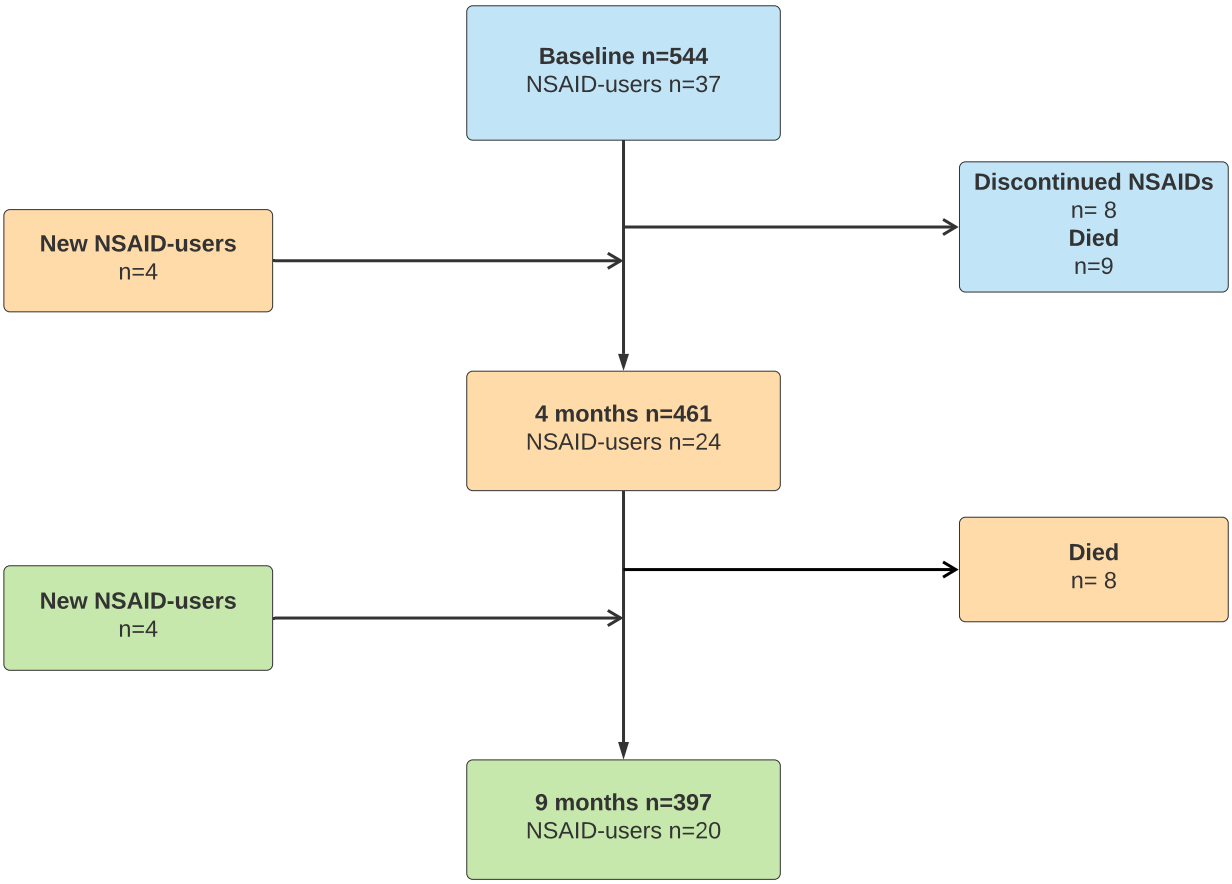


Fig 3.1 Users of regular or PRN oral NSAIDs at baseline, four and nine months.

During the study, there were 11 regular and 26 PRN oral NSAID-use at baseline, 10 regular and 14 PRN oral NSAID-users at 4 months, and 8 regular and 12 PRN oral NSAID-users at 9 months.

Besides, ibuprofen was the most frequently used oral NSAID among the population during the study, with a total of 24 users (53% of oral NSAID-users), followed by diclofenac 10 users (22%). The majority of the oral NSAID-users used NSAIDs PRN, but 12 (27%) of the

users were prescribed regular NSAIDs, which corresponds to 2.2% of the entire study population. The different oral NSAIDs used at any time are summarized in Table 3.2.

Table 3.2 Commonly used regular or PRN oral NSAIDs among participants during the study

NSAIDs	**Regular or PRN n (% of oral NSAID users)** *N*=45*
Diclofenac	
Regular	3(7)
PRN	7 (16)
Meloxicam	
Regular	1 (2)
PRN	-
Ibuprofen	
Regular	2 (2)
PRN	22 (49)
Ketoprofen	
Regular	2 (4)
PRN	5 (11)
Naproxen	
Regular	-
PRN	2 (4)
Celecoxib	
Regular	3 (7)
PRN	-
Etoricoxib	
Regular	2 (4)
PRN	2 (4)

* *N*=45 oral NSAID users, two patients used two different regular oral NSAIDs (diclofenac and ibuprofen) and one PRN oral NSAID (ketoprofen). One patient used one regular (celecoxib) and two PRN oral NSAIDs (ibuprofen and diclofenac) during the study.

3.3 Indications for oral NSAIDs use during the study

The different indications registered for oral NSAIDs use are presented in Table 3.3.

Table 3.3 Number of users (n) and indications registered for the use of different oral NSAIDs regularly or PRN during the study

Oral NSAID (n)*	**Indications (n)**
Celecoxib (3)	Rheumatoid arthritis (2), and bile duct inflammation due to gallstone (1)
Diclofenac (10)	Rheumatoid arthritis (6), and osteoarthritis (4)
Etoricoxib (4)	Osteoarthritis (4)
Ibuprofen (24)	Pain (6), and rheumatoid arthritis (18)
Ketoprofen (7)	Rheumatoid arthritis (7)
Meloxicam (1)	Ankylosing spondylitis (1)
Naproxen (2)	Rheumatoid arthritis (2)

* *N*=45 oral NSAID users, two patients used two different regular oral NSAIDs (diclofenac and ibuprofen) and one PRN oral NSAID (ketoprofen). One patient used one regular (celecoxib) and two PRN oral NSAIDs (ibuprofen and diclofenac) during the study.

Rheumatoid arthritis was the most frequent indication for use of NSAIDs and registered in a total of 35 patients, which is 78 % of oral NSAID-users, followed by osteoarthritis in 8 patients (18%).

3.4 Concomitant use of NSAIDs and CV-medicines or PPIs

3.4.1 Use of medicines for cardiovascular diseases by patients taking regular oral NSAID

The study has observed regular cardiovascular medicines used in the ATC groups of B01 and C01-C10 by regular oral NSAID-users during the research. In addition, regular oral NSAID-users have used diuretics (by 50% of regular oral NSAID-users and antithrombotic and beta-blockers (by 33% of regular oral NSAID-users) commonly during the study, and is summarized in table 3.4.

Table 3.4 Use of regular cardiovascular medicines in the ATC groups B and C by regular oral NSAID users (*N*=12) compared to non-regular oral NSAID-users (*N*=532), during the study

Medications* (ATC-code)	**n (% of regular oral NSAID-users*)**	**n (% of non-regular oral NSAID-users*)**
Any regular CV-medicine*	9 (75)	384 (72)
Antithrombotic (B01)	4 (33)	258 (48)
Cardiac therapy (C01)	1 (8)	45 (8)
Diuretics (C03)	6 (50)	176 (33)
Beta blockers (C07)	4 (33)	126 (24)
Calcium channel blockers (C08)	2 (17)	45 (8)
Agents acting on the renin-angiotensin system (C09)	3 (25)	116 (22)
Lipid modifying agents (C10)	3 (25)	77 (14)

*used at any time during the study period

*Regular CV medicine use are defined as the use of medicines in the ATC group of B01 and C01-C10 regularly.

Among the regular oral NSAID-users, 9 patients (75 % of regular oral NSAID-users) had used CV-medicines, and 384 patients (72%) of non-regular oral NSAID-users had CV-medicines disease. No difference in prevalence of use of regular CV medicines was found between regular oral NSAID-users and the study population not using regular oral NSAIDs (Chi-square test, p=0.791). No association was found when adjusting for age and sex using logistic regression analysis, (OR=1.164, 95% confidence interval 0.3-4.4, p=0.822) (table 3.5)

Table 3.5 Association between the use of regular cardiovascular medicine and regular oral NSAID

Crude, n=544			**Adjusted, n=542[a]**	
Independent	OR (95% CI)	p-value (0.05)	OR (95% CI)	p-value (0.05)
Regular Oral NSAID-use[b]	1.134 (0.584-2.201)	0.710	2.214 (1.178-4.162)	0.755

a: Adjusted for age, and sex, 2 missing age and/or sex

b: Regular oral NSAID use defined as the use of NSAID in the ATC group MO1 regularly. Regular CV medicine use are defined as the use of medicines in the ATC group of B01 and C01-C10 regularly.

3.4.2 Use of proton pump inhibitors (PPIs) among oral NSAID-users

The use of regular PPI in regular oral NSAID-users compared those not using oral NSAIDs regularly is presented in table 3.6.

Table 3.6 Use of regular PPI at any time by regular oral NSAID-users compared to those not using oral NSAIDs regularly during the study.

Proton pump inhibitors (A02BC)	**PPI used by regular oral NSAID-users** *n (% of regular oral NSAID-users)* ***N*=12**	**PPI used by non-regular oral NSAID-users** *n (% of non-regular oral NSAID-users)* ***N*=533**
Any regular PPI*	5 (42)	144 (27)
Esomeprazole	4(33)	60 (11)
Omeprazole	1(8)	21 (4)
Pantoprazole	-	65 (12)

* Regular PPI use defined as the use of PPI in the ATC group A02BC regularly

During the study, 5 (42%) of oral NSAID-users were taking regular PPIs, whereas 144 (27%) of non-regular oral NSAID-users took PPIs regularly. No difference in the prevalence of use of regular PPIs was found between regular oral NSAID-users and the study population not using oral NSAIDs regularly (Chi-square test, p=0.281). No association was found when adjusting for age and sex using logistic regression analysis, (OR=1.929, 95% confidence interval 0.6-6.2, p=0.268) (table 3.7).

Table 3.7 Association between regular PPI use and regular oral NSAID use

Crude, n=544			**Adjusted, n=542[a]**	
Independent	OR (95% CI)	p-value (0.05)	OR (95% CI)	p-value (0.05)
Regular Oral NSAID-use[b]	1.902 (0.590-6.133)	0.281	1.929 (0.603-6.176)	0.268

a: Adjusted for age, and sex, 2 missing age and/or sex
b: Regular Oral NSAID use defined as the use of oral NSAID in the ATC group MO1 regularly

3.5 Deaths among oral NSAID-users during the study period

One hundred twelve patients died in the study period, of whom 17 were taking oral NSAIDs, daily or on-demand. The cause of death and use of CV-medicines in oral NSAID-users who died during the study period is summarized in table 3.8.

Table 3.8 Reported cause of death and use of regular cardiovascular medication in users of oral NSAID who died during the study.

Patient	NSAID	CV medicines	Cause of death
1	Celecoxib (R)	low dose ASA	Dementia
2	Ibuprofen (PRN)	low dose ASA	Unspecified bleeding
3	Ibuprofen (PRN)	warfarin	Pneumonia
4	Ketoprofen (R)	bumetanide, valsartan, isosorbidmononitrate	Pulmonary edema, cardiac arrest
5	Ibuprofen (PRN)	digoxin, furosemid, warfarin	Dementia
6	Diclofenac (PRN)	-	Urinary tract Infection
7	Diclofenac (R)	metoprolol	Pneumonia, dementia
8	Ibuprofen (PRN)	low dose ASA, glyseroltrinitrat	Dementia
9	Naproxen (PRN),	bumetanide, valsartan	cardiac arrest
10	Ketoprofen (PRN)	low dose ASA, clopidogrel, atorvastatin, metoprolol	Pneumonia, chronic obstructiv pulmonary disease (COPD)
11	Ketoprofen (PRN)	low dose ASA, metoprolol, ramipril, glyseroltrinitrat	Pneumonia
12	Arcoxia (PRN)	low dose ASA	Infection
13	Ibuprofen (PRN)	low dose ASA, losartan, metoprolol	Cardiac arrest
14	Diclofenac (PRN)	rivaroxaban	Due to age
15	Ibuprofen (PRN)	low dose ASA, atorvastatin, irbesartan	Unspecified
16	Ketoprofen (PRN)	omega-3 triglycerides	Multi-organ failure
17	Naproxen (PRN)	enalapril, metoprolol, Low dose ASA	Stroke

Note: R: Regularly use of oral NSAID. PRN: Pro Re Nata/on demand use of oral NSAID.

4. DISCUSSION

4.1 Method discussion

4.1.1 Study population

This thesis is based on data material from the COSMOS study of 544 NH patients. The study participants are included from 67 long-term-care nursing homewards from eight large and small, wealthy and less prosperous Norwegian municipalities, to give a representative sample of the nursing home population in Norway, which does this thesis have a higher population validity.

In the study population, there is a possibility of more health issues and using more medications than the general home living elderly. Studies have reported that chronic cardiovascular diseases are common among nursing home residents [59], and elderly patients, and particularly fragile patients suffering from multimorbidity are particularly vulnerable to adverse effects, such as drop in orthostatic blood pressure, increased blood pressure, and gastrointestinal discomfort [49, 50]. So, choosing the COSMOS population as our study population could specifically explain the use of different medicines (polypharmacy) and multimorbidity among elderly patients in a nursing home population, which contributes to external validity.

4.1.2 Data collection

I did not participate in the data collection process or the baseline assessment. But to my knowledge, internal validity was strengthened during the data collection process by performing structured interviews and education by the researchers to enhance systematic evaluations and medication reviews [56, 57]. Taking not part in the data collection process is a limitation in this study. The data collected by the COSMOS study had a different aim than ours, and using the COSMOS data somehow lacks some outcome variables such as the comorbidity index, that could be helpful to our research. So, if I had conducted the data collection, other ideas and perspectives could have been reflected based on our study aim.

Longitudinal data were collected in the COSMOS-study but in this thesis, they are treated as cross-sectional data because the aim is to study prevalence of use, not changes over time. Besides, the strength of converting longitudinal data into cross-sectional data is that it allows studying multiple variables at a single point in time [60], which is helpful to answer our study aim.

4.1.3 Medication list

The medication list was revised and prepared by interviewing the NH patients and their primary caregivers simultaneously. The strength of the medication list is that since it was filled by interviewing both the patients and caregivers, it minimized the participants' risk of underreporting or overreporting the medicinal use. However, it is difficult to distinguish whether the list reflects actual use or prescribed use during the COSMOS study, which is a limitation. In addition, the study population gets medication PRN with prescription [61]. Therefore, any prescribed PRN medication will be registered in the system regardless of whether it is used often or never at all. All regression analyses were restricted to oral NSAIDs prescriptions for regularly scheduled use as an outcome to minimize the risks for overreporting of PRN use. However, this creates a limitation in the thesis, where an association between oral NSAID-use and CV-medicine use or PPI-use only applies for regular NSAID-use, were exclusion av PRN use could have led to under-reporting of oral NSAID-use during the regression analysis.

Data on the use of NSAIDs among home-dwelling elderly Norwegians can be acquired from the Norwegian Prescription Database. For instance, data from a larger population using the Norwegian Prescription Database could increase power and provide more reliable estimates on both uses of NSAIDs and CV-medicines or PPI in an elderly population. However, the Norwegian Prescription Database does not include medicines used at institutions, and it couldn't describe the use of NSAIDs among elderly patients in NH with cardiovascular disease or using proton pump inhibitors. This study aimed to investigate the use of NSAIDs in a NH population, and using data from the COSMOS study could specifically describe NSAID use among Nursing home patients using cardiovascular medicines or proton pump inhibitors concomitantly.

4.1.4 Statistical methods

A Chi-square test is used to test if there was a significant group difference in the use of NSAIDs according to gender. Binomial logistic regression is chosen to analyze the statistical section of this thesis. Because our dependent variables were in dichotomous form and the independent variables were in categorical form, a binomial logistic regression is well established to test these types of variables [62]. Furthermore, a medication list was used during the statistical analysis to find the association between the use of regular oral NSAIDs and regular CV medicines or regular PPIs.

Despite registering diagnoses and Charlson index during a pilot period, it was not filled out for the remaining participants and thus were not available for this study. However, we assess using the medication list as a more appropriate measure for concomitant cardiovascular risk factors and gastrointestinal prophylaxis as the gathered data on medication use has been thoroughly validated. It is more convenient using the ATC-system compared to the wide range of ICPC-codes. Because it makes us able to compare different drug utilization among the elderly based on the ATC classification.

4.2 Discussion of the results

4.2.1 Baseline characteristics of the study population

Patients' age and gender distribution were in concordance with the general NH population in Norway [33, 53], which contributes to external validity. According to the Norwegian Statistics (2009-2017), gender distribution in nursing homes shows that the proportion of women is highest in all age groups. In total, about 6 out of 10 who are living in nursing homes are women. Most of the patients living in nursing homes are in the age groups of 65 years or older [63]. Thus, the finding from the Norwegian statistics shows relatively similar finding to the present study. In this study, 544 patients were included, of which 143 (26,3%) were men, and 401 (73,7%) were women. Besides, the study population was in the age group of 66 to 104 (Table 3.1).

Use of medicines was prevalent in the study population as only two people (0.4%) reported no use of medications, 32 participants (5.9%) used 1 to 4 regular medications, while 510

participants (94%) used five or more regular medications, qualifying for polypharmacy according to a systemic review of definition [58]. Similarly, different European studies have reported an increase in the prevalence of polypharmacy among the elderly [64-66]. PRN medications were excluded due to uncertainty on the frequency of use. This systematic selection bias could have led to a certain underestimation of total medication use.

4.2.2 Prevalence and type of oral NSAIDs in the study population

We found that 45 (8%) of the study population were prescribed oral NSAIDs regularly or on-demand during the study, of which 12 (2%) used NSAIDs regularly, and 33 (6%) used NSAIDs on-demand. Ibuprofen was the most frequently used oral NSAID with 24 users (53% of oral NSAID users), which corresponds to 4% of the study population, followed by diclofenac with 10 users (22%), which corresponds to 2% of the study population (Table 3.2).

Comparatively, a Polish study (2016) aimed to study the use of analgesics among 392 nursing home residents aged 75 years and above, found that 51 people (13%) used different oral NSAIDs regularly and 11(3%) used NSAIDs on-demand. Diclofenac, ibuprofen, and ketoprofen were among the most commonly used regular oral NSAIDs [67]. A German study (2016), which included 685 elderly from 21 nursing homes, reported that about one-fifth used at least one NSAID. Besides, 117 (17%) used oral NSAIDs on-demand whereas 38 (6%) used regular oral NSAIDs. The most commonly used NSAIDs during the study were oral ibuprofen with 127 users (18.5 %), followed by oral diclofenac with 23 users (14.7%) [68]. To summarize, previous studies have found the use of oral NSAIDs between 4 and 13%, substantially higher than the prevalence of 2% in the present study. Besides the use of PRN oral NSAIDs in previous studies, was between 3 and 17% which is close to the findings from this thesis, which was 6% of the study population.

Furthermore, in the present study, some patients were taking more than one oral NSAIDs during the study. Among the oral NSAID users (N=45), two patients used two different regular oral NSAIDs and one PRN oral NSAID, while one patient used one regular and two PRN oral NSAIDs during the study. In comparison, a Polish study found that several nursing home residents were taking concomitantly different types of regular and/or PRN oral NSAIDs during the study [67].

In the present study, only 2.2% of the study population used oral NSAIDs regularly, whereas the majority of the NSAID-users used oral NSAIDs PRN (Table 3.2). A French cohort study (2013) aimed to study persistent analgesic use in patients with mild to moderate Alzheimer's disease (n= 595) found that 4% used regular oral NSAIDs [69]. A Finnish study (2017) which included 67215 home-dwelling elderly, reported that 13.3% used regular oral NSAIDs. Besides, the study interestingly found a reduction in the number of prescribed NSAIDs among people diagnosed with dementia in 2012 compared to those diagnosed with dementia in 2005. This indicates that prescribers have become more aware of the potential hazards associated with NSAID use in the elderly, leading to a corresponding change in prescribing practice [70]. This development could explain why a small fraction of the participants in our study used regular oral NSAIDs.

4.2.3 Characteristics of oral NSAID users

The proportion of regular or PRN oral NSAIDs use was 8% (Table 3.1) and there was no significant difference between men and women (p=0.862). In comparison, studies from Sweden and Canada have reported a higher yearly prevalence of NSAIDs use among women than men [33, 71, 72]. Since we have few oral NSAID-users in the study population, the generalizability of the results is limited.

4.2.4 Indications for NSAID use during the study

In this study, different oral NSAIDs have been used for various indications related to musculoskeletal pain. Rheumatoid arthritis (RA) was the most frequent indication, followed by osteoarthritis (Table 3.3). RA is among the most common inflammatory disease in older age groups [73], and the reason for the use of different oral NSAIDs could be to relieve pain and stiffness, especially in the morning, which are common problems among patients with RA, and where use of NSAIDs is well established. An Australian study (2007) reported that 15–20% of individuals over the age of 65 take oral NSAIDs regularly because of musculoskeletal pain [74], which is higher than this study's findings, which is by 8% of the study population. In the present study, the indications reported for use of NSAIDs complies with labelling approved by the Norwegian Medicines Agency [75].

4.2.5 Use of medicines for cardiovascular diseases by patients taking regular oral NSAID

Nine patients (75%) among the regular oral NSAID-users and 384 patients (72%) of non-regular oral NSAID-users used CV medicines. As NSAIDs increase risk of adverse cardiovascular events, we explored the association between the use of regular CV medicine between regular oral NSAID-users and non-regular oral NSAID-users. There was no significant difference in the prevalence of use of regular CV medicine between regular oral NSAID-users and non-regular oral NSAID-users (p=0.791). Logistic regression analysis was performed to explore associations between the use of regular oral NSAID and regular CV medicine, and we adjusted the model for gender and age (Table 3.5). We hypothesized lower odds of using CV-medicines in regular oral NSAIDs users as NSAIDs are contraindicated in patients with CV disease [23, 24, 26, 34, 76-80]. However, no significant association between regular oral NSAID use and regular CV medicine use were detected, which can be explained by sample size. A sample size that is too small increases the likelihood of decreasing the power of the study, in which the probability of finding existing differences will be less [81]. This could be why we got a non-significant association between regular oral NSAID use and regular CV medicine due to a small number of users. Another reason could be there is actually no significant difference or little difference in the prevalence of use of regular CV medicine between regular oral NSAID-users and non-regular oral NSAID-users, which results in non-significant results.

Furthermore, CV medicines that interacts with oral NSAIDs have been reported used by 2% of the study population, in which diuretics (by 1%) and antithrombotic and beta blockers (both 0.2%) were most common. In addition, regular oral NSAID-users were taking calcium channel blockers, beta blockers, lipid modifying agents, or agents acting on the renin-angiotensin system, during the study (Table 3.4). Other studies have shown that inappropriate medicine combinations with NSAIDs were used by 7% of the elderly [53, 55], which is higher than this study's findings, which is by 2% of the study population. A Norwegian study (2012) among elderly who had been admitted to an intermediate care nursing home unit (INHU), found that combinations of NSAIDs and agents acting on RAAS (3.4%), NSAIDs and diuretics (2.8%), while NSAIDs and warfarin and other anticoagulants were used by 0.3% of the participants [53]. Another Norwegian study (2008), reported that 86 000 elderly

patients had received one or more prescriptions, whereas 18,4% of them received pharmacologically inappropriate prescriptions. Among these, NSAIDs were prescribed for 7% of the elderly patients in combination with a diuretic, warfarin, or ACE inhibitor. 1% of the population received NSAIDs + ACE inhibitor or Angiotensin II receptor blocker (A2-blocker) and a diuretic, whereas 0.2% received NSAIDs + ACE inhibitor or A2-blocker and SSRIs [55].

Improper drug combinations with NSAIDs are a major concern in several clinical settings, increasing the risk of possible adverse effects among the elderly [23, 24, 34, 76-80]. The use of NSAID and CV medicine is associated with increased CV adverse effects [34]. For instance, the use of beta-blockers, calcium antagonists, or diuretics concomitant with NSAIDs causes an increase in blood pressure by attenuating the antihypertensive effect. Whereas the use of warfarin and other anticoagulants along with NSAIDs is associated with an increased risk of GI bleeding [43], and excess thrombotic events [77].

4.2.6 Use of Proton pump inhibitor by patients taking oral NSAID

In total, 5 (42%) of regular oral NSAID-users, were taking regular PPI during the study. Similarly, a Dutch study (2003) found 6.6% of NSAID-users have received PPI either as prophylaxis or as a treatment of non-steroidal anti-inflammatory drug-induced upper gastrointestinal side-effects [82]. Different studies have reported that GI risks associated with NSAIDs are reduced when NSAID treatment is combined with PPIs. Besides, PPIs have been shown more effective for healing ulcers in patients who continuously use NSAIDs [83-85], which could be why regular PPIs have been observed among regular oral NSAID users during our study.

Moreover, in the present study, logistic regression analysis was performed to explore a possible association between the use of regular oral NSAID and regular PPI adjusted for sex and age. No difference was found in the odds of using regular PPI between the participants using oral NSAIDs regularly compared to non-regular oral NSAID-users (p=0.281), neither when adjusting for age and gender (OR=1.929, p=0.268). An increased odds of using PPI among regular oral NSAID-users was expected as different studies reported an increased risk of GI-related adverse effects among NSAID-users compared to non-users [32, 34, 86-89].

Possible reasons for finding an insignificant difference in the use of PPIs between regular oral NSAIDs users and non-regular oral NSAIDs users could be small sample size. Besides, in our study, the use of different antithrombotic drugs has been observed in both groups (Table 3.4), where various studies have reported major GI bleeding among patients receiving antithrombotic medicines, in which PPIs are administered together to reduce the risk of gastrointestinal bleeding [90-92]. Therefore, this could increase the number of PPI-users in both groups resulting in a non-significant result. Another reason for finding insignificant results could be the overuse of PPI among the elderly. Different studies have reported a high prevalence of PPI use in nursing home residents where PPIs are used over a longer period [93, 94]. This could affect the number of PPI users in our study, which results in non-significant results.

4.2.7 Future studies

Future studies should investigate, although in this study there is limited use of NSAIDs in nursing home patients, NSAIDS related adverse effects should be investigated as these are vulnerable to side effects. Besides, future studies should explore countries where NSAIDs' related health risks are exceptionally high such as Tanzania and other low-middle income countries where NSAIDs are used highly as an over-the-counter product [78]. It is essential to examine how the evidence about the safe use of NSAIDs has translated into practice in a country like Tanzania, where the prevalence of the cardiovascular disease has been increasing, as has been the case in many other low-middle income countries.

5. Conclusion

In the present study, 8% of nursing home residents were prescribed oral NSAIDs for regularly scheduled or PRN use. The majority used NSAIDs PRN, but 12 (27%) of the users were prescribed regular NSAIDs, corresponding to 2.2% of the study population. Ibuprofen and diclofenac were the most frequently used oral NSAIDs. Rheumatoid arthritis was the most frequent indication, followed by osteoarthritis. The use of cardiovascular medicines and PPI was common in regular oral NSAID-users, but no significant association was found between the use of regular oral NSAID and use of CV medicines or PPIs.

6. REFERENCE LISTS

1. *WHO Collaborating Centre for Drug Statistics Methodology: Structure and principles*. 2018 [cited 2021 Jan. 26]; Available from: https://www.whocc.no/atc/structure_and_principles/.
2. Pahwa R, G.A., Bansal P, Jialal I., *Chronic Inflammation*, in *StatPearls*. 2020: Treasure Island (FL).
3. Celsus, *De Medicina, Vol. III*, ed. S. WG. 1953, London: Heinemann.
4. Brune K, H.B., *The discovery and development of antiinflammatory drugs.* Arthritis Rheum, 2004. **50**(8): p. 2391-9.
5. Ritter, J.M.F., Rod J. Henderson, Graeme Loke, Yoon Kong MacEwan, David Rang, Humphrey P., *Local hormones 2: peptides and proteins*, in *Rang & Dale's Pharmacology*. 2015, Churchill Livingstone. p. 225-229.
6. James R, R.F., Graeme H, Humphrey R. , *Anti-inflammatory and immunosuppressant drugs*, in *Rang & Dale's Pharmacology*. 2015, Churchill Livingstone. p. 317-320.
7. James Ritter, R.F., Graeme Henderson, Humphrey Rang., *Local hormones 1: histamine and the biologically active lipids*, in *Rang & Dale's Pharmacology*. 2015, Churchill Livingstone. p. 214-216.
8. Ricciotti E, F.G.A., *Prostaglandins and inflammation.* Arterioscler Thromb Vasc Biol, 2011. **31**(5): p. 986-1000.
9. Fookes C, B. *Nonsteroidal anti-inflammatory drugs*. 2018; Available from: https://www.drugs.com/drug-class/nonsteroidal-anti-inflammatory-agents.html.
10. Hutchinson, F., *New highly selective COX-2 inhibitors.* 1998.
11. Brooks P, E.P., Evans JF, Fenner H, Hawkey CJ, Patrono C, Smolen J, Breedveld F, Day R, Dougados M, Ehrich EW, Gijon-Baños J, Kvien TK, Van Rijswijk MH, Warner T, Zeidler H., *Interpreting the clinical significance of the differential inhibition of cyclooxygenase-1 and cyclooxygenase-2, Rheumatology.* 1999. **38**(8): p. 779-788.
12. Kaci Durbin, M. *Diclofenac*. 2020 Dec 1. [cited 2020 Dec 17.]; Available from: https://www.drugs.com/diclofenac.html.
13. Sanjai, S. *Aspirin*. 2020 [cited 2020 Dec 18]; Available from: https://www.drugs.com/aspirin.html.
14. Omudhome, O. *Aspirin*. 2020 [cited 2021 oct.12]; Available from: https://www.medicinenet.com/acetylsalicylic_acid/article.htm#what_is_aspirin_how_does_it_work_mechanism_of_action.
15. *Direktoratet for e-helse no; Reseptfrie smertestillende medisiner*. 2019 [cited 2021 Oct.13]; Available from: https://www.helsenorge.no/medisiner/reseptfrie-smertestillende-legemidler.
16. Sibbald, B., *Rofecoxib (Vioxx) voluntarily withdrawn from market.* Cmaj, 2004. **171**(9): p. 1027-8.
17. Bresalier RS, S.R., Quan H, Bolognese JA, Oxenius B, Horgan K, Lines C, Riddell R, Morton D, Lanas A, Konstam MA, Baron JA. , *Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial.* N Engl J Med, 2005. **352**(11): p. 1092-102.
18. Beilin, L.J., *Non-steroidal anti-inflammatory drugs and antihypertensive drug therapy.* J Hypertens, 2002. **20**(5): p. 849-50.
19. Varga Z, S.S., Vargova V., *Cardiovascular Risk of Nonsteroidal Anti-Inflammatory Drugs: An Under-Recognized Public Health Issue.* Cureus, 2017. **9**(4): p. e1144.

20. Schmidt M, S.H.T., Pedersen L., *Diclofenac use and cardiovascular risks: series of nationwide cohort studies.* Bmj, 2018. **362**: p. k3426.
21. Kearney PM, B.C., Godwin J, Halls H, Emberson JR, Patrono C., *Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomised trials.* BMJ, 2006. **332**(7553): p. 1302-8.
22. Trelle S, R.S., Wandel S, Hildebrand P, Tschannen B, Villiger P M et al., *Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis.* Bmj, 2011. **342**: p. c7086.
23. Caldwell B, A.S., Weatherall M, Shirtcliffe P, Beasley R., *Risk of cardiovascular events and celecoxib: a systematic review and meta-analysis.* J R Soc Med, 2006. **99**(3): p. 132-40.
24. Aldington S, S.P., Weatherall M, Beasley R., *Systematic review and meta-analysis of the risk of major cardiovascular events with etoricoxib therapy.* N Z Med J, 2005. **118**(1223): p. U1684.
25. Scott P. A, K.G.H., Smith C. M, Choy E. H, Scott D. L., *Non-steroidal anti-inflammatory drugs and myocardial infarctions: comparative systematic review of evidence from observational studies and randomised controlled trials.* Ann Rheum Dis, 2007. **66**(10): p. 1296-304.
26. Garcia Rodriguez L. A, T.S., Patrignani P., *Role of dose potency in the prediction of risk of myocardial infarction associated with nonsteroidal anti-inflammatory drugs in the general population.* J Am Coll Cardiol, 2008. **52**(20): p. 1628-36.
27. Solomon SD, W.J., Finn PV, Fowler R, Viner J, Bertagnolli MM, Arber N, Levin B, Meinert CL, Martin B, Pater JL, Goss PE, Lance P, Obara S, Chew EY, Kim J, Arndt G, Hawk E. , *Cardiovascular risk of celecoxib in 6 randomized placebo-controlled trials: the cross trial safety analysis.* Circulation, 2008. **117**(16): p. 2104-13.
28. McGettigan P, H.D., *Cardiovascular risk with non-steroidal anti-inflammatory drugs: systematic review of population-based controlled observational studies.* PLoS Med, 2011. **8**(9): p. e1001098.
29. Varas-Lorenzo C, R.-G.N., Calingaert B, Castellsague J, Salvo F, Nicotra F, Sturkenboom M, Perez-Gutthann S., *Myocardial infarction and individual nonsteroidal anti-inflammatory drugs meta-analysis of observational studies.* Pharmacoepidemiol Drug Saf, 2013. **22**(6): p. 559-70.
30. Bhala N, E.J., Merhi A, Abramson S, Arber N, Baron JA, Bombardier C, Cannon C, Farkouh ME, FitzGerald GA, Goss P, Halls H, Hawk E, Hawkey C, Hennekens C, Hochberg M, Holland LE, Kearney PM, Laine L, Lanas A, Lance P, Laupacis A, Oates J, Patrono C, Schnitzer TJ, Solomon S, Tugwell P, Wilson K, Wittes J, Baigent C., *Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials.* Lancet, 2013. **382**(9894): p. 769-79.
31. Schjerning Olsen AM, F.E., Lindhardsen J, Folke F, Charlot M, Selmer C, Lamberts M, Bjerring Olesen J, Køber L, Hansen PR, Torp-Pedersen C, Gislason GH., *Duration of treatment with nonsteroidal anti-inflammatory drugs and impact on risk of death and recurrent myocardial infarction in patients with prior myocardial infarction: a nationwide cohort study.* Circulation, 2011. **123**(20): p. 2226-35.
32. García Rodríguez LA, J.H., *Risk of upper gastrointestinal bleeding and perforation associated with Individual non-steroidal anti-inflammatory drugs.* 1994. **343**(8900): p. 769-772.

33. Mamdani M, R.P., Juurlink DN, et al. , *Observational study of upper gastrointestinal haemorrhage in elderly patients given selective cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs.* BMJ, 2002. **325**(7365): p. 624.
34. Vonkeman H. E, V.d.L.M.A., *Nonsteroidal anti-inflammatory drugs: adverse effects and their prevention.* Semin Arthritis Rheum, 2010. **39**(4): p. 294-312.
35. Whelton, A., *Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications.* Am J Med, 1999. **106**(5b): p. 13s-24s.
36. Pannu N, N.M.K., *An overview of drug-induced acute kidney injury.* Crit Care Med, 2008. **36**(4 Suppl): p. S216-23.
37. Harirforoosh S, J.F., *Renal adverse effects of nonsteroidal anti-inflammatory drugs.* Expert Opin Drug Saf, 2009. **8**(6): p. 669-81.
38. Dr Delwyn Dyall-Smith FACD, D. *Non-steroidal anti-inflammatory drugs and their skin side effects*. 2010 [cited 2020 Dec 18.]; Available from: https://dermnetnz.org/topics/non-steroidal-anti-inflammatory-drugs-and-their-skin-side-effects/.
39. Lo P. C, T.Y.T., Lin S. K, Lai J. N., *Risk of asthma exacerbation associated with nonsteroidal anti-inflammatory drugs in childhood asthma: A nationwide population-based cohort study in Taiwan.* Medicine (Baltimore), 2016. **95**(41): p. e5109.
40. Ms Joanna Sturtevant, C.P. *NSAID-induced Bronchospasm: A Common and Serious Problem*. 1999 [cited 2020 Dec 17.]; Available from: https://www.medsafe.govt.nz/profs/PUarticles/nsaid-induced.htm.
41. Lattuca B, K.Z., Malclès G, Davy JM, Leclercq F., *Drug Interactions between Non-Steroidal Anti-Inflammatory Drugs and Cardiovascular Treatments (Except Anti-Agregant Therapy), Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry.* 2013.
42. Shad M. U, M.C., Preskorn S. H., *The economic consequences of a drug-drug interaction.* J Clin Psychopharmacol, 2001. **21**(1): p. 119-20.
43. *Statens legemiddelverk: Interaksjonssøk*. 2020 [cited 2020 Dec. 15]; Available from: https://www.legemiddelsok.no/sider/Interaksjoner.aspx.
44. *Statistisk sentralbyrå: population* 2021 [cited 2021 Jan, 20]; Available from: https://www.ssb.no/en/befolkning/statistikker/folkemengde/aar-per-1-januar.
45. *Pensjonistforbundet: Fakta om eldre i Norge*. 2018 [cited 2021 Jan, 20]; Available from: https://www.pensjonistforbundet.no/side/64-fakta-om-eldre-i-norge.
46. *Statistisk sentralbyrå: Care services*. 2020 [cited 2021 Jan, 20]; Available from: https://www.ssb.no/en/pleie/.
47. *Statista: Population in Norway from 2010 to 2020, by age group*. 2020 [cited 2021 Jan, 20]; Available from: https://www.statista.com/statistics/586378/total-population-by-age-group-in-norway/.
48. *NHI.NO: Legemiddelbehandling av eldre mennesker*. 2018 30.04.2018 [cited 2021 Jan.20]; Available from: https://nhi.no/forskning-og-intervju/legemiddelbehandling-av-eldre/.
49. Ebbesen J, B.I., Erikssen J, Brørs O, Hilberg T, Svaar H, Sandvik L., *Drug-related deaths in a department of internal medicine.* Arch Intern Med, 2001. **161**(19): p. 2317-23.
50. Beijer H. J, d.B.C.J., *Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies.* Pharm World Sci, 2002. **24**(2): p. 46-54.
51. *Folkehelseinstituttet; Statistikk fra Reseptregisteret*. 2021 [cited 2021 Oct.2]; Available from: http://www.reseptregisteret.no/Prevalens.aspx.

52. Jokanovic N, T.E., Dooley MJ, Kirkpatrick CM, Bell JS., *Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review.* 2015. **16**.
53. Bakken MS, R.A., Engeland A, Ruths S. , *Inappropriate prescribing for older people admitted to an intermediate-care nursing home unit and hospital wards.* 2012.
54. Rognstad S, B.M., Fetveit A, Spigset O, Wyller TB, Straand J., *The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study.* Scand J Prim Health Care, 2009. **27**(3): p. 153-9.
55. Brekke M, R.S., Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J, Furu K, Gjelstad S, Bjørner T, Dalen I., *Pharmacologically inappropriate prescriptions for elderly patients in general practice: How common? Baseline data from The Prescription Peer Academic Detailing (Rx-PAD) study.* Scand J Prim Health Care, 2008. **26**(2): p. 80-5.
56. Husebø BS, B.C., Aarsland D, Selbaek G, Slettebo DD, Gulla C, Aasmul I, Habiger T, Elvegaard T, Testad I, Flo E., *The Effect of a Multicomponent Intervention on Quality of Life in Residents of Nursing Homes: A Randomized Controlled Trial (COSMOS).* J Am Med Dir Assoc, 2019. **20**(3): p. 330-339.
57. Husebo BS, F.E., Aarsland D, Selbaek G, Testad I, Gulla C, Aasmul I, Ballard C., *COSMOS--improving the quality of life in nursing home patients: protocol for an effectiveness-implementation cluster randomized clinical hybrid trial.* Implement Sci, 2015. **10**: p. 131.
58. Masnoon N, S.S., Kalisch-Ellett L, Caughey Gillian E., *What is polypharmacy? A systematic review of definitions.* 2017.
59. Joseph J, K.M., Aronow W. S., *Prevalence of moderate and severe renal insufficiency in older persons with hypertension, diabetes mellitus, coronary artery disease, peripheral arterial disease, ischemic stroke, or congestive heart failure in an academic nursing home.* J Am Med Dir Assoc, 2008. **9**(4): p. 257-9.
60. Nicola Di Girolamo, C.M., *Fowler's Zoo and Wild Animal Medicine Current Therapy: Research Study Design.* 2019. **9**: p. 59-62.
61. *Forskrift om legemiddelhåndtering for virksomheter og helsepersonell som yter helsehjelp*. 2008 [cited 2021 Aug.17]; Available from: https://lovdata.no/dokument/SF/forskrift/2008-04-03-320.
62. *Binomial Logistic Regression.* . 2021; Available from: https://amstatisticalconsulting.com/banking-fees-2-9/.
63. KARLSEN, H. *Flest kvinner rehabiliteres i institusjon*. 2018 [cited 2021 May 10]; Available from: https://www.ssb.no/helse/artikler-og-publikasjoner/flest-kvinner-rehabiliteres-i-institusjon.
64. Wastesson J. W, M.L., Tan E. C. K, Johnell K., *An update on the clinical consequences of polypharmacy in older adults: a narrative review.* Expert Opin Drug Saf, 2018. **17**(12): p. 1185-1196.
65. Morin L, J.K., Laroche ML, Fastbom J, Wastesson JW., *The epidemiology of polypharmacy in older adults: register-based prospective cohort study.* Clin Epidemiol, 2018. **10**: p. 289-298.
66. Guthrie B, M.B., Hernandez-Santiago V. et al. , *The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995–2010.* 2015.
67. Neumann-Podczaska A, N.T., Suwalska A, Łojko D, Krzymińska-Siemaszko R, Kozak-Szkopek E, Wieczorowska-Tobis K., *Analgesic use among nursing homes residents, with and without dementia, in Poland. Clin Interv Aging.* . 2016. **11**: p. 335-340.

68. Dörks M, H.-R.S., Schmiemann G, Hoffmann F., *Use of nonsteroidal anti-inflammatory drugs and renal failure in nursing home residents-results of the study "Inappropriate Medication in Patients with Renal Insufficiency in Nursing Homes".* Wien Klin Wochenschr, 2016. **128**(7-8): p. 287-90.
69. Gallini A, G.V., Vellas B, Lapeyre-Mestre M, Andrieu S, Brefel-Courbon C. , *Persistent use of analgesic medications in mild-to-moderate Alzheimer's disease.* 2013: p. 30(6): 439–445.
70. Hamina A, T.H., Tanskanen A, Tolppanen AM, Tiihonen J, Hartikainen S., *Differences in analgesic use in community-dwelling persons with and without Alzheimer's disease.* Eur J Pain, 2017. **21**(4): p. 658-667.
71. Backryd, E., *Gender differences in dispensed analgesics in Sweden during 2006-2015 - an observational, nationwide, whole-population study.* Int J Womens Health, 2018. **10**: p. 55-64.
72. Dominick K. L, A.F.M., Gold C. H, Heller, D. A., *Gender differences in NSAID use among older adults with osteoarthritis.* Ann Pharmacother, 2003. **37**(11): p. 1566-71.
73. Serhal L, L.M., Holroyd C, Edwards CJ., *Rheumatoid arthritis in the elderly: Characteristics and treatment considerations.* 2020. **19**(6).
74. Day R.O, G.G.G., *NSAIDs and their Indications.* 2007.
75. *Statens legemiddelverk: Legemiddelsøk*. 2021 [cited 2021 27.04]; Available from: https://www.legemiddelsok.no/.
76. Mené P, P.F., Patrono C., *The effects of nonsteroidal anti-inflammatory drugs on human hypertensive vascular disease.* Semin Nephrol, 1995. **15**(3): p. 244-52.
77. Schjerning Olsen AM, G.G., McGettigan P, Fosbøl E, Sørensen R, Hansen ML, Køber L, Torp-Pedersen C, Lamberts M., *Association of NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction.* Jama, 2015. **313**(8): p. 805-14.
78. McGettigan P, H.D., *Use of non-steroidal anti-inflammatory drugs that elevate cardiovascular risk: an examination of sales and essential medicines lists in low-, middle-, and high-income countries.* PLoS Med, 2013. **10**(2): p. e1001388.
79. McGettigan P, H.D., *Cardiovascular risk and inhibition of cyclooxygenase: a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2.* JAMA, 2006. **296**(13): p. 1633-44.
80. Page J, H.D., *Consumption of NSAIDs and the development of congestive heart failure in elderly patients: an underrecognized public health problem.* Arch Intern Med, 2000. **160**(6): p. 777-84.
81. MO Columb, F.F., MS Atkinson, FRCA FFICM, *Statistical analysis: sample size and power estimations.* May 2016. **16**(5): p. 159–161.
82. Sturkenboom MC, B.T., Dieleman JP, Tangelder MJ, Lee F, Goldstein JL., *Underutilization of preventive strategies in patients receiving NSAIDs.* Rheumatology (Oxford), 2003. **42 Suppl 3**: p. iii23-31.
83. Walan A, B.J., Classen M, Lamers CB, Piper DW, Rutgersson K, Eriksson S., *Effect of omeprazole and ranitidine on ulcer healing and relapse rates in patients with benign gastric ulcer.* N Engl J Med, 1989. **320**(2): p. 69-75.
84. Agrawal NM, C.D., Safdi MA, Lukasik NL, Huang B, Haber MM., *Omeprazole compared with misoprostol for ulcers associated with nonsteroidal antiinflammatory drugs. Omeprazole versus Misoprostol for NSAID-induced Ulcer Management (OMNIUM) Study Group.* N Engl J Med, 1998. **338**(11): p. 727-34.
85. Agrawal NM, C.D., Safdi MA, Lukasik NL, Huang B, Haber MM., *Superiority of lansoprazole vs ranitidine in healing nonsteroidal anti-inflammatory drug-associated*

gastric ulcers: results of a double-blind, randomized, multicenter study. NSAID-Associated Gastric Ulcer Study Group. Arch Intern Med, 2000. **160**(10): p. 1455-61.
86. MacDonald TM, M.S., Robinson GC, Shield MJ, McGilchrist MM, Murray FE, McDevitt DG., *Association of upper gastrointestinal toxicity of non-steroidal anti-inflammatory drugs with continued exposure: cohort study.* BMJ, 1997. **315**(7119): p. 1333-7.
87. Hernández-Díaz S, R.L.A., *Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding/perforation: an overview of epidemiologic studies published in the 1990s.* Arch Intern Med, 2000. **160**(14): p. 2093-9.
88. Wang FW, T.M., Mar GY, Chuang HY, Yu HC, Cheng LC, Hsu PI., *Prevalence and risk factors of asymptomatic peptic ulcer disease in Taiwan.* World J Gastroenterol, 2011. **17**(9): p. 1199-203.
89. Garrow D, D.M.H., *Risk factors for gastrointestinal ulcer disease in the US population.* Dig Dis Sci, 2010. **55**(1): p. 66-72.
90. Agewall S, C.M., Collet JP, Andreotti F, Lip GY, Verheugt FW, Huber K, Grove EL, Morais J, Husted S, Wassmann S, Rosano G, Atar D, Pathak A, Kjeldsen K, Storey RF. , *Expert position paper on the use of proton pump inhibitors in patients with cardiovascular disease and antithrombotic therapy.* 14 June 2013. **34**(23): p. 1708–1713.
91. Lettino, M., *Inhibition of the antithrombotic effects of clopidogrel by proton pump inhibitors: facts or fancies?* Eur J Intern Med, 2010. **21**(6): p. 484-9.
92. Bolek T, S.M., Škorňová I, Kovář F, Galajda P, Staško J, Kubisz P, Mokáň M. , *Proton Pump Inhibition in Patients Treated With Novel Antithrombotic Drugs: Should We Worry About Thrombosis?* J Cardiovasc Pharmacol, 2018. **72**(1): p. 71-76.
93. Pasina L, N.A., Elli C, Nobili A, Ianes A., *Overuse of proton pump inhibitors in nursing homes: An Italian multicenter observational study.* Pharmacoepidemiol Drug Saf, 2020. **29**(4): p. 461-466.
94. Braxton, P., *Long-Term PPIs May Be Overused in Nursing Homes.* 2017. **18**(8).

Pasient: Utfyller Dato:

7. APPENDICES

7.1 Appendix 1 Questionnaire from the COSMOS study

Innsamling til KOMSOS-studien

Navn på pasienten _____ _____

Sykehjem _____ _____

Pleierne skal fylle ut:

-Side 5

-Side 10 til2

Pasient: Utfyller Dato:

Pasient: Utfyller Dato:

KOSMOS pasientnr:_____

Datainnsamling Baseline. Oversikt over utfylte spørreskjema:

Spørreskjema (aktuelttidsrom)	Utfylt	Kommentar
Pleiepersonalet		
Bakgrunnsopplysninger		
Medisinliste		
Diagnoseliste		
Pleier utfylt		
Pasient		
MOBID-2		
MMSE		
Til legevisitt		

Pasient: Utfyller Dato:

Pasient: Utfyller Dato:

Bakgrunnsopplysninger om beboeren

Personopplysninger

1. Kjønn a) ❑Mann b) ❑Kvinne c) ❑Fødselsår: _____

2. Sivilstand: a) ❑Ugift b) ❑Gift c) ❑Enke/-mann

3. Vekt:_____kg (maks 4 uker gammel) 4. Høyde:_____m

5. Blodtrykk:_____/_____mmHg (maks 2 uker gammelt)

6. Puls måles i 1 minutt:_____slag/minutt

Pasient: Utfyller Dato:

Faste medisiner

Medikament	Døgndose i mg	ATC kode	Indikasjon Ja/Nei
a)			
b)			
c)			
d)			
e)			
f)			
g)			
h)			
i)			
j)			
k)			
l)			
m)			
n)			
o)			

7. Behovsmedisiner

Medikament	Indikasjon Ja/Nei	ATC kode
a)		
b)		
c)		
d)		
e)		
f)		
g)		
h)		
i)		
j)		
k)		
l)		
m)		
n)		
o)		

Pasient: Utfyller Dato:

8. Smertediagnoser

a) ❑ Muskel og skjelettplager
b) ❑ Gammelt brudd
c) ❑ Gikt
d) ❑ Hud/sår/gangren
e) ❑ Hodepine
f) ❑ Gyn/urologisk smerte
g) ❑ Muskelspasmer
h) ❑ Nevropati i forbindelse med diabetes, slag, herpes zoster ++
i) ❑ Osteoporose
j) ❑ Artritt
k) ❑ Kontrakturer
l) ❑ Kreftrelatert smerte
m) ❑ Magesmerte
n) ❑ Tannpine eller smerte i munnen

Demensdiagnoser

i) ❑ Alzheimer
j) ❑ Alzheimer + vaskulær
k) ❑ Lewylegme
l) ❑ Andre
e) ❑ Vaskulær
f) ❑ Frontotemporal
g) ❑ Parkinson med demens
h) ❑ Ukjent

Pasientens diagnoser og eventuelle diagnosekoder

a)	k)
b)	l)
c)	m)
d)	m)
e)	o)
f)	p)
g)	q)
h)	r)
i)	s)
j)	t)

9. Charlsons komorbiditetsindeks

Tilstand	Ja	Beskrivelse
a) Hjerteinfarkt	❑	Akutt/gammelt hjerteinfarkt
b) Hjertesvikt	❑	Hjertesvikt, kardiomyopati
c) Perifer vaskulær sykdom	❑	Aortaaneurismer, aortadisseksjon, status med implantat/protese i kar, claudicatio, vaskulær skade tarm, aterosklerose, gangren
d) Cerebrovaskulær sykdom	❑	TIA, ameurosis fugax, Hjerneblødning, inkl subaraknoidalblødning, alle iskemiske slag, sekvele etter hjernekarsykdommer
e) Demens	❑	Alle former for demens
f) Kronisk lungesykdom	❑	Kroniske sykdommer i nedre luftveier
g) Bindevevssykdom	❑	Revmatoid artritt, polymyalgia revmatika, temporalisarteritt, systemisk lupus og andre systemiske bindevevssykdommer og vaskulitter
h) Magesår	❑	Ulcus ventriculi, duodeni, uspesifisert ulcus og gastrojejunalt sår
i) Mild leversykdom	❑	Alkoholisk cirrhose/fibrose, kronisk hepatitt, toksisk leversykdom med cirrhose/fibrose, levercirrose, leverfibrose, fettlever, primær eller sekundær biliær cirrhose, biliær cirrhose, levertransplantert
j) Diabetes	❑	Diabetes mellitus I og II og uspesifisert uten komplikasjoner, evt med ketoacidose
k) Hemiplegi eller paraplegi	❑	Hemiplegi eller paraplegi
l) Moderat til alvorlig nyresykdom	❑	Kronisk eller uspesifisert nefrittisk syndrom, raskt progredierende nefrittisk syndrom, kronisk nyresvikt (stadie I-V), dialyse, transplantert
m) Diabetes komplikasjoner	❑	Diabetes mellitus I og II med nyre-, øye-, sirkulasjons- og/ellers nevrologiske komplikasjoner
n) Kreft	❑	Alle typer ondarta svulster
o) Leukemi	❑	
p) Lymfom	❑	
q) Moderat til alvorlig leversykdom	❑	Leversvikt, hepatorenalt syndrom og portal hypertensjon, øsofagusvaricer
r) Kreft med spredning	❑	Alle typer kreft med spredning

Pasient: Utfyller Dato:

FAST

Functional Assessment Staging (FAST) (B.Reisberg, 1984)

SKÅR:

Kryss av for det nivå som samsvarer suksessivt best med pasientens funksjonsnivå.

1) ❑ Ingen vanskeligheter med hukommelsen, hverken subjektivt eller objektivt.

2) ❑ Klager over å ha forlagt ting. Opplever selv vanskeligheter med å utføre arbeidsoppgaver.

3) ❑ Redusert arbeidsfunksjon, åpenbart for kolleger. Vanskeligheter med å reise til nye steder ved egen hjelp. Redusert evne til å organisere arbeid og andre oppgaver.

4) ❑ Redusert evne til å utføre sammensatte oppgaver, ivareta privat økonomi (glemmer å betale regninger) som å arrangere middagsselskap etc

5) ❑ Behøver assistanse for å kle seg adekvat for anledningen, i det daglige eller ved spesielle anledninger/høytider.

6)

A. ❑ Behøver assistanse til å kle seg ordentlig (glemmer å ta av pyjamasen først, tar skoene på feil fot, greier ikke å kneppe knapper etc).
B. ❑ Kan ikke bade selv (vansker med å finne riktig temperatur på badevannet etc). Av og til, eller oftere de siste ukene.
C. ❑ Kan ikke gjennomføre toalettbesøk alene (glemmer å trekke i snoren, tørke seg ordentlig, glemmer å kaste toalett papir etc.). Av og til, eller oftere de siste ukene.
D. ❑ Inkontinent for urin. Av og til, eller oftere de siste ukene.
E. ❑ Inkontinent for avføring. Av og til, eller oftere de siste ukene.

7)

A. ❑ Ordforrådet er begrenset til ca 6-10 forskjellige ord, som brukes i løpet av en vanlig dag eller de kommer frem under samtale/grundig intervju.
B. ❑ Ordforrådet er begrenset til et enkelt ord. Dette repeteres gjerne om igjen.
C. ❑ Redusert evne til å bevege seg rundt. Må ha hjelp til å gå.
D. ❑ Er ikke i stand til å sitte oppreist uten støtte fra stolens armlene.
E. ❑ Har mistet evnen til å smile.
F. ❑ Kan ikke løfte hodet ved egen hjelp

Pasient: Utfyller Dato:

Cornell skala for depresjon – siste uke

Utredningsverktøy til bruk for HELSEPERSONELL OG SYKEHJEMSLEGER

Cornell – skala for depresjon

Alexopoulos et al., 1988. Til norsk Årsland D.

Pasientens navn: _____ Dato for utredning: .....

Utfylt av: _____

Skåringen baseres på symptomer og tegn som har vært til stede siste uke før evalueringen. Skåringen skal ikke baseres på kroppslig funksjonshemning eller sykdom.

NB: Spørsmål nummer 8 og 11 skåres hvis endring har oppstått raskt, for eksempel i løpet av en måned, uansett når, ikke begrenset til siste måned.

Svaralternativ
a. *Lar seg ikke evaluere*
0. *Ikke til stede*
1. *Moderat eller bare periodevis til stede*
2. *Mye til stede*

	a	0	1	2
A: Stemningssymptomer				
1. Angst, engstelig uttrykk, grubling, bekymring	☐	☐	☐	☐
2. Tristhet, trist uttrykk, trist stemme, tar til tårene	☐	☐	☐	☐
3. Manglende evne til å glede seg over hyggelige hendelser	☐	☐	☐	☐
4. Irritabilitet, lett irritert	☐	☐	☐	☐
B: Forstyrret atferd				
5. Agitert, rastløs, vrir hendene, river seg i håret	☐	☐	☐	☐
6. Retardasjon, langsomme bevegelser, langsom tale, reagerer sent	☐	☐	☐	☐
7. Uttalte kroppslige plager (skår 0 hvis bare mage/tarm symptomer)	☐	☐	☐	☐
8. Tap av interesse, mindre opptatt av vanlige aktiviteter (skåre 1 eller 2 bare hvis endringen har skjedd raskt, dvs. i løpet av en måned, ellers 0)	☐	☐	☐	☐
C: Kroppslige uttrykk				
9. Redusert appetitt, spiser mindre enn ellers	☐	☐	☐	☐
10. Vekttap (skår 2 hvis større enn 2 kg i løpet av en måned)	☐	☐	☐	☐
11. Tap av energi, blir fort trett, klarer ikke holde ut aktiviteter (skår 1 eller 2 bare hvis forandringen har oppstått raskt, dvs. i løpet av en måned, ellers 0)				
D: Døgnvariasjoner				
12. Døgnvariasjoner i humør, humør verst om morgenen	☐	☐	☐	☐
13. Innsovningsvansker, sovner senere enn det som er vanlig for pasienten	☐	☐	☐	☐
14. Hyppige oppvåkninger i løpet av natten	☐	☐	☐	☐
15. Tidlig morgenoppvåkning, tidligere enn vanlig for denne pasienten	☐	☐	☐	☐
E: Tankeforstyrrelser				
16. Selvmord, føler livet ikke er verd å leve, har selvmordstanker, gjør selvmordsforsøk	☐	☐	☐	☐
Dårlig selvbilde, selvbebreidelse, selvnedvurdering, skyldfølelse	☐	☐	☐	☐
Pessimisme, ser svart på framtiden	☐	☐	☐	☐
17.				
19. Vrangforestillinger som samsvarer med å være deprimert				
18. (for eksempel forestillinger om fattigdom, sykdom eller tap)				
Cornell sum skåre	☐	☐	☐	☐

Pasient: Utfyller Dato:

NPI – sykehjemsversjon – siste uke

Variabel	N/A	Ikke tilstede 0	Hyppighet 1-4	Intensitet 1-3	Belasting 0-5
1. Vrangforestillinger					
2. Hallusinasjoner					
3. Agitasjon/aggresjon					
4. Depresjon/dysfori					
5. Angst					
6. Oppstemthet/eufori					
7. Apati/likegyldighet					
8. Manglende hemninger					
9. Irritabilitet/labilitet					
10. Avvikende motorisk adferd					
11. Søvn					
12. Apetitt- /spiseforstyrrelser					

Hyppighet - hvor ofte skjer adferden?
1. Av og til- sjeldnere enn en gang per uke
2. Ofte - omtrent en gang per uke
3. Hyppig - flere ganger per uke men sjeldnere enn hver dag
4. Svært hyppig - daglig eller oftere

N/A – kan ikke vurderes

Intensitet – hvor ille er det for pasienten?
1. Mild - medfører liten belastning for beboeren
2. Moderat - forårsaker uvanlig eller merkelig atferd
3. Alvorlig - forstyrrende og forårsaker mye uvanlig eller merkelig atferd.

Belastning – hvor belastende er dette for pleierne?
0. Ikke i det hele tatt
1. Minimalt
2. Mild
3. Moderat
4. Alvorlig
5. Svært alvorlig eller ekstremt

Pasient: Utfyller Dato:

1. Vrangforestillinger
Har beboeren oppfatninger som du vet ikke er riktige? For eksempel, insistere på at folk prøver å skade ham/henne eller stjele fra ham/henne. Har han/hun sagt at familiemedlemmer eller personale ikke er den de utgir seg for å være, eller at ektefellen er utro? Har beboeren hatt andre uvanlige oppfatninger

2. Hallusinasjoner
Har beboeren hallusinasjoner, det vil si ser, hører eller opplever ting som ikke er til stede? (Hvis ja, be om et eksempel for å verifisere at det virkelig er en hallusinasjon). Snakker beboeren til personer som ikke er der?

3. Agitasjon/aggresjon
Har beboeren perioder der han/hun motsetter seg hjelp fra andre? Er han/hun vanskelig å ha med å gjøre? Skaper han/hun mye støy eller samarbeider dårlig? Prøver beboeren å skade eller slå andre?

4. Depresjon/dysfori
Virker beboeren trist eller deprimert? Sier han/hun at han/hun føler seg trist eller deprimert? Hender det at beboeren gråter?

5. Angst
Er beboeren svært nervøs, bekymret eller skremt uten noen åpenbar grunn? Virker han/hun veldig anspent eller ute av stand til å slappe av? Er beboeren redd for å være adskilt fra deg eller andre som han/hun stoler på?

6. Oppstemthet/Eufori
Virker beboeren altfor munter eller altfor lykkelig uten spesiell grunn? Jeg mener ikke normal glede, men for eksempel det å le av ting som andre ikke synes er morsomme?

7. Apati/Likegyldighet
Sitter beboeren rolig uten å legge merke til ting som foregår rundt ham/henne? Har han/hun mistet interessen for å gjøre ting eller mangler motivasjon for å delta i aktiviteter? Er det vanskelig å engasjere ham/hun i samtale eller felles aktiviteter?

8 Manglende hemning
Gjør eller sier beboeren ting som man vanligvis ikke gjør eller sier offentlig? Virker det som om han/hun handler impulsivt uten å tenke? Sier beboeren ting som er ufølsomme eller sårende?

9 Irritabilitet/Labilitet
Blir pasienten lett irritert eller urolig? Er humøret hans/hennes svært skiftende? Er han/hun ekstremt utålmodig?

10. Avvikende motorisk atferd
Har beboeren gjentatte handlinger eller "vaner" som han/hun utfører om og om igjen, slik som vandring, kjøre rullestol fram og tilbake, plukke på ting eller tvinne på tråder og snorer? (Ikke inkluder vanlig tremor eller tungebevegelser)

11. Søvn
Har beboeren søvnvansker (symptomet er ikke til stede hvis pasienten må opp på toalettet en eller to ganger om natten for deretter straks å sovne igjen)? Er han/hun våken om nettene? Vandrer han/hun om nettene, kler på seg, eller går inn på andres rom?

12 Appetitt- og spiseforstyrrelser
Har beboeren hatt en ekstremt god eller dårlig matlyst, vektendring, eller uvanlige spisevaner (skår som NA hvis pasienten ikke er i stand til å spise selv og må mates)? Har det vært noen endring i type mat han/hun foretrekker?

Pasient: Utfyller Dato:

CMAI – siste 2 uker

COHEN-MANSFIELD AGITATION INVENTORY - Lang versjon

Oversatt av Arvid Skjerve og Harald A. Nygaard

Navn:_____ Dato: _____

Les gjennom hver av de 29 agiterte atferdstypene, og sett en ring rundt tallet som angir hvor ofte (fra 1-7) hver av dem har forekommet de siste 2 ukene:

	Aldri	Mindre enn en gang i uken	En eller to ganger i uken	Flere ganger i uken	En eller to ganger om dagen	Flere ganger om dagen	Flere ganger i timen
	1	2	3	4	5	6	7
1. Vandrer frem og tilbake, formålslas vandring	1	2	3	4	5	6	7
2. Kler paseg eller av seg paen upassende mate	1	2	3	4	5	6	7
3. Spytter (også under måltid)	1	2	3	4	5	6	7
4. Banning eller verbal aggresjon	1	2	3	4	5	6	7
5. Konstant krav om oppmerksomhet eller hjelp	1	2	3	4	5	6	7
6. Gjentar setninger eller sparsmål	1	2	3	4	5	6	7
7. Slår (inkludert seg selv)	1	2	3	4	5	6	7
8. Sparker	1	2	3	4	5	6	7
9. Griper, tar tak i andre	1	2	3	4	5	6	7
10. Skubber	1	2	3	4	5	6	7
11. Kaster gjenstander	1	2	3	4	5	6	7
12. Lagermerkelige lyder (underliglatter eller gråt)	1	2	3	4	5	6	7
13. Skriker, roper	1	2	3	4	5	6	7
14. Biter	1	2	3	4	5	6	7

Pasient: Utfyller Dato:

	Aldri	Mindre enn en gang i uken	En eller to ganger i uken	Flere ganger i uken	En eller to ganger om dagen	Flere ganger om dagen	Flere ganger i time
	1	2	3	4	5	6	7
15. Klorer	1	2	3	4	5	6	7
16. Forsaker â komme til et annet sted (f.eks. ut av rommet, bygningen)	1	2	3	4	5	6	7
17. Faller med vilje	1	2	3	4	5	6	7
18. Klager	1	2	3	4	5	6	7
19. Negativisme	1	2	3	4	5	6	7
20. Spiser/drikker noe som ikke er beregnet til â spises/drikkes	1	2	3	4	5	6	7
21. Skader seg selv eller andre (sigarett, varmt vann, etc.)	1	2	3	4	5	6	7
22. Hândterer gjenstander pa en upassende mate	1	2	3	4	5	6	7
23. Gjemmer gjenstander	1	2	3	4	5	6	7
24. Samler sammen gjenstander	1	2	3	4	5	6	7
25. River eller sdelegger gjenstander	1	2	3	4	5	6	7
26. Utfarer til stadighet repeterende stereotype bevegelser	1	2	3	4	5	6	7
27. Gjsr verbale seksuelle tilnzerminger	1	2	3	4	5	6	7
28. Gjsr fysiske seksuelle tilnzerminger	1	2	3	4	5	6	7
29. Generell rastlsshet	1	2	3	4	5	6	7

Kilde: Cohen-Mansfield, J., Marx, M.S., & Rosenthal, A. S. (1989). A description of agitation in a nursing home. Journal of Gerontology: Medical Sciences, 44(3), M77-M84.

Pasient: Utfyller Dato:

ADL

Utredningsverktey til bruk for **HELSEPERSONELL** OG SYKEHJ **EMSLEGER**

ADL-vurdering, aktiviteter i dagliglivet

Physical Self-Maintenance **Scale** (PSMS) kartlegger personna°re aktiviteter i dagliglivet, som hygiene, spising og mobilitet. Diagnosen demens innebzerer at det foreligger kognitiv svikt av en slik grad at det medferer sviktende ferdigheter til å klare dagliglivets aktiviteter. Skjemaet har ingen definert grenseverdi, og svarene som gis vurderes pa hvert enkelt område. Skjemaet kan brukes både til å fastslå om det fore- ligger et ferdighetstap som kan skyldes en demenstilstand, og til å beskrive hva pasienten klarer eller ikke klarer. Dette gir et overblikk over hvilke hjelpetiltak som er nedvendig å sette inn.

ADL-vurdering

Lawton og Brody, 19b9

Pasientens navn: __ _____ _____ _____ Dato forutredning: _____

Utfylt av: _____ _____

Utlflling g v algende skjeriio skol boseres på helsepersonell sine observosjorier g v pasienten i s/kehjemmet.

Utgangspunkt for avkrysning er hva pasienten faktisk utferer i hverdagen og ikke hva han/hun kan klare eller er i stand til å mestre fysisk sett.

Jo heyere skare pa et omrtde, jo mer sannsynlig er det at pasienten kan ha behov for av hjelp pa det omradet.

0 skares kun dersom omradet ikke er aktuelt.

Personlige aktiviteter i dagliglivet(P-ADL)

A. Toalett

0 0 Ikke aktuelt
10 Klarer seg selv p6 toalettet
2 0 Trenger I bli paminnet. og/eller hjelp til I vaske seq, har sjelden uhell (heyst en gang i uken)
3 Er inkontinent (bla°re eller tarm) i sevne mer enn en gang i uken
4 ☐ Er inkontinent (bla°re eller tarm) i vtken tilstand mer enn en gang i uken
s *D* Ingen kontroll over bla°re eller tarm

B. Spicing

0 0 Ikke aktuelt
1 0 Spiser uten hjelp
2 Q Trenger litt hjelp under maltidene, eller trenger spesialtilberedte mtltider, eller trenger annen hjelp i mtltidssituasjonene
3 0 Spiser med moderat hjelp og "seler"
4 Q Trenger mye hjelp ved alle maltider
5 0 Spiser ikke selv, og motsetter seq forsek pa a bli matet av andre

Pasient: Utfyller Dato:

C. Pâkledning

00 Ikke aktuelt

1 Q Kler av og pâ seg selv, velger ut kla r fra egen garderobe

2 0 Kler av og pa seg selv med noe hjelp

30 Trenger moderat hjelp ved påkledning og/eller utvelgelse av kla•r

4 0 Trenger mye hjelp ved påkledning, men samarbeider med den som hjelper

50 Motsetter seg aktivt andres hjelp til person fig stell

D. Personlig stell (hâr, negler, hender, ansilrt, *klmrl*

0 Q Ikke aktuelt

1 0 Alltid pent kledd og velstelt, uten hjelp

20 Steller seg selv, men trenger f.eks hjelp til barbering

3 0 Trenger moderat og regelmessig hjelp eller veiledning til personlig stell

S 0 Trenger hjelp til alt personlig stell, men holder seg ren og velstelt ved hjelp fra andre

5 0 Motsetter seq aktivt andres hjelp til personlig stell

E. Fysisk bev'egefse

00 Ikke aktuelt

1 Q Går utenders, i jevnt og ulendt terreng 2 Q Går i na'rmiIjeet.

3 Q Kan forflytte seq ved hjelp av (kryss av en) Q

A. Annen person

D B. rekkverk

Q C. Spaserstokk D

D. Gâstol

Q E1. Rullestol, kommer i og ut pâ egen hând Q

E2. Rullestol, trenger hjelp til â komme i og ut

40 Kan ikke gâ, men sitter oppreist uten stette i stol eller rullestol, men kan ikke bevege seq uten hjelp

50 Sengeliggende mer enn halvparten av tiden

F. Boding

0 0 Ikke aktuelt

1 0 Bader selv uten hjelp (badekar, dusj)

2 0 Bader selv, men trenger hjelp i og ut av badekaret/dusjen

3 0 Vasker kun ansikt og hender, og kan ikke bade/vaske resten av kroppen

40 Vasker seg ikke selv, men er samarbeidsvillig når andre hjelper

5 0 Vasker seg ikke selv og gjer motstand når andre gjer et forsek pa â hjelpe

Kommentarer:

Pasient: Utfyller Dato:

AKTIVITET

1. Har det vært store endringer for pasientens aktivitetstilbud den siste måneden (4 uker)?

❑ Ja ❑ Nei ❑ Ikke aktuelt

1a. Hvis ja, hva skyldes endringene?
❑ Pasientens helsetilstand ❑ Ressurser/bemanning ❑ Annet: _____

2. Har pasienten en tilpasset ukeplan med aktiviteter?
❑ Ja ❑ Nei ❑ Ikke aktuelt

3. Har pasienten deltatt i aktivitet med fysisk utfoldelse/bevegelse?
❑ Ja ❑ Nei ❑ Ikke aktuelt

4. Har pasienten deltatt i aktivitet med tenkning, hukommelse, refleksjon?
❑ Ja ❑ Nei ❑ Ikke aktuelt

5. Har pasienten deltatt i sosiale aktiviteter?
❑ Ja ❑ Nei ❑ Ikke aktuelt

6. Omtrent hvor mye tid er ukentlig brukt på aktiviteter?

_____timer_____minutter

6a. Omtrent hvor mye av denne tiden var i regi av pårørende?

_____timer_____minutter

Pasient: Utfyller Dato:

KOMMUNIKASJON

1. I løpet av den siste måneden:

…har det blitt invitert til felles samtale med lege?
❑ Ja ❑ Nei ❑ Ikke aktuelt ❑ Vet ikke

…har pasient og pårørende hatt en felles samtale med primærkontakt?
❑ Ja ❑ Nei ❑ Ikke aktuelt ❑ Vet ikke

…har dere hatt telefonkontakt med familien?
❑ Ja ❑ Nei ❑ Ikke aktuelt ❑ Vet ikke

…har dere hatt kontakt med pårørende?
❑ Ja ❑ Nei ❑ Ikke aktuelt ❑ Vet ikke

Er kommunikasjonen dokumentert?
❑ Ja ❑ Nei ❑ Ikke aktuelt ❑ Vet ikke

2. Ved felles samtale den siste måneden, inkluderte samtalen følgende spørsmål:

Hvor involvert har dere som pårørende vært og hvor mye vil dere inkluderes?
❑ Ja ❑ Nei ❑ Vet ikke

Hva har dere (pasient og pårørende) forstått om situasjonen og sykdommen?
❑ Ja ❑ Nei ❑ Vet ikke

Hva trenger dere for å forstå mer?
❑ Ja ❑ Nei ❑ Vet ikke

Hva bør vi vite om pasientens liv for å gi optimal behandling – hva gir hverdagen og livet mening?
❑ Ja ❑ Nei ❑ Vet ikke

Hvilke mål, tanker og forventinger har dere til sykehjemsoppholdet?
❑ Ja ❑ Nei ❑ Vet ikke

Belastes pasienten med uoppgjorte spørsmål?
❑ Ja ❑ Nei ❑ Vet ikke

3. Har dere tidligere snakket om behandling i livets slutt? For eksempel sykehusinnleggelse v/ akutt sykdom
❑ Ja ❑ Nei ❑ Vet ikke

Pasient: Utfyller Dato:

Vurdering av IivsL:valitet

Livskvaliteten til pasienten vurderes med skalaen: Livskvalitet ved langtkommen demens (QUALID) skala, som baseres pa informasjon fra pårerende eller personale som har daglig omgang med pasienten. Vurderingen gjeres pa bakgrunn av konkret, observerbar atferd og felelsesuttrykk hos pasienten.

Livskvalitet ved lan@kommen demens (Qt/AUD) skala •

Weiner et ml 2000

Norsk o versettelse: Knut Engedol, Irene Raen, Eivind Aakhus, Sverre Bergh, Susan Juell, Geir Selba•k

Pasientens navn: _____ Dato for utredning: _____

Utfylt av:

Kryss av for svaralternativet som best beskriver pasienten gjennom den siste uken. Totalskaren vil ligge mellom 11 og 55, med 11 som uttrykk for heyest livskvalitet.

Hvilket svaralternativ beskriver pasienten best gjennom den siste uken...

A. Personen smiler

1 D spontant en eller flere ganger daglig
2 D spontant, men sjeldnere enn en gang daglig
30 bare som respons pa ytre stimuli, minst en gang daglig
40 bare som respons pa ytre stimuli, sjeldnere enn en gang daglig
5 D sjelden eller aldri

B. Personen virker trist

1 D sjelden eller aldri
2 D bare som respons pa ytre stimuli, sjeldnere enn en gang daglig
30 bare som respons pa ytre stimuli. minst en gang daglig
ñ D uten apenbar grunn, sjeldnere enn en gang daglig
5 D uten apenbar grunn, en eller flere ganger daglig

C. Personen gråter

1 D sjelden eller aldri
2 D bare som respons pâ ytre stimuli, sjeldnere enn en gang daglig
30 ba re som respons pa ytre stimuli, minst en gang daglig
ñ D uten apenbar grunn, sjeldnere enn en gang daglig
5 Q uten apenbar grunn, en eller flere ganger daglig

D. Personen har et ansiktsuttrykk som uttrykker u6ehag — virker ulyk:k:elig eller smerteR•"virket (ser belcymret ut, sk:jzerer grimaser, rynker pannen eller slår ned blikket)

1 D sjelden eller aldri
2 D sjeldnere enn en gang daglig
3 D minst en gang daglig
4 D nesten halvparten av dagen
50 mesteparten av dagen

E. Personen viser kroRR•!"g ubehag
- hun/han vrir på seq, virker utilpass, skitter stadig stilling

10 sjelden eller aldri
20 sjeldnere enn en gang daglig 3
Q minst en gang daglig
40 nesten halvparten av dagen
50 mesteparten av dagen

F. Personen kommer med Stringer eller lager lyder som tyder R misnaye, *tristhet eller ubehag (klager, stanner, roper/skriker)*

10 sjelden eller aldri
2 Q bare som respons pa ytre stimuli, **sjeldnere enn en** gang daglig
30 bare som respons pa ytre stimuli, minst en gang daglig
40 uten Apenbar grunn, sjeldnere enn en gang daglig
5 0 uten Apenbar grunn, en eller flere ganger daglig

C. Personen er irritabel og aggressiv (blir sint, banner, dytter eller forseker å skade andre)

l 0 sjelden eller aldri
2 0 bare som respons pa ytre stimuli, sjeldnere enn en gang daglig
3 0 bare som respons pa ytre stimuli, minst en gang daglig
40 uten Apenbar grunn, sjeldnere enn en gang daglig
50 uten Apenbar grunn, en eller flere ganger daglig

H. Personen nyter å spise

1 0 ved de fleste måltidene, og mellom måltider 2 0 ved minst to måltider daglig
30 ved minst ett måltid daglig
40 sjeldnere enn daglig 5
0 sjelden eller aldri

I. Personen liker berering/ kroRR• kontak:I

0 nesten alltid, tar nesten alltid initiativ til berering
20 mer enn halvparten av tiden, tar av og til initiativ til berering
30 halvparten av tiden, tar aldri initiativ til berering men motsetter seg ikke å bli berert
4Q mindre enn halvparten av tiden, motsetter seg ofte å bli berert/bli tatt på
50 sjelden eller aldri, motsetter seg nesten alltid berering/bli tatt på

J. Personen fiker samvmr med andre

10 nesten alltid, tar nesten alltid initiativ til samva•r med andre
20 mer enn halvparten av tiden, tar av og til initiativ til samva°r med andre
3 Q halvparten av tiden, tar aldri initiativ til samva°r med andre men motsetter seg ikke samva•r med andre
40 mindre enn halvparten av tiden, motsetter seg ofte samva°r med andre
50 sjelden eller aldri, motsetter seg nesten alltid samva•r med andre

K. J ersonen virker fefefsesmess/g rolig og avslappet

10 mesteparten av dagen
20 mer enn halvparten av dagen
30 halvparten av dagen
40 mindre enn halvparten av dagen
5 ☐ sjelden eller aldri

_____ ***Totalskår***
(summen av skåringene på alle spersmålene).

Skåringen varierer mellom 11 til 55 hvor laveste sum representerer heyest livskvalitet

Pasient: Utfyller Dato:

QALIDEM – siste uka

Spørreskjemaet har 40 spørsmål. Målet er at du sammen med en kollega, skal svare på spørsmålene om hva dere har observert hos beboeren den siste uken. Svar på alle spørsmålene. Hvis dere står mellom to svaralternativer kan dere sette en sirkel rundt det svaret som stemmer mest med deres observasjoner. Et svar er aldri feil, men det indikerer hva dere synes er nærmest virkeligheten. Ikke tenk for lenge på svarene; det første svaret som slår dere er ofte det beste. Prøv å bli enige der du og din kollega har forskjellige oppfatninger.

Aldri = Aldri **Sjelden** = Ikke mer enn en gang per uke

Noen ganger = Et par ganger per uke **Ofte** = Nesten hver dag

	Aldri	**Sjelden**	**Noen ganger**	**Ofte**
1. Er munter				
2. Gjør rastløse bevegelser				
3. Har kontakt med andre beboere				
4. Avviser hjelp fra pleiere				
5. Utstråler tilfredshet				
6. Virker engstelig				
7. Er sint				
8. Er i stand til å glede seg over ting i hverdagen				
9. Vil ikke spise				
10. Er i godt humør				
11. Er trist				
12. Reagerer positivt på henvendelser				
13. Viser at han/hun kjeder seg				
14. Har konflikter med pleiere				
15. Nyter måltider				
16. Blir avvist av andre beboere				
17. Anklager andre				
18. Tar seg av andre beboere				
19. Er urolig				
20. Åpenlyst avviser kontakt med andre				

Pasient: Utfyller Dato:

	Aldri	Sjelden	Noen ganger	Ofte
21. Har et smil om munnen				
22. Har et anspent kroppsspråk				
23. Gråter				
24. Verdsetter hjelp han eller hun får				
25. Stenger seg ute fra omgivelsene				
26. Finner på ting å gjøre uten hjelp fra andre				
27. Gir inntrykk av at han eller hun ønsker mer hjelp				
28. Gir inntrykk av at han eller hun føler seg innelåst				
29. Har en vennlig tone med en eller flere beboere				
30. Liker å ligge nedpå i senga				
31. Godtar hjelp				
32. Roper				
33. Kritiserer den daglige rutinen				
34. Føler seg avslappet i andres selskap				
35. Gir inntrykk av å ikke være i stand til å gjøre noe				
36. Føler seg hjemme i avdelingen				
37. Gir inntrykk av å føle seg verdiløs				
38. Liker å hjelpe til med oppgaver i avdelingen				
39. Vil komme vekk fra avdelingen				
40. Humøret kan påvirkes positivt				

Pasient: Utfyller Dato:

(RUD) Helseøkonomisk spørreskjema

Pasientens bruk av helsevesenets ressurser

Trenger beboeren hjelp i en av de følgende eller sammenlignbare aktiviteter?

Toalettbesøk, spising, av- og påkledning, hygiene, bading, gangfunksjon.

a) ❑Ja b) ❑Nei

Hvis nei: gå til spørsmål 2

Hvis ja: Vær vennlig å svar på følgende spørsmål

1.1. På hvor mange dager i løpet av de siste fire ukene hjalp du eller en annen pleier beboeren i disse aktivitetene?

_____dager (28 = daglig, 4 = en gang i uken)

1.2. På disse dagene, hvor mange minutter brukte du eller en annen pleier i gjennomsnitt per døgn på å hjelpe beboeren med disse aktivitetene?

_____minutter (per 24 timer)

2. Trenger beboeren hjelp i en av de følgende eller sammenlignbare aktiviteter?

Ta medisiner, telefonsamtaler, enkle innkjøp/gå til frisøren, utføre administrative aktiviteter (fylle ut skjemaer, åpne brev osv), følge utenfor hjemmet.

a) ❑Ja b) ❑Nei

Hvis nei: gå til spørsmål 3

Hvis ja: Vær vennlig å svar på følgende spørsmål

2.1. På hvor mange dager i løpet av de siste fire ukene hjalp du eller en annen pleier beboeren i disse aktivitetene?

_____dager (28 = daglig, 4 = en gang i uken)

2.2. På disse dagene, hvor mange minutter brukte du eller en annen pleier i gjennomsnitt per døgn på å hjelpe beboeren med disse aktivitetene?

_____minutter (per 24 timer)

Pasient: Utfyller Dato:

Brukte du eller en annen pleier tid den siste måneden individuell personrettet tid til å hjelpe beboeren (tid som ikke er inkludert i spørsmål 1 og 2). For eksempel til å:

- Forhindre farlige situasjoner som vandring som kunne ført til at beboeren utsatte seg for fare
- Tilby hjelp til å finne fram, for eksempel til rommet
- Stoppe oppførsel som hindrer friheten til andre personer som plage/irritere andre beboere?

b) ❑Ja b) ❑Nei

Hvis nei: gå til spørsmål 4
Hvis ja: Vær vennlig å svar på følgende spørsmål

3.1. På hvor mange dager i løpet av de siste fire ukene hjalp du eller en annen pleier beboeren i disse aktivitetene?

_____dager (28 = daglig, 4 = en gang i uken)

3.2. På disse dagene, hvor mange minutter brukte du eller en annen pleier i gjennomsnitt per døgn på å hjelpe beboeren med disse aktivitetene?

_____minutter (per 24 timer)

Er det familie, venner eller bekjente som hjelper beboeren med en eller flere av områdene i spørsmål 1-3?

c) ❑Ja b) ❑Nei

Hvis nei: du har fullført spørreskjemaet
Hvis ja: Vær vennlig å svar på følgende spørsmål

4.1. Får beboeren hjelp av familie, venner eller bekjente til aktiviteter beskrevet under punkt 1 (bruk av toalettet, spising osv)?

a) ❑Ja b) ❑Nei

Hvis nei: gå til spørsmål 4.2
Hvis ja: Vær vennlig å svar på følgende spørsmål

4.1.1. Hvor mange dager i løpet av de siste 4 ukene?

_____dager (28 = daglig, 4 = en gang i uken)

4.1.2. På disse dagene, hvor mange minutter?

_____minutter (per 24 timer)

4.2. Får beboeren hjelp av familie, venner eller bekjente til aktiviteter beskrevet under punkt 2 (følge utenfor hjemmet, ta medisiner osv)?

a) ❑Ja b) ❑Nei

Hvis nei: gå til spørsmål 4.3
Hvis ja: Vær vennlig å svar på følgende spørsmål

4.2.1. Hvor mange dager i løpet av de siste 4 ukene?

_____dager (28 = daglig, 4 = en gang i uken)

4.2.2. På disse dagene, hvor mange minutter?

_____minutter (per 24 timer)

4.3. Får beboeren hjelp av familie, venner eller bekjente til aktiviteter beskrevet under punkt 3 (individuell person-relatert hjelp ikke inkludert i punkt 1 og 2)?

a) ❑Ja b) ❑Nei

Hvis nei: Du er ferdig med spørreskjemaet
Hvis ja: Vær vennlig å svar på følgende spørsmål

4.3.1. Hvor mange dager i løpet av de siste 4 ukene?

_____dager (28 = daglig, 4 = en gang i uken)

4.3.2. På disse dagene, hvor mange minutter?

_____minutter (per 24 timer)

Pasient: Utfyller Dato:

EQ-5d

Vis hvilke utsagn som passer best på din helsetilstand i dag ved å sette et kryss i en av rutene utenfor hver av gruppene nedenfor.

Kryss av for om det er besvart av pasient eller helsepersonell:

❑ Pasient ❑ Helsepersonell (Pasient MMSE <10)

Gange

Jeg har ingen problemer med å gå omkring. ❑

Jeg har litt problemer med å gå omkring. ❑

Jeg er sengeliggende. ❑

Personlig stell

Jeg har ingen problemer med personlig stell. ❑

Jeg har litt problemer med å vaske meg eller kle meg. ❑

Jeg er ute av stand til å vaske meg eller kle meg. ❑

Vanlige gjøremål *(f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter).*

Jeg har ingen problemer med å utføre mine vanlige gjøremål ❑

Jeg har litt problemer med å utføre mine vanlige gjøremål. ❑

Jeg er ute av stand til å utføre mine vanlige gjøremål. ❑

Smerte/ubehag

Jeg har verken smerte eller ubehag. ❑

Jeg har moderat smerte eller ubehag. ❑

Jeg har sterk smerte eller ubehag. ❑

Angst/depresjon

Jeg er verken engstelig eller deprimert. ❑

Jeg er noe engstelig eller deprimert. ❑

Jeg er svært engstelig eller deprimert. ❑

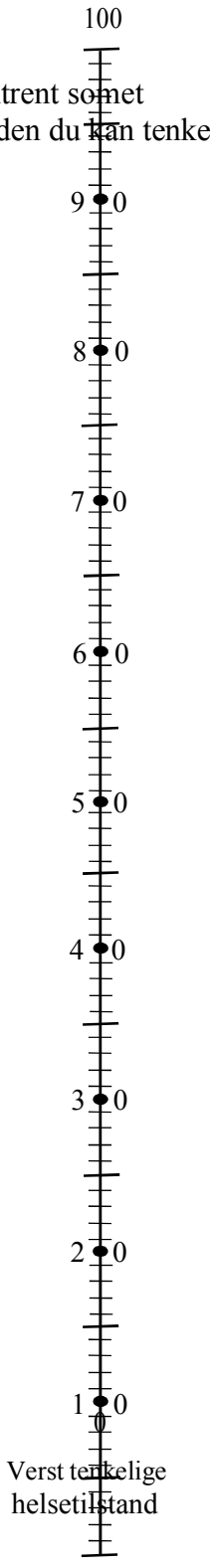
Pasient: Utfyller Dato:

For å hjelpe folk til å si hvor god eller dårligen helsetilstand er, har vi laget en skala (omtrent somet termometer)hvordenbestetilstandendu kan tenke deg er merket 100 og den verste tilstanden du kan tenke deg er merket 0.

Vi vil gjerne at du viser på denne skalaen hvor god eller dårlig helsetilstanden din er i dag, etter din oppfatning. Vær vennlig å gjøre dette ved å trekke en linje fra boksen nedenfor til det punktet på skalaen som viser hvor god eller dårlig din helsetilstand er i dag.

Din egen helsetilstand

Sett inn tallether:



Pasient: Utfyller Dato:

MMSE

MMSE-NR

TL starter med felgende spersmål: Synes du hukommelsen har blitt dårligere7 ja Q Nei deg skal nå stifle deg noen spersmål, som vi sper alle am. Svar så godt du kan. Instruksjon kan gjentas, unntatt på oppg. 12 og 17. ☐ Vetikke ☐

TIDSORIENTERING	*Poeng*	
1. Hvilket årstall har vi nå? (kun fullt årstall med 4 sifre gir poeng)	0	1
2. Hvilken årstid har vi nå? (ta hensyn til va•r og geografiske forhold) _____	0	1
3. Hvilken måned har vi nå7 (kun riktig navn pa måned gir poeng) _____	0	1
4. Hvilken ukedag har vi i dag? (kun riktig navn pa dag gir poeng) _____	0	1
5. Hvilken dato har vi i dag7 (kun dagsledd trenger å va°re riktig for å få poeng)	0	1

STEDSORIENTERING

På spersmål 7 brukes "Landsdel" ved testing i Oslo, "Fylke" utenfor Oslo. Sett ring rundt valgt stedsord for spersmål 8 og 9.

6. Hvilket land er vi i nå? _____	0	1
7. Hvilket fylke/landsdel er vi i nå7 (Ser-Norge gir også poeng for landsdel) _____	0	1
8. Hvilken by/kommune er vi i nå7 _____	0	1
9. Hva heter dette stedet/bygningen/sykehuset/Iegekontoret/hvor er vi nå?	0	1
10. I hvilken etasje er vi nå? (Spersmål stilles også om man er i 1. etasje) _____	0	1

UMIDDELBAR C•)ENKALLING/REC•ISTRERING

Ved retesting: [2. adm: STOL-BANAN-MYNT], [3. adm: SAFT-LAMPE-BAT], [S. adm: KATT-AVIS-L6K], [5. adm: FLY-EPLE-SKO].

11. Her godt etter. deg vil si 3 ord som du skal gjenta etter at jeg har sagt dem, og som du skal preve å huske, for jeg kommer også til å sperre deg om dem senere. Klar7 Nå kommer ordene;... HUS *\pause],* KANIN *\pause\,* TOC *\pause}.* Nå kan du gjenta disse ordene.

Dersom pasienten ikke gjentar alle 3 ord, repeteres alle ord inntil alle gjengis i samme forsek, maks. 3 presentasjoner. Det gis kun poeng etter I. presentasjon, rekkefelge pasienten sier ordene eruten betydning. Antall presentasjoner: stk.

HUS *\Ofd Ved* CAUSE: .....] _____	0	1
KANIN *\Ord ved retest:*	0	1
TOG *[Ord ved* refest:	0	1

Husk disse ordene, for jeg vil be deg gjenta dem senere.

OPPMERKSOMHET Oc HODEREcNlNc (Va r oppmerksom på eventuell distraksjonsbetingelse**)

Bruk felgende starttall ved retesting: [2. adm: 50], [3. adm: 90], [4. adm: 40], [5. adm: 60]. Sett ring rundt start- tall, skriv ned tallwar. Poeng gis når war er akkurat 7 fra forrige tall, uavhengig av om forrige tall var riktig.

12. Kan du trekke 7 fra 80? *\Dersom pasienten ikke gir et tallsvar, si:* Hva er 80 minus 7?] [Reft *etter tallsvar, gis videre instruksjon):* Og så fortsetter du å trekke 7 fra tallet **du kommer til, helt til** jeg sier stopp *[Instruksjon gis kun én gang}.* Dersom pasienten heller ikke nå gir et tallsvar, gå videre til distraksjonsbetingelsen**.

Starttall:	80	50	90	40	60			
	[73]	[43]	[83]	[33]	[53]	_____	0	1
Om nedvendigsi: også videre...	[66]	[36]	[76]	[26]	[46]	_____	0	1
Om nedvendigsi: også videre...	[59]	[29]	[69]	[19]	[39]	_____	0	1
Om nedvendigsi: ogsåvidere...	[52]	[22]	[62]	[12]	[32]	_____	0	1
Om nedvendigsi: også videre...	[45]	[15]	[55]	[5]	[25]	_____	0	1

Etter 5 subtraksjoner si: Fint, det holder *[Gå til oppg.* IN].

• •*Eventuell distroksjonsbetingelse — OBS, er ik:k:e poenggivendel*

Dersom pasienten ikke vil utfere eller kan besvare oppg. 12 med 5 avgitte tallsvar, skal distraksjonsbetingelsen brukes for å sikre kartlegging av langtidshukommelse pa oppg. 13. Be da pasienten telle baklengs fra 100 ca. 30 sek. med felgende instruksjon: (Tell baklengs fra 100 på denne måten: 99, 98, 97..., helt til jeg sier stopp. Var så god!)

Pasient: Utfyller Dato:

MMSE-NR

UTSATT G)ENKALLING ***Poeng***

13. **Hvilke** 3 ord var det jeg ba deg om â **huske?** *Ikke gi hjelp/stikkord]*

HUS	*[Ord ved retest:.....]*	0	1
KANIN	*[Ord ved retest:.....]*	0	1
TOG	*\Ord ved retest:.....]* _	0	1

Nevnes mer enn 3 ord, må pasienten velge hvilke 3 ord som skal va•re svaret. Rekkefelge er uten betydning. Det gis kun poeng for eksakt gjengivelse, dvs. bolighus, hytte, hare. kanindyr, togbane, lokomotiv etc. gir ikke poeng.

BENEVNING

14.	Hva heter dette? *\Pek på en blyant}*	0	1
15.	Hva heter dette? *Pek på et armbåndsur]*	0	1

Bruk kun blyant og armbåndsur, gjelder også retesting. Alternative poenggivende svar: Penn, gråblyant, klokke, ur etc.

REPETISJON

16. Gjenta ordrett det jeg sier. Er du klar? *\Si tydelig}:* "Aldri annet enn om og men" 0 1

TL kan si frasen 3 ganger. Poeng gis kun etter 1. presentasjon. Dialektvariasjoner godtas.

Antall presentasjoner:_____stk.

FORSTJELSE

Legg et blankt A4-ark på bordet midt foran pasient, kortsiden mot pasienten. TL legger egen hånd pa arket til all instruksjon er gift. Gi poeng for hver utfert delhandling, også dersom pasienten bretter arket med én hånd eller legger arket foran TL.

17. Her godt etter, for jeg skal be deg gjere 3 ting i en bestemt rekkefelge. Er du klar? Ta arket med én hand *\pause],* brett arket på midten én gang med begge hender samtidig *\pause),* og gi arket til meg. *[pause]* Var så god! *\Instruksjon gis kun én gany)*

TAR ARKET MED KUN EN HAND _____	0	1
BRETTER ARKET PA MIDTEN KUN EN GANG _____	0	1
LEGGER ARKET PA BORDET FORAN TL ELLER GIR ARKET TIL TL _____	0	1

LEANING

18. Nå vil jeg at du gjer det som star på arket *\Vis pasienten teksten).*
Pasienten må lukke eynene for poeng.

LUKK ØYNENE DINE _____ 0 1

5KRIVNINC/SETNINC•SC•ENERERINC•

Legg MMSE-NR skjema side 4 med kortsiden foran pasienten og gi vedkommende en blyant.

19 Skriv en meningsfu setning her *\Pek på* evre *del av side d]* .

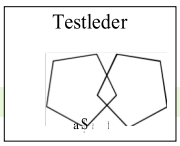
Skriver ikke pasienten noe, si: Skriv om vwret. _____ 0 1

Skrives imperativsetning med kun ett ord, f.eks. "Spis", si: Skriv en lengre setning. Skrives tidligere gitt setning/frase, f.eks. "Lukk eynene dine", "En meningsfull setning", si: Skriv en setning du lager selv.

Setningen må vure forståelig, men trenger ikke inneholde objekt. Se eksempler i manual*. Det gis poeng ved riktig utferelse selv etter supplerende instruksjon. Ignorer stave- og grammatikalske feil.

TEGNING/FI‹fiURKOPIERING

Legg figurark over setningen pasienten skrev, viskeIa•r ved siden av.



20. Kopier figuren så neyaktig du kan her *\Pek på nedre del av side d).* 0 1
Du kan bruke viskelwr. Ta deg god tid. Si fra når du er ferdig.

Det gis poeng når tegningen består av to 5-kantede figurer som former en 4-sidet figur der 5-kantene overlapper. Tegnet figur trenger ikke va•re identisk med modellen. Se slcâringseksempler manual*.

TOTAL POENcSUM --_____/30. Presiser hva pasienten hadde utfall (feilsvar) på:

Pasient: Utfyller Dato:

Til legevisitt

Spørreskjema	Skår
MMSE	
Cornells depresjonskala ved demens	
MOBID-2 ≥3?	

- Husk MOBID-2 i 2 eksemplarer, 1 til forsker og en til legevisitt
- Husk å fylle ut sjekklisten
- Husk å bestille og ta blodprøver

Mini mental status - MMSE

0-30, jo høyere skår jo bedre mental fungering.

Cornell skala for depresjon hos demente

0 – 38. Skår 7-11 indikerer mild grad og 12 og mer indikerer moderat eller svær grad av depresjon

Mobilization Observation Behavior Intensity Dementia - MOBID-2 Pain Scale

0-10. 3 eller mer på total skår betegnes som for høy smerte

Pasient: Utfyller Dato: