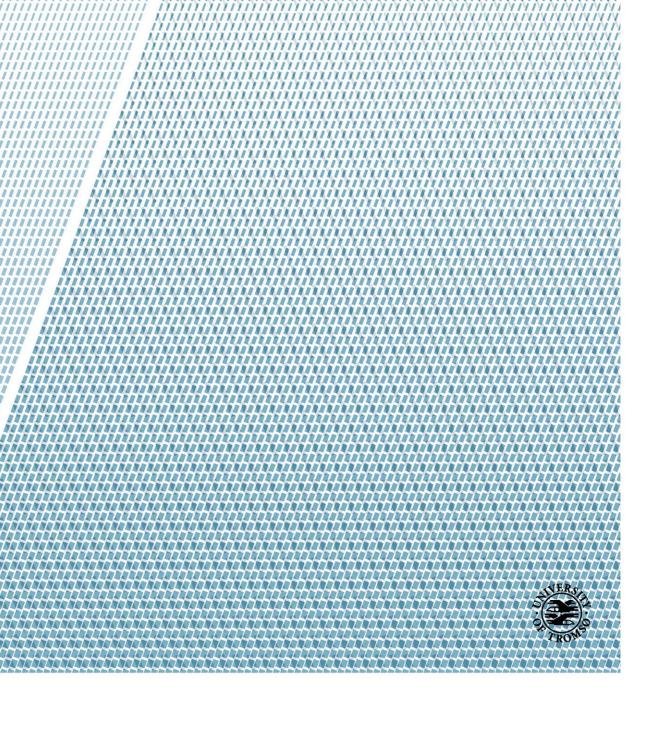


Faculty of health sciences / Department of community medicine

# Use of non-prescription (OTC) analgesics – utilization pattern and user characteristics in Norway, The Tromsø study: Tromsø 6

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## **Abstract**

Background: Drug policies in western countries, as well as countries in most other parts of the world, support self-medication with Over-The-Counter (OTC) drugs. The switch from prescription (Rx)-to-OTC has been most common in the Nordic countries, Great Britain and Germany in the last decades and deregulations were done to make it possible to sell OTC analgesics other places than under the pharmacy monopoly. Individual registration of OTC drugs cannot be done and therefore it is important to do public surveys to get information on consumption patterns of those drugs. The aim of the study is to describe where the different OTC analgesics are bought and how they are used in the population, and to assess whether or not recommended guidelines are followed.

**Material and method:** A cross-sectional study was conducted based on data from the sixth survey of the Tromsø study, Tromsø 6, in 2007-2008. The data included information from questionnaires and physical examinations of the 30-89 years study population (n=12981). A specific questionnaire was given, on OTC analgesic use within the last four weeks before the interview, for the users of OTC analgesics.

The wholesaler-based drug statistics from Norwegian Institute of Public Health (NIPH) was used to compare the consumption of OTC analgesics over time and to get ideas about changes in use since OTC analgesics became available outside pharmacy, in grocery shops and petrol stations etc. in 2003.

**Results:** There was a 45.3 % prevalence of OTC analgesic use within last 4 weeks before the interview (54.9 % women and 33.6 % men). Most of the OTC analgesics were used seldom (less than every week) by 73.5 % of users, and in a small daily dose, (1-2 tablets) by 78.4 %.

There was 70.0 percent women and 60.5 percent men who bought OTC analgesics from the pharmacies only, while 6.3 percent women and 15.8 percent men bought OTC analgesics from non-pharmacy outlets only.

The total sales (OTC+Rx) of paracetamol, ibuprofen, naproxen, diclofenac, ASA and phenazone-caffeine, in Defined Daily Dose/1000 inhabitants/day, increased by 40 %, from the year 2003 to 2016 according to statistics from Norwegian Institute of Public Health (NIPH). The prescription of those medicines doubled from 2003 to 2016. The OTC sales on the other hand went down by 4.5 %.

Conclusions: The majority of the adult OTC analgesic users in the present study follow the guidelines for use of OTC analgesics. Most of the OTC analgesics were used seldom and in a small daily dose. A small number of the participants report adverse effect from OTC analgesics. It is headache, muscle and joint pain and backache that is the main reasons for using OTC analgesics. The majority of the OTC analgesic users, use to buy there OTC analgesics at the pharmacy.

**Key words:** Population study, Public Health, Pharmacoepidemiology, Non-prescription analgesics, Self-medication, OTC analgesics, OTC drugs, Pain, Norway

# List of abbreviations

ADEs Adverse Drug Events

ATC Anatomical Therapeutic Chemical Classification

ASA Acetylsalicylic acid

BMI Body Mass Index

CI Confidential Interval

DDD Defined Daily Dose

GI Gastro Intestinal

GP General Practitioner (fastlege)

LUA "Legemidler Utenom Apotek" Sales of OTC drugs outside pharmacies

NSAID Non-steroidal Anti-Inflammatory Drugs.

NIPH Norwegian Institute of Public Health (Folkhelseinstituttet)

OR Odds Ratio

OTC Over-The-Counter (medicine sold without prescription)

POM Prescription only medicines

Rx Prescription (medicine sold with prescription)

WHO World Health Organisation

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#### 1 Introduction

#### 1.1 The importance of the study and reasons for use of OTC analgesic

# 1.1.1 The importance of doing population studies on use of non-prescription OTC analgesics.

Drug policies in western countries, as well as countries in most other parts of the world, support self-medication with Over-The-Counter (OTC) drugs. According to European Union Directive 92/96, "a drug should be sold without a prescription unless its use without medical supervision is dangerous, it is frequently used incorrect, it is a new chemical entity or it is administrated parenterally". Of the European countries, prescription (Rx)-to-OTC switches has been most common in the Nordic countries, Great Britain and Germany during the 1980s and early 1990s. In most European countries OTC drugs are sold in pharmacies only [1].

It is important to do public surveys that can give us information on consumption patterns of OTC drugs. It is a suitable way to do such studies to get information about the pattern of utilization. Through health surveys, the population are asked about drug use patterns and it is possible to study if the patterns differ among people with different living conditions, socioeconomic status, age, gender, education, pain conditions or intensity, and lifestyle choices. OTC drugs are by definition not prescribed by a physician and the use by individuals are therefore not registered. By such a survey, we can explore how these drugs are used, the preferential drug of choice, frequency of use, concomitant of overuse, purpose of use and side effects. We can also gather information about buying habits and if use of OTC analgesics follow the given guidelines for the use of the drugs.

#### 1.1.2 Reasons for use of OTC analgesics according to other studies

Pain and pain-related disease obviously represent the most common reason for analgesic use. Headache, ache in shoulders, joints and muscles, backache are treated with OTC analgesics as well as cold or flu symptoms [2,3,4]. There is, however, reason to believe that factors other than pain are important in the use of these drugs. Studies show that analgesics are more often used by women [2,3,4,5]. Overweight women have a higher total use of prescription medicines than other women do[6]. Health status is very important for drug use in general and for analgesic use in particular. Physical function and lifestyle are closely related to health status, and it has been suggested that physical functioning is also related to analgesic drug use. Analgesic use has also been found related to mental health. Psychological symptoms such as depression, insomnia and anxiety have been significantly related to analgesic use in some studies [2,3,7,8].

#### 1.1.3 What other studies reports about OTC analgesic frequency use

To compare the prevalence of OTC analgesic use and the share of OTC users in the different studies is difficult because it is measured in different length of time. In the Tromsø study 2007-2008 there were 60% women and 37% men using analgesics in the last four weeks [9]. Another Norwegian study (HUNT 3) 2006-08, reported 47% prevalence of OTC analgesic use among men and women at least once per week in the last month [10]. In a computer aided telephone survey, in Australia in 2009, there was 55% prevalence use at least once per month among those who have reported ever using an OTC analgesic [11]. In a study in Scotland, a postal survey in 2002, 37% reported OTC analgesic use within the last two weeks [4]. From a recent, randomly selected population study (web), in Sweden (2013), they reported 47% OTC analgesic users with use of analgesics at least monthly or more in the 6 months prior to the study [12].

#### 1.1.4 Characteristics of OTC analgesic users according to other studies

Women use more OTC analgesic than men do. In the Tromsø Study 1986-87 there was more than double use of analgesic among women [3], in Sweden 1988/89 it was more than 50% higher use for women [2]. In Scotland 2002 the prevalence of women was higher compared to men OR 1.70 (CI 95% 1.33-2.18) [4]. In a German survey from 2011, the women had higher prevalence of analgesic drug use than men OR=1.58 (CI 95%1.35-1.85) [5]. In an Australian study from 2009, regular users of analgesics were more likely to be female (57%, n=1297/2276) [11]. In the HUNT3 population 2006-2008, there was 33% higher use of OTC analgesic among women compared to men [10], and in Tromsø 2007-08, there was 62% higher total analyseic use among women compared to men [13]. Younger people use more OTC analgesic than older people do. Porteous et al reported in 2005 an unadjusted OR=2.70 (CI 95% 2.11-3.46) and multi-adjusted OR=1,52 (CI 95% 1.05-2.20) of OTC analgesic use in the group of people under 60 years, compared to those 60 years and above [4]. Sarganas et al reports in 2015 that Use of OTC analgesics is lower among older adults (65-79 years) OR=0.31 (CI 95% 0.22-0.44) compared to all other groups [5]. Stocik et al. reported in 2011 that "More people under the age 54 years reported regular use of OTC analgesics than did those aged 55 years or more" [11]. Håkonsen et al. reported in 2016 "participants in the age range 20-39 years reported more frequent use of OTC drugs compared with the other age groups" [12]. Dale et al reported from the HUNT3 study that OTC paracetamol is used almost at the same level in all age groups, but ASA is used more among those who are older than 60 years and NSAID is used more among those who are younger than 60 years [10].

People with self-reported bad health use more OTC analgesic than those with good health. Self-perceived health explained much of analgesic use in the Swedish study

(1988-89) OR=1.56 (CI 95%1.30-1.87) for men and OR=1.42 (CI 95% 1.20-1.69) for women [2]. Porteous et al. reported from a Scottish study that those with "good or very good" or "fair or poor" were twice as likely to use non-prescription analysis as those reporting "excellent" health [4]. This finding has been confirmed in another study. [9].

#### 1.2. Background, Terminology and Explanations

#### 1.2.1 Pain

IASP (International Association for the Study of Pain) has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [14].

"Pain is a personal experience that cannot be detected or ruled out by objective methods. It is therefore meaningless to question a patient's pain experience. Pain may occur without being possible to detect any tissue damage". "It is important to distinguish between acute and persistent pain. In case of acute pain, it is often easier to determine a likely pain cause and prescribe effective treatment."" The persistent pain is usually multifactorial and in many cases means a therapeutic challenge" [15,pp 889-890].

"Injury does not only produce pain, it also leads to stress, which the body attempts to deal with by achieving homoeostasis. This process involves neural, hormonal, and behavioural activities derived from genetically determined repertoires. These homoeostatic repertoires exist at the injury site (cytokine release, for example), in the adrenal cortex (release of corticosteroids), the immune system, and in widely distributed areas in the brain" [16].

#### 1.2.2 Analgesics

Analgesics are among our most commonly used drugs[17,18]. They are used in the treatment of both acute and chronic pain. Analgesics, also called painkillers, are pharmaceuticals used to relief pain and can be divided into opioid and non-opioid

analgesics. Opioids acts on the central nervous system (CNS) as depressants and stimulants, often with a good effect on pain, but causes also addiction among other adverse effects. That is the main reason to avoid them. The World Health Organisation (WHO) recommend a pain ladder[19] where the first step is to use non-opioids such as Paracetamol and/or non-steroidal anti-inflammatory drug (NSAID). At step two, you continue with week opioids such as codeine or tramadol in combination with non-opioids and then goes further on to a stronger opioid such as oxycodone, morphine or fentanyl also in combination with non-opioids until you receive pain relief. A good analgesic drug, should in a proper dose, relieve pain without giving side effects.

#### 1.2.3. Over-The-Counter (OTC) drugs

Over-The-Counter (OTC) drugs represent the drugs that are sold without prescription in and outside pharmacies. People may also buy them on the internet or abroad.

#### 1.2.4 Sales of OTC drugs outside pharmacy/"Legemidler utenom apotek" (LUA)

In Norway, some drugs were released for selling outside pharmacy in grocery shops, petrol station etc. in the year 2003. A new reform was established through political decision. The monopoly of the pharmacies was abolished and enabled supermarkets, grocery stores, convenience stores and petrol stations (non-pharmacy outlets), to sell some specific drugs i.e. analgesics, nicotine replacement medicines, nasal decongestants, expectorants, motion sickness tablets and antihistamine[20]. The reform is called LUA "Legemiddel utenom apotek"[21]. Emergency contraceptives, allergy medicine, hydrocortisone dermatological and agents used for treatment of dyspepsia, antacids, were included from January 2009 [22,p12].

# 1.2.5 OTC analgesics sold in pharmacy and outside pharmacy

The OTC analgesics available in Norway are paracetamol, acetylsalicylic acid (ASA), ibuprofen, naproxen, diclofenac (was not sold as OTC between 2005 and 2008) and phenazone in combination with caffeine. There are limitations on which strength and size of package that are sold as OTC analgesic. The only analgesics sold outside pharmacy today are paracetamol and ibuprofen. Phenazone-caffeine was sold outside pharmacy until the 1 February 2011 [22,p.16]. Paracetamol is the most common sold analgesic not only in Norway but also worldwide. The NSAIDs, ibuprofen and naproxen are then the second and third most common sold OTC analgesics. The sales of ASA as an analgesic is very low. It was much more common earlier, but because of its serious side effect, other analgesics has been promoted as the drug of choice[23]. Phenazone-caffeine is a product that has a long tradition in Norway only, and has been sold since 1930. England has no product with phenazone and phenazone preparations were withdrawn from the US market after a report from US Food and Drug administration (FDA) in the 1990s that stated that the drug was neither safe nor effective [24,p.8-9]. Phenazone has not been promoted for years and the sales has declined considerably in Norway [24,p.17-22].

#### 1.2.6 Defined Daily Dose (DDD)

The use of DDDs as units of measurement offers better possibilities for comparisons between alternative medicinal products, independent of price differences. A DDD is defined as the assumed average maintenance dose per day for a drug used on its main indication in adults. The sales figures are given as the number of DDDs/1000 inhabitants/day. Ten DDDs/1000 inhabitants/day corresponds to a daily use of this drug by 1% of the population. This estimate is, however, only valid if there is good correlation between the DDD and the actual consumed dose[22]. Despite of that, these figures will be

useful when we compare the use over time, and the use between different generic products.

# 1.2.7 Anatomical Therapeutic Chemical Classification (ATC)

In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the body organ or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs are classified in groups at five levels. The drugs are divided into 14 main groups (1st level), with pharmacological/therapeutic subgroups (2nd level). The 3rd and 4th levels are chemical/pharmacological/therapeutic subgroups and the 5th level is the chemical substance[25]. Paracetamol, acetylsalicylic acid and phenazone caffeine are all classified under the ATC group, *N-nervous system* and its subgroup *N02B other analgesics and antipyretics*. Ibuprofen, naproxen and diclofenac are classified under ATC group *M-Musculo-skeletal system* and its subgroup *anti-inflammatory nonsteroid drugs*.

#### 1.2.8 Sales statistics: General trends concerning OTC analgesics

The sales of analgesics has increased considerably in Norway over the last three decades. The sales of NSAIDs more than doubled, paracetamol tripled, while high-dose ASA declined substantially in Norway from 1990 to 2016 [26,pp 66-73]. The sales of OTC drugs accounted for 13% of total sales measured in Defined Daily Doses (DDDs) [26,p.12].

#### 1.3 The OTC analgesics

#### 1.3.1 Paracetamol

Paracetamol is safe and effective when used properly and can be used both by children and adults. It also acts as a fever depressant. Paracetamol is recommended as the first choice in the treatment of pain. However, the number of inquiries into poison information board about paracetamol has increased [27,28,29]. Paracetamol is one of the most commonly used drugs in Norway. OTC sales correspond to almost two packs per person per year or on average 36 tablets in 2016 [26,p.12]. "The total sales of paracetamol, both OTC and Rx, measured in DDDs have increased gradually. OTC sales have been relatively stable since 2010." "The sale of Rx paracetamol in large packages is the reason for the increase in total sales of paracetamol. Increased prescribing for use in chronic pain that are reimbursed has probably contributed to this" [30].

#### 1.3.2 Nonsteroidal Anti-inflammatory Drugs (NSAID)

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed because of their analgesic and anti-inflammatory properties. Their use is associated with the occurrence of serious adverse drug events (ADEs), particularly of the gastrointestinal, cardio-vascular, and renal tract. In general, short-term use of NSAIDs is considered relatively safe, provided it is used in OTC-doses by adults without contraindications or interacting medications[31]. OTC Ibuprofen is sold both in and outside pharmacies while OTC naproxen and OTC diclofenac are sold in pharmacy only (diclofenac was not sold as OTC in the year 2005-2007).

#### 1.3.3 Acetylsalicylic acid (ASA)

ASA is an old analgesic and antipyretic drug that has been used a lot worldwide.

Indications for OTC ASA in Norway are analgesic, antipyretic and anti-inflammatory use.

Because of its dangerous side effects with gastrointestinal bleedings and risk of other inner bleedings, guidelines from the health authority has recommended other analgesics than ASA for treatment of pain[32,pp.1237-1240].

#### 1.3.4 Phenazone with caffeine

Phenazone is an analysesic and antipyretic drug. Phenazone caffeine has been sold both in and outside pharmacies from 2003-2011. Today it is sold in the pharmacies only [22].

#### 1.4 Adverse effects of OTC analgesics

OTC analgesics sold from non-pharmacy outlets, are advocated particularly to be safe and well tolerated. However, inappropriate use, abuse or concomitant use with other OTC drugs or prescribed drugs can lead to adverse effects. These adverse effects include upper gastrointestinal (GI) bleeding and perforation, renal failure, heart failure and damage on the liver [32,pp.1237+1292]. The decision to use any analgesic is a balance of benefit and risk. In the case of analgesics, it is important to balance the therapeutic benefit against both the risk in therapeutic use and the risk in overdose. Some analgesics have adverse effects in therapeutic doses; all analgesics are toxic in overdose[33].

#### 1.4.1 Adverse effects of Paracetamol

Paracetamol is recommended because of few side effects, when used for short time and in therapeutic doses, even though it might not be as effective as some NSAID products [34,p24], [35,p1061]. Paracetamol does not affect the thrombocyte aggregation and does not cause damage to the gastrointestinal mucous membrane as NSAID products does. It can give allergically reactions, leukopenia, thrombocytopenia and haemolytic anaemia. Use over long time can also give chronically headache. There are risk for liver and cardiovascular damages with prolonged use of large doses. Also in ordinary doses, it can

cause damages to patients with poor nutritional status and to patients with chronic alcohol abuse[32,p.1292]. Liver and kidney damage is a big risk associated with self-injury and poisoning of paracetamol. Antidote treatment with acetyl cysteine will give complete protection of liver damage if started 8 hours after intake[36]. Potential risk of severe damage of vital organs are there and intensive treatment and care are required for several days. Liver transplantations can be a consequence if treatment do not start in time[33].

#### 1.4.2 Adverse effect of NSAID and ASA

NSAID and ASA has a wide spectrum of gastrointestinal side effects from dyspeptic symptoms to life threatening bleeding and perforation. Gastric and duodenal changes is frequently and most clinically important. Advanced age, previous ulcer disease, concomitant use of glucocorticoids increases the risk of gastrointestinal complications (severe ulcers, gastrointestinal bleeding, and perforation). "There is a correlation between dose of NSAIDs and the development of ulcer disease, and one should always strive to use the lowest possible effective dose for the shortest possible time" [35]. In patients with renal failure or severe heart failure, NSAID can lead to further reduction in renal function with renal blood flow and sodium retention. Worsening or provocation of hypertension have been reported, as well as heart failure. Caution is advised in patients with coronary artery disease. 2400 mg or more ibuprofen per day increases the risk of cardiovascular disease. Diclofenac is contraindicated in patients with coronary disease.

Bronchoconstriction can be triggered or worsened in especially vulnerable patients having allergies or asthma, as well as in persons with a known hypersensitivity to ASA. [32,p.1237].

#### 1.4.3 Adverse effect of phenazone-caffeine

Adverse effects are rare. Poisoning risk is probably small. There is a risk of anaphylactic reactions. It may cause headaches on withdrawal - "habituation headache" [32,p.1291]. Overdose may give nausea, vomiting, circulatory disorders, excitation, convulsions and coma [37,p.762]. Chronic use of large doses may cause risk of renal complications. Prolonged use creates the risk of allergic reactions, gastrointestinal and renal side effects. Caffeine doses of 1 g (10 times recommended dose) for adults can cause reactions of the central nervous system and circulatory disorders with tachycardia, extra systoles and increased respiratory rate. Nausea, headache, dizziness, agitation, tinnitus, tremor, excitation, tachypnea and increased urine output [38].

#### 1.4.4 Abuse and overdose of OTC analgesics

There are indications that some individuals use OTC analgesics to treat psychological problems and stress [7,8,39]. Overdose is also related to self-medication of OTC analgesics. Adverse drug reaction related to self-medication resulted more frequently in neurologic and psychiatric side effects compared to ADR caused by a medical prescription[40]. The principal factor in the frequency of paracetamol overdose is ease of access. Availability of paracetamol in large quantities contributes to its use in overdose. Limiting availability could prove an effective strategy for reducing the frequency of paracetamol overdose and self-poisoning [29,41,42,43].

# 1.6 Aims and study questions

#### 1.6.1 Aims

The aim of the project is to describe how the different OTC analgesics are bought and used in the population, to characterize the users of OTC analgesics and to assess whether or not recommended guidelines are followed.

#### 1.6.2 Study questions

- Is self-medication of OTC analgesics in accordance with guidelines?
- Do people experience adverse effects from OTC analgesics?
- What kind of pain problems do people self-medicate with OTC analgesics?
- How many purchase OTC analgesics on the internet and abroad, and are there
  differences in the user characteristics of people buying OTC analgesics in the pharmacy
  compared to non-pharmacy outlets, difference in regards to demographics, social
  economic factors, lifestyle and health status.

#### 2. The Tromsø study. Study population and design

#### 2.1 The Tromsø Study

The Tromsø Study is a population-based, prospective study of various health issues, symptoms, and chronic diseases. Seven surveys have been carried out 6–7 years apart, referred to as Tromsø 1–7. The surveys have been carried out in the municipality of Tromsø, Northern Norway from 1974 to 2016 [44].

The Tromsø Study was initiated in 1974 in an attempt to help combat the high mortality due to cardiovascular diseases in Norway.

The primary aim of the Tromsø Study was to determine the reasons for the high mortality of cardiovascular disease, and to develop ways of preventing heart attacks and strokes.

The study was gradually expanded to include many other chronic diseases and other problems such as rheumatism, neurological and mental diseases, skin diseases, stomach and bowel-related diseases, cancer and osteoporosis.

In all, a total of more than 45 000 different people have participated in one or more of the seven surveys that are completed since 1974.

The Tromsø Study cohort consists of people living in the municipality of Tromsø, Norway, situated at 69° N. In 2007-2008 when the sixth survey was conducted, Tromsø consisted of 70,000 inhabitants, about 60,000 people lived in the city area, while the rest was scattered throughout the whole municipality (2558 square kilometres). Tromsø is a centre of education, research, administration and fishing related activities. The population is growing and dominated by Caucasians of mainly Norwegian origin, but also includes a Sami minority. Tromsø may be considered as representative of a Northern European, white, urban population[44].

#### 2.2 Study population and design

Participants are from the sixth wave of the Tromsø study, Tromsø 6. Tromsø 6 was conducted in 2007–08 among men and women 30–87 years old living in the municipality of Tromsø. A total of 19,762 people were invited and 12,984 of them were examined (65.7%). A personal invitation, an information folder, and a four-page questionnaire Q1 (Appendix 2), were posted to the participants about 2 weeks before the suggested appointments.

All residents aged 40–42 and 60–87(n=12,578), a 10% random sample of individuals aged 30–39 (n=1056) and a 40% random sample of individuals aged 43–59 (n= 5787) were invited to the sixth wave of The Tromsø study.

In addition study subjects who had attended the second visit of Tromsø 4, (included ultrasound examination of the carotid arteries, echocardiography, and bone scan), if not already included in the three groups above and still residing in Tromsø municipality September 2007, (n=341), were also invited[44].

#### 2.3 Questionnaires

In the first questionnaire Q1, participants were asked, "How often have you during the last four weeks used painkillers without prescription?" Out of 12 693 of the participants (288 missing), 5 275 (41.6 %) answered that they had used OTC analgesics during the last four weeks. The participants of Tromsø 6 answered the second questionnaire (Q2), that was handed out to the participants and either returned at the study site or sent back by mail, and 12 440 participants (95.8%) answered Q2.

Those participants that confirmed in Q1 that they had used OTC analgesics within last four weeks were asked to answer a specific section of Questionnaire 2 (Q2) part 16 called

use of OTC analgesics. There were 4 292 men and women that answered what type of OTC analgesic they have used during last four weeks (figure 1, flow chart).

In Q1, the participants got questions concerning: health and diseases, use of health service and medicines, socio-demography, lifestyle and questions concerning women and pregnancy.

In Q2 the participants are asked more detailed questions about use of OTC analgesics (appendix 3) as, a) type of OTC analgesics that are used and how often they are taken, within last four weeks, b) daily dose taken, c) reasons using the medicine, d) side effects, e) if they are combined with prescribed analgesics, f) questions on were OTC analgesics are bought, pharmacy, grocery, petrol station, internet or abroad.

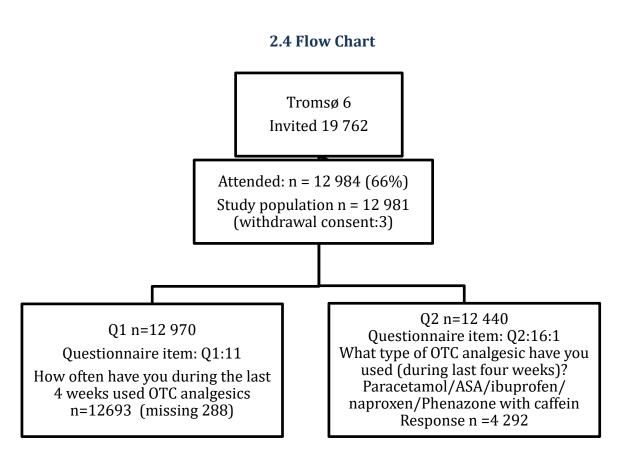


Figure 1. Flow chart for participants in the study. Tromsø study: Tromsø 6

#### 2.5 Measurements

Height and weight. BMI is defined as the body mass divided by the square of the body height (kg/m2),

#### 2.6 Variables:

For a complete list of variables with response alternatives (appendix 4).

#### 2.6.1 Questionnaire1 (Q1)

- Age per 31.12.2007
- Sex (male, female)
- How do you in general consider your own health to be? (very bad, good, neither good nor bad, bad, very bad)
- How often have you during the last four weeks used the following medication?
   Painkillers non-prescription (not used the last four weeks, less than every week, every week but not daily, daily)
- What is the highest level of education you have completed? (primary/secondary school, technical school/vocational school, high school diploma, collage university less than 4 years, 4years or more)
- Describe your exercise and physical exertion in leisure time (reading/watching TV/ other sedentary activity? Walking/cycling/other forms of exercise at least 4 hours a week? Participation in recreational sports/heavy gardening etc. at least 4 hours a week? Participation in recreational sports competition, regularly several times a week?).
- How often do you usually drink alcohol? (never, monthly or less frequently,2-4 times a month, 2-3times a week, 4 or more times a week)
- Do you/did you smoke daily? (yes now, yes previously, never)

#### 2.6.2 Questionnaire 2 – section 16 (Q2; 16)

- Which OTC analgesics have you used? paracetamol (not used, not every week, every week-but not daily, daily) acetyl salicylic acid (not used, not every week, every week-but not daily, daily) ibuprofen (not used, not every week, every week-but not daily, daily) naproxen (not used, not every week, every week-but not daily, daily) phenazone-caffeine (not used, not every week, every week-but not daily, daily)
- What is your normal daily dose when taking paracetamol? (Number of tablets)
- What is your normal daily dose when taking acetyl salicylic acid? (Number of tablets)
- What is your normal daily dose when taking ibuprofen? (Number of tablets)
- What is your normal daily dose when taking naproxen? (Number of tablets)
- What is your normal daily dose when taking phenazone-caffeine? (Number of tablets)
- What reasons do you have for taking non-prescription analgesics headache? Yes, menstrual pain? Yes, migraine? Yes, backache? Yes, muscle ache/joint pains? Yes, tooth ache? Yes, other than headache, menstrual pain, migraine, backache, muscle ache/joint pains, tooth pain? Yes
- Have you experienced side effects taking the OTC analgesics paracetamol? Yes/No, acetyl salicylic acid? Yes/No, ibuprofen? Yes/No, naproxen? Yes/No, phenazone-caffeine? Yes/No.
- Where do you normally buy OTC analgesics pharmacy? Yes, grocery? Yes, petrol station? Yes, abroad? Yes, internet? Yes.

# 2.7 Definitions of concept and expressions in the result

The educational groups are formed from how many years studies that are expected for each group, primary or 1-2 years secondary school = "up to 9 years", vocational or high secondary school (A-level) = "10-12 years" collage/university, = "more than 13 years". Self-reported health: "bad" = bad and very bad, "good" = good and excellent.

Activity: Exercise and physical exertion in leisure time.

"Low activity" = reading watching TV, or other sedentary activity. "Walking /cycling >4 hours/week" = Walking, cycling, or other forms of exercise at least 4 hours a week. "Sport activity/Hard training" = participation in recreational sport, heavy gardening etc. or participating in hard training and sport competition, several times a week.

Use of alcohol: Table 7 and 9, "Never or seldom" = never or monthly or less frequently. "2-4 times/month" is the same in the questionnaire. "Several times/week" = 2-3 times a week or four or more times a week.

Daily smoking: yes/no, no = former smokers or not daily smokers.

OTC analgesic use: "Seldom use" = use less than every week within last four weeks, "frequent use" = weekly or daily use within last four weeks.

#### 2.8 Wholesalers-based drug statistics, NIPH

Norwegian Institute of Public Health and their wholesaler-based drug statistics was used to compare the use of OTC analgesics over time and study the changes in consumption since 2003 when the OTC analgesics were allowed to be sold in non-pharmacy outlets. The statistics includes sales of paracetamol, ibuprofen, naproxen, diclofenac, acetylsalicylic acid and phenazone-caffeine. The table gives sales figures on both Rx and OTC analgesics and shows sales from both the pharmacies and non-pharmacy outlets.

#### 2.9 Statistical analysis

Statistical analyses were conducted in IBM SPSS statistics 24. Statistical analyses were done with Pearson's chi-square test, log linear analysis and logistic regression,

## 2.10 Missing and inaccurate data

The 288 participants in the study who did not answer the question about non-prescription painkillers in Q1 was not included in the study. Those who also did not answer questions about health 0.7%, education 1.2%, activity 7.8%, alcohol 1.2%, smoking 1.3% and those without measurements to calculate BMI 0.3% were not included in those analysis.

In the analysis of use of different OTC analgesics, all the participants who answered on one or more of the question about which OTC analgesic they had used in the last four weeks was included, n = 4292 out of the 5275 participants that gave a positive answer on the question about OTC- analgesics (non-prescription painkillers) in Questioner 1. Participants, who on the question about "amount of tablets used daily" did not answer or wrote zero tablets, were not included in the analysis.

All original survey documents that included any extreme value of tablets used daily were controlled and corrected or not included in the analyses, if found incongruous.

#### 2.11 Systematic review of literature

Systematic reviews of the literature in the field was carried out in the beginning of the study, in the middle of the study, and in the end of the study. Through Ovid Databases, EMBASE, MEDLINE, Cochrane library and PubMed, literature search was performed in January 2016, in April 2017 and in January 2018. Search was done to find articles concerning population studies in the field of Over-The-Counter, OTC analgesic, non-prescription analgesics use and purchase of OTC analgesics focusing on Northern Europe

and the Nordic countries. Literature search was done in English and the Scandinavian languages. Some articles in German language was also browsed. Throughout the study period search has been done through Ovid databases at the university library, UiT and through google scholar search on the World Wide Web on use of OTC analgesics, purchase habits, efficiency, side effect, and user characteristics. Search has also been done concerning abuse and self-intended injury with OTC analgesics focusing on the Scandinavian countries. Literature and articles have also been given through people knowing the research field, including supervisor. Several articles have been found through other researches reference list.

#### 2.12 Ethical aspects

The Regional Committee for Medical and Health Research Ethics of North Norway (REK Nord), and The Norwegian Data Protection Authority have approved the Tromsø study. The Tromsø study complies with the Declaration of Helsinki, International Ethical Guidelines for Biomedical Research Involving Human Subjects and the International Guidelines for Ethical Review of Epidemiological Studies. Participation was voluntary and each subject gave written informed consent prior to participation [44,45].

#### 3. Results

#### 3.1 Sales of OTC analgesics in Norway.

**Table 1** shows sales statistics for OTC analgesics in Norway 2003-2016. From the year 2003, OTC analgesics were also sold at non-pharmacy outlets. Table1 describes the sales of OTC analgesics (in DDD/1000 inhabitants/day) both in the pharmacies and in grocery stores, petrol stations etc. There are also information about sales of the prescription (Rx) analgesics and the total sales of each drug.

In the period 2003-2016, the total sales of paracetamol (OTC+Rx) steadily increased from 23.3 to 38.2 DDD/1000 inhabitants/day, an increase of 64.0 percent over these years. In 2003, paracetamol was mostly sold as OTC, (73.4 %), however, this share was reduced to 39.3 percent in 2016. Out of the total sale of OTC paracetamol 54.6 percent were sold at non-pharmacy outlets 2016.

Ibuprofen increased steadily its total sales from 2003 to 2011 from 10.9 to 19.8 DDD/1000inhabitants/day, (81.7 %). Since 2011, there has been a decrease in the sales with 3.0 DDD/1000 inhabitants /day, (15.2 %). Totally, in the period 2003 to 2016 the increase in the sales of ibuprofen was from 10.9 to 16.8 DDD/1000 inhabitants/day (54.1 %). In 2016, 54.8 percent of the total sale of ibuprofen were sold as OTC analgesics. The share of OTC and Rx has been almost the same for ibuprofen over these 14 years. Out of the total sale of OTC ibuprofen 39.1 percent were sold at non-pharmacy outlets in 2016. Diclofenac increased steadily its sales from 2003 to 2011 from 5.3 to 11.4 DDD/1000 inhabitants/day, (115 %). Since then, there has been a decrease in the sales with 4.2 DDD/ 1000 inhabitants/day, (36.8 %). In the period 2003-2016 the increase in the total sales of diclofenac was from 5.3 to 7.2 DDD/1000 inhabitants /day, (35.8 %).

The sales of acetylsalicylic acid as an analgesic drug has declined steadily from 2003-2016 from 0.7 to 0.2 DDD/1000 inhabitants/day, (71.4%). Phenazone-caffeine has also declined steadily in the period from 3.6 to 1.4 DDD/1000 inhabitants/day, (61.1 %). Both ASA and phenazone caffeine are sold as OTC only in pharmacy. Phenazone-caffeine was sold in non-pharmacy outlets from 2003 to 2010.

 $Table \ 1. \ Sales \ of \ OTC \ analgesics \ from \ the \ pharmacies \ and \ the \ non-pharmacy \ outlets \ in \ Norway \ 2003-2016, \ DDD/1000 \ inhabitants/day.$ 

Source: The Norwegian Wholesaler-based drug statistics, Norwegian Institute of Public Health.

Year	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Paracetamol	2003	2004	2003	2000	2007	2000	2003	2010	2011	2012	2013	2014	2013	2010
OTC Pharmacy	16.9	12.4	11.4	10.4	10.2	9.5	9.2	8.3	8.0	8.0	7.6	7.1	6.8	6.8
OTC Grocery etc.	0.2	4.1	5.9	7.0	7.8	8.0	8.1	7.7	8.0	8.0	7.9	7.8	8.1	8.2
Total OTC	17.1	16.6	17.3	17.4	18.0	17.5	17.3	16.0	16.0	16.0	15.5	14.9	14.9	15.0
Total Rx	6.3	7.1	8.7	10.1	11.3	13.0	14.5	15.9	17.8	19.2	20.2	20.6	21.5	23.2
Total DDD	23.3	23.6	26.0	27.5	29.3	30.5	31.8	31.9	33.8	35.2	35.7	35.5	36.4	38.2
Ibuprofen														
OTC Pharmacy	5.8	5.0	5.3	5.5	6.1	6.6	6.6	6.3	6.8	6.4	6.1	5.8	5.6	5.6
OTC Grocery etc.	0.1	2.0	2.8	3.3	3.7	4.0	4.1	4.1	4.2	4.1	3.7	3.5	3.7	3.6
Total OTC	5.9	7.0	8.1	8.8	9.8	10.6	10.7	10.4	11.0	10.5	9.8	9.3	9.3	9.2
Total Rx	5.1	5.7	5.9	6.4	7.0	7.6	8.1	8.2	8.8	8.6	7.9	7.9	7.7	7.6
Total DDD	10.9	12.7	14.0	15.2	16.8	18.2	18.8	18.6	19.8	19.1	17.7	17.2	17.0	16.8
Naproxen														
Total OTC	1.3	1.2	1.0	1.0	1.0	0.9	0.9	0.8	0.8	0.7	0.7	0.8	0.9	0.8
Total Rx	3.5	3.1	3.6	3.5	3.4	3.3	3.3	3.1	3.2	3.2	3.1	3.3	3.5	3.6
Total DDD	4.8	4.3	4.6	4.5	4.4	4.2	4.2	3.9	3.9	3.9	3.8	4.1	4.3	4.4
Diclofenac														
Total OTC	0.0	0.0	0.0	0.0	0.0	0.1	0.4	0.4	0.5	0.6	1.2	0.7	0.8	0.7
Total Rx	5.3	5.4	7.7	8.7	9.6	10.7	10.6	10.9	11.0	10.2	8.9	7.6	7.2	6.6
Total DDD	5.3	5.4	7.7	8.7	9.6	10.9	11.0	11.4	11.4	10.8	10.1	8.3	8.0	7.2
Acetylsalicylic acid	d													
Total DDD/OTC	0.7	0.6	0.5	0.4	0.4	0.4	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.2
Phenazone-caffei	ne													
OTC pharmacy	3.5	3.1	2.8	2.5	2.4	2.3	2.0	1.8	2.0	1.9	1.8	1.7	1.5	1.4
OCT grocery etc.	0.0	0.4	0.5	0.4	0.4	0.4	0.4	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Total DDD	3.6	3.5	3.2	3.0	2.8	2.7	2.5	2.3	2.0	1.9	1.8	1.7	1.5	1.4

Figures based on numbers from Table 1: Sales of OTC analgesics in pharmacy and non-pharmacy outlets 2003-2016

Sales of paracetamol have increased with 64 %, 2003-2016. OTC sales were reduced while the sales of Rx paracetamol have increased substantially.

From 2003-2016 sales of ibuprofen increased from 10.9-16.8 DDD/1000/day. In 2011, there was a top of 19.8 DDD/1000/day. About 40% of the OTC ibuprofen was sold in non-pharmacy outlets.

Naproxen was mostly sold as a prescription drug. Only 18% was sold as OTC in pharmacy. ASA was only bought as OTC and the sales has declined. Phenazone-caffeine sales were reduced 2.5 times within 14 years.



Fig. 2: Sales of paracetamol (DDD/1000 inhabitants/day) in 2003-2016. Source: Wholesaler-based drug statistics, NIPH

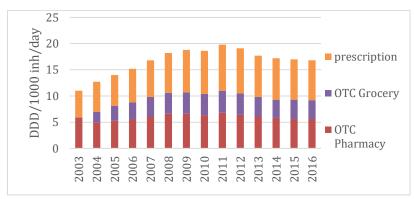


Figure 3: Sales of ibuprofen (DDD/1000 inhabitants/day) in 2003-2016. Source: Wholesaler-based drug statistics, NIPH

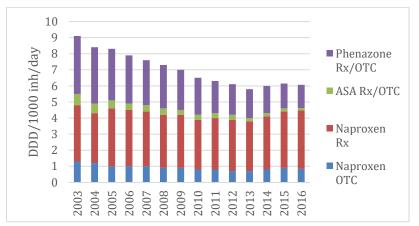


Figure 4: Sales of naproxen, ASA and phenazone-caffeine, (DDD/1000 inhabitants/day) in 2003-2016.

Source: Wholesaler-based drug statistics, NIPH

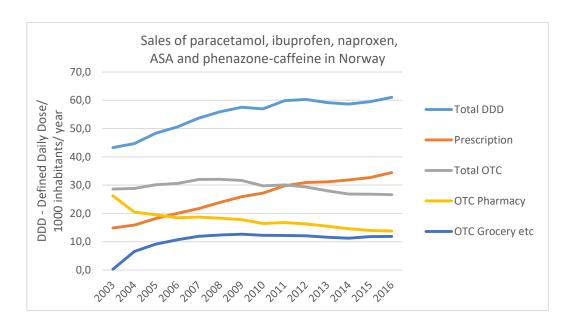


Figure 5: Sales of paracetamol, ibuprofen, naproxen, ASA, and phenazone-caffeine in Norway 2003-2016. Source: Wholesaler-based drug statistics, NIPH

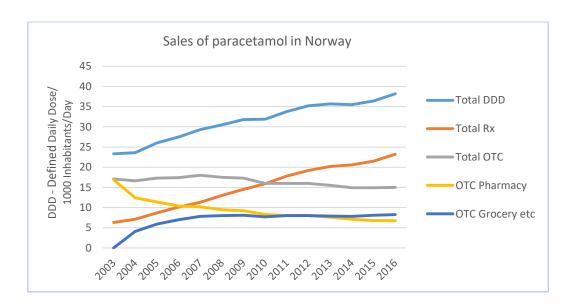


Figure 6: Sales of paracetamol in Norway 2003-2016. Source: Wholesaler-based drug statistics, Norwegian Institute of Public Health, NIPH

Diagrams in figure 5 and 6 are compiled from figures in Table 1, page 22. Figure 5 gives the total amount of those drugs but are mostly influenced by the dominated sales trends of Paracetamol. The other drug sales (ibuprofen, naproxen, ASA and phenazone-caffeine) are illustrated separately in figure 3 and 4.

Tables with specified numbers are available in Appendix 1.

## 3.2. Characteristics of the study population

Table 2 shows that age is lower in the subpopulation compared to the total population of the study. There also are more in women the subpopulation compared to the total population. There are only small differences in education, health, activity and alcohol consumption between the groups. There are more smokers and more people with chronic pain in the subpopulation than in the total population. All are users of OTC analgesic in subpopulation compared with the total population where 41.6 % had used OTC analgesics within last four weeks.

Table 2. Characteristics of the study population. The Tromsø Study: Tromsø 6.

The Tromsø Stud	ly: Tromsø	6.	
		Total	Subpopulation
		population	N=4292 (%)
		N=12981 (%)	
Age, years (means	<u>+</u> SD)	57.5 (12.7)	54.1 (12.3)
Age n	30-39	509 (3.9)	240 (5.6)
	40-49	3574 (27.4)	1569 (36.6)
	50-59	2436 (18.8)	873 (20.3)
	60-69	4102 (31.6)	1106 (25.8)
	70-79	1829 (14.1)	408 (9.5)
	80-89	531 ( 4.1)	96 (2.2)
Sex	Women	6928 (53.4)	2861 (66.7)
	Men	6053 (46.6)	1431 (33.3)
Education		(n=12798)	(n=4250)
Up to 9 years		3673 (28.7)	1078 (25.4)
10-12 years		4289 (33.5)	1494 (35.2)
More than 13 year	S	4836 (37.8)	1678 (39.5)
Self-reported heal	th	(n=12863)	(n=4262)
Bad		699 (5.4)	277 (6.5)
Neither good or ba	d	3699 (28.8)	1386 (32.5)
Good		6592 (51.2)	2109 (49.5)
Excellent		1873 (14.6)	490 (11.5)
Activity in leisure t	ime	(n=11921)	(n=4040)
Low activity		2452 (20.6)	848 (21.0)
Walking/cycling >4		7104 (59.6)	2487 (61.6)
hours/week		2173 (18.2)	657 (16.3)
Sport activity >4 ho	ours/week	192 (1.6)	48 (1.2)
Hard training x sev			
Alcohol consumpti	ion	(n=12790)	(n=4259)
Never		1449 (11.3)	404 (9.5)
<monthly _<="" td=""><td></td><td>3670 (28.7)</td><td>1208 (28.4)</td></monthly>		3670 (28.7)	1208 (28.4)
2-4 times/month		4873 (38.1)	1756 (41.2)
2-3 times/week		2160 (16.9)	710 (16.7)
>4 times/week		638 (5.0)	181 (4.2)
Smoking		(n=12784)	(n=4244)
	Yes now	2610 (20.4)	970 (22.9)
	Yes before	5407 (42.3)	1729 (40.7)
	Never	4767 (37.3)	1545 (36.4)
BMI		(n=12937)	(n=4277)
	nderweight	84 (0.6)	27 (0.6)
	ormal range	4490 (34.7)	1522 (35.6)
	verweight	5728 (44.3)	1826 (42.7)
	oese I-III	2635 (20.4)	902 (21.1)
Chronic Pain	Vos	(n=12948)	(n=4289)
	Yes	4242 (32.8)	1916 (44.7)
	No	8706 (67.2)	2373 (55.3)
Use of OTC analge		(n=12693)	(n=4292)
	Yes	5280 (41.6)	4292 (100.0)
	No	7413 (58.4)	0 (0.0)

#### 3.3. Use of OTC analgesics

**Table 3** shows use of OTC analgesics within last four weeks according to sex, age, self-reported health, level of education, physical activity, use of alcohol, smoking and BMI. The participants have answered how often they had used OTC analgesics within the last four weeks.

There was a big sex difference in the use of OTC analgesics. The proportion of users were 52.0 and 29.7 percent in women and men respectively who had used OTC analgesics within the last 4 weeks, (OR gender 2.57, (95% CI 2.39-2.77)). An age adjustment with the figures from SSB Statistics Norway, 10-year age groups of Norwegian population 1of January 2008, gives higher figures. When we adjusted for age women use was 54.9 percent, men use of OTC analgesics was 33.6 percent.

Younger people used more OTC analgesics than elderly people did. When we compared the youngest with the oldest age group, women had an OR of 2.41 (95% CI 2.09-2.78), while men had an OR of 2.84 (95% CI 2.37-3-41).

Younger people mostly used OTC analgesics less than every week.

Most of the OTC analgesics are used among those who have a bad self-reported health. When we compare those with bad health to those with excellent health, women had an OR of 2.60 (95% CI 2.04-3.30), while men had an OR of 2.96 (95% CI 2.20-3.99). It is even greater difference among the frequent users (weekly/daily use), when we compare those with bad to those with excellent health, for women OR=15.01 (95%CI 10.44-21.59) men OR=10.42 (95%CI 5.97-18-21). There were 39.9 and 19.0 percent that consider their health as bad who, where using OTC analgesic weekly or daily in women and men, respectively. Out of women, 63.6 percent and 42.0 percent men with bad health

had used OTC analgesic within last 4 weeks. However, also some with excellent health had used OTC analgesics frequently (women 4.2 percent and men 2.2 percent). Those with less education used OTC analgesic more frequently compared to those with higher education. Women OR=1.59 (95% CI 1.35-1.87), Men OR=1.79 (95% CI 1.38-2.32).

Less OTC analgesics were used among those with high physical activity compared to those with low physical activity, women OR=0.81 (CI 95% 0.68-0.96) men OR=0.79 (CI 95% 0.67-0.94), Frequent use: Women OR=0.47 (CI 95% 0.37-0.60) men OR=0.59 (CI 95% 0.43-0.80).

Those with some use of alcohol (2-4 times/month) used OTC analgesics mostly. There were more frequent use of OTC analgesics among those who did not use alcohol compared to those with high consumption, women OR=2.00 (CI 95% 1.34-2.96) men OR=2.36 (CI 95% 1.26-4.41).

Daily smokers had used OTC analgesics last four weeks more than non-smoking people, women OR=1.35 (CI 95% 1.20-1.52), men OR=1.30 (CI 95% 1.14-1.50) also among the frequent users, women OR=1.73 (CI 95% 1.50-2.00), men OR=1.54(CI 95% 1.22-1.96). There was a higher percent of OTC analgesic users, among those who had a high BMI than in the group with normal range of BMI, women OR=1.27 (CI 95% 1.11-1.44), men OR=1.20 (CI 95% 1.02-1.41). Among women there are more users with frequent use (weekly/daily use) of OTC analgesic, in the group with high BMI, OR=1.67 (CI 95% 1.41-1.97) than in the group of women with normal range of BMI.

Table 3. Use of OTC analgesics within the last 4 weeks, according to different characteristics. The Tromsø Study: Tromsø 6

	Women	Men	Women					Men				
			Use	d within last 4 weeks	Less than every week		eekly or daily use requent use)	Use	d within last 4 weeks	Less than every week		ekly or daily use equent use)
	number	number	% OR (95% CI) %	%	%	OR (95% CI)	%	OR (95% CI)	%	%	OR (95% CI)	
Sex												n=12693
Women	6743	-	52.0	2.57 (2.39-2.77)	35.4	16.6	2.84 (2.51-3.20)	-	-	-	-	-
Men	-	5950	-	-	-	-		29.7	1.0 (reference)	23.1	6,6	1.0 (reference)
Age adjusted 10 year age gro	ups 1 Jan 20	08*	54.9	-	38.2	16.8	-	33.6	-	27.3	6.3	-
Total unadjusted Men and W	omen		41.6	-	29.6	11.9	-	-	-	-	-	-
Total age adjusted Men and v	women		45.3	-	33.3	12.0	-	-	-	-	-	-
Age												n=12693
30-49	2194	1863	63.3	2.41 (2.09-2.78)	46.8	16.5	0.85 (0.71-1-02)	40.8	2.84(2.37-3.41)	33.2	7.6	1.22 (0.90-1.66)
50-59	1267	1131	55.9	1.78 (1.52-2.08)	39.1	16.8	0.87 (0.71-1.07)	30.1	1.78(1.45-2.18)	24.1	6.0	0.94 (0.66-1.34)
60-69	2054	1963	43.8	1.09 (0.95-1.26)	28.4	15.4	0.79 (0.65-0.95)	23.9	1.30(1.07-1-56)	17.9	6.0	0.94 (0.69-1.30)
70-89	1228	993	41.7	1 (reference)	22.9	18.8	1 (reference)	19.5	1.0 (reference)	13.2	6.3	1.0 (reference)
Self-reported health												n=12598
Bad	393	269	63.6	2.60 (2.04-3.30)	23.7	39.9	15.01(10.44-21.59)	42.0	2.96(2.20-3.99)	23.0	19.0	10.42(5.97-18.21)
Neither good nor bad	1923	1655	59.6	2.19 (1.88-2.59)	32.0	27.6	8.59 (6.25-11.80)	34.9	2.19(1.79-2.68)	24.5	10.3	5.13 (3.14-8.41)
Good	3329	3172	50.0	1.49 (1.29-1.71)	38.6	11.4	2.92 (2.12-4.02)	28.6	1.64(1.36-1.98)	23.9	4.7	2.18 (1.33-3.58)
Excellent	1037	820	40.2	1 (reference)	36.0	4.2	1 (reference)	19.6	1 (reference)	17.4	2.2	1 (reference)
Level of education												n=12544
Up to 9 years	2083	1453	47.4	0.81 (0.72-0.91)	28.5	18.9	1.59 (1.35-1.87)	28.4	0.94 (0.81-1.08)	19.7	8.7	1.79 (1.38-2.32)
10-12 years	2133	2089	55.6	1.12 (1.00-1.26)	37.2	18.4	1.53 (1.30-1.80)	30.9	1.06 (0.93-1.20)	24.2	6.7	1.35 (1.05-1.74)
More than 13 years	2445	2341	52.8	1( reference)	40.0	12.8	1 (reference)	29.8	1 (reference)	24.8	5.1	1(reference)

Table 3. Use of OTC analgesics within the last 4 weeks, according to different characteristics. The Tromsø Study: Tromsø 6 Continuous from last page

	Women	n Men	Women					Men				
			Used	within last 4 weeks	Less than every week		eekly or daily Use requent use)	Use	d within last 4 weeks	Less than every week		ekly or daily Use equent use)
	n	n	%	OR (95% CI)	%	%	OR (95% CI)	%	OR (95% CI)	%	%	OR (95% CI)
Activity												n=11707
Low activity	1214	1177	54.6	1 (reference)	32.5	22.2	1 (reference)	33.8	1 (reference)	25.3	8.5	1 (reference)
Walking /cycling >4 h/week	4077	2897	53.0	0.94 (0.82-1.06)	37.2	15.8	0.66 (0.56-0.77	29.2	0.81 (0.70-0.93)	22.9	6.3	0.73 (0.56-0.94)
Sport activity/Hard training	830	1512	49.3	0.81 (0.68-0.96)	37.5	11.8	0.47 (0.37-0.60)	28.8	0.79 (0.67-0.94)	23.6	5.2	0.59 (0.43-0.80)
Use of alcohol												n=12536
Never	929	444	45.1	0.62 (0.54-0.73)	24.7	20.5	2.00 (1.34-2.96)	26.8	0.79 (0.63-0.99	17.6	9.2	2.36 (1.26-4.41)
< monthly	2053	1534	51.8	0.82 (0.73-0.92)	35.0	16.6	1.57 (1.08-2.30)	28.9	0.87 (0.76-1.01)	22.2	6.8	1.69 (0.95-2.99)
2-4 times/month	2339	2468	56.8	1 (reference)	40.2	16.6	1.54 (1.05-2.25)	31.7	1 (reference)	25.6	6.1	1.49 (0.85-2.61)
2-3 times/week	1023	1118	51.6	0.81 (0.70-0.94)	37.5	14.1	1.27 (0.85-1-90)	29.0	0.88 (0.75-1.03)	22.0	7.0	1.74 (0.97-3.12)
> 4 times/week	289	339	42.2	0.56 (0.43-0.71)	30.8	11.4	1 (reference)	26.3	0.77 (0.59-0.99)	22.1	4.1	1 (reference)
Smoking												n=12531
Smoking	1437	1133	58.0	1.35 (1.20-1.52)	34.9	23.0	1.73 (1.50-2.00)	34.3	1.30 (1.14-1.50)	25.4	8.9	1.54 (1.22-1.96)
Non-smoking	5205	4756	50.5	1 (reference)	35.7	14.7	1 (reference)	28.6	1 (reference)	22.7	6.0	1 (reference)
BMI												n=12651
Underweight, < 18.5	63	18	42.9	0.74 (0.45-1.23)	27.0	15.9	1.16 (0.59-2.31)	38.9	1.67 (0.64-4.33)	22.2	16.7	3.04 (0.87-10.68)
Normal range, 18.5 - < 25	2731	1670	50.3	1 (reference)	36.4	14.0	1 (reference)	27.6	1 (reference)	21.4	6.2	1 (reference)
Overweight, 25- <30	2569	3033	52.0	1.07 (0.96-1.19)	34.9	17.1	1.28 (1.10-1.48)	30.1	1.13 (0.99-1.29)	23.9	6.1	0.99 (0.78-1.27)
Obese, 30 and above	1354	1213	56.2	1.27 (1.11-1.44)	34.9	21.3	1.67 (1.41-1.97)	31.3	1.20 (1.02-1.41)	23.2	8.0	1.38 (1.00-1.78)

<sup>\*</sup> Norwegian population, figures from SSB Statistics Norway.

### 3.4 Use of different OTC analgesics

**Table 4**. There were 4292 participants who filled in Questionnaire 2 about analysics, and they answered what type of analysics and how often they had used OTC analysics in the last four weeks. Out of this population, there was 52.2 percent who had used two or more OTC analysics and 9.0 percent that had used three or more OTC analysics.

Paracetamol was the most used OTC analgesics, 86.5 percent use for women and 85.7 percent use for men within the last four weeks. There is no statistical significant difference in use within the last four weeks between the age groups. However, women used paracetamol more frequently (weekly or daily use) than men in all age groups. Among women, 30.2 percent had used paracetamol weekly or daily, while among men it was 19.7 percent who used this drug frequently OR=1.77 (95% CI 1.52-2.06.) In the elderly age group (70-89 years) they used paracetamol more frequently (weekly/daily use) than in the younger age group (30-49 years), women OR=2.34 (95% CI 1.83-2.99), men OR=1.62 (95% CI 1.06-2.50)

Ibuprofen was used within the four weeks period by 57.2 percent women and 56.6 percent men, no statistically gender difference OR=1.03(95% CI 0.91-1.17). Ibuprofen was used more, within the last four weeks, among young people (30-49 years) than among the elderly participants (70-89 years), women OR=5.42 (95% CI 4.20-7.01), men OR=3.68 (95% CI 2.51-5.39). Women used ibuprofen more frequently (weekly or daily use) than men OR=1.54 (95% CI 1.27-1.78).

Naproxen was mostly used among the women OR=1.45 (95% CI 1.08-1-93) compared to men, and especially among the younger women (30-49 years) OR=2.19 (95% CI 1.21-3.97) compared to older women (70-89 years). The users of OTC-naproxen do not use it frequently, only 1.2 percent of the female and 0.8 of the male OTC analgesic users used naproxen weekly or daily.

Men were using OTC-Acetylsalicylic acid almost two times more than women were in most of the age groups. Total use women OR=0.50 (95% CI 0.40-0.61) compared to men. The most frequent users are men 60-79 years old OR=1.86 (95% CI 1.27-2.74) compared to 30-49 years old men.

Phenazone-caffeine was used by 3.7 percent men and 4.0 percent women within last 4 weeks. Phenazone caffeine was used less frequently (weekly/daily) among the younger men OR= 0.12 (95% CI 0.03-0.57) and women OR=0.30 (95% CI 0.13-0.66) compared to the 60-69 years old population.

Table 4. Use of different OTC analgesics within, the last 4 weeks according to type of analgesics, sex and age. The Tromsø study: Tromsø 6.

	Women	Men	Women	nes within, the la	· <u> </u>			total n=4292				
			Used	within the last 4 weeks	less than every week		Weekly or daily Use (frequent use)		within the last 4 weeks	less than every week		eekly or daily Use requent use)
Paracetamol	n	n	%	OR (95% CI)	%	%	OR (95% CI)	%	OR (95% CI)	%	%	OR (95% CI)
30-49	1156	653	87.7	1 (reference)	62.3	25.4	1 (Reference)	89.0	1 (reference)	71.5	17.5	1 (reference)
50-59	602	271	83.9	0.73(0.55-0.96)	56.3	27.6	1.12 (0.89-1.39)	84.9	0.70 (0.46-1.05)	67.2	17.7	1.02 (0.70-1.48)
60-69	740	366	86.6	0.91(0.69-1.19)	53.6	33.0	1.44 (1.18-1.77)	81.9	0.56(0.39-0.81)	59.0	22.9	1.41 (1.03-1.93)
70-89	363	141	86.8	0.92(0.65-1.30)	42.4	44.4	2.34 (1.83-2.99)	82.3	0.58 (0.35-0.96)	56.7	25.5	1.62 (1.06-2.50)
Total	2861	1431	86.5	1.07(0.89-1.28)*	56.3	30.2	1.77(1.52-2.06)**	85.7	1 (ref. sex)*	66.0	19.7	1 (ref. sex)**
Ibuprofen												
30-49	1156	653	70.8	5.42 (4.20-7.01)	51.6	19.1	1.86 (1.30-2.65)	66.9	3.68 (2.51-5.39)	54.7	12.3	1.27 (0.70-2-31)
50-59	602	271	61.7	3.60 (2.73-4.75)	44.2	17.5	1.66 (1.13-2.44)	56.8	2.40 (1.57-3.65)	46.1	10.7	1.09 (0.56-2.13)
60-69	740	366	45.5	1.87 (1.44-2.44)	32.3	13.2	1.20 (0.81-1.77)	45.9	1.54 (1.03-2.31)	35.8	10.1	1.02 (0.53-1.95)
70-89	363	141	30.9	1 (reference)	19.6	11.3	1 (reference)	35.5	1 (reference)	25.5	9.9	1 (reference)
Total	2861	1431	57,2	1.03(0.91-1.17)*	41.0	16.2	1.54(1.27-1.87)**	56.6	1 (ref. sex)*	45.4	11.2	1 (ref sex)**
Naproxen												
30-49	1156	653	7.5	2.19 (1.21-3.97)	6.5	1.0	1 (reference)	4.3	0.97 (0.39-2.40)	3.9	0.4	1 (reference)
50-59	602	271	6.3	1.81 (0.95-3.45)	5.8	0.5	0.48 (0.13-1.70)	5.9	1.41 (0.54-3.69)	4.8	1.1	1.46 (0.77-2.75)
60-69	740	366	6.6	1.91 (1.02-3.57)	5.0	1.6	1.57 (0.70-3.52)	4.7	1.10 (0.42-2.84)	3.3	1.4	1.13 (0.61-2.10)
70-89	363	141	3.6	1 (reference)	1.4	2.2	2.15 (0.87-5.30)	4.1	1 (reference)	3.5	0.7	1.03 (0.42-2-54)
Total	2861	1431	6,5	1.45(1.08-1.93)*	5.3	1.2	1.60(0.81-3.16)**	4.6	1 (ref. sex)*	3.8	0.8	1 (ref. sex)**
Acetylsalicylic	c acid											
30-49	1156	653	4.5	1 (reference)	4.3	0.2	1 (reference)	9.3	1 (reference)	8.6	0.8	1 (reference)
50-59	602	271	8.1	1.88 (1.26-2.81)	6.1	2.0	11.74(2.62-52.61)	12.2	1.35 (0.86-2.11)	11.1	1.1	1.45 (0.34-6.12)
60-69	740	366	8.0	1.84 (1.25-2.70)	6.4	1.6	9.51 (2.12-42.62)	16.2	1.86 (1.27-2.74)	13.7	2.5	3.27 (1.09-9.82)
70-89	363	141	6.1	1.37 (0.82-2.29)	4.7	1.4	8.06 (1.56-41.72)	14.9	1.70 (1.00-2.90)	11.3	3.5	4.77(1.36-16.68)
Total	2861	1431	6.4	0,50(0.40-0.61)*	5.3	1.1	0.70(0.41-1.22)**	12.1	1 (ref. sex)*	10.6	1.5	1 (ref. sex)**
Phenazone-ca	affeine											
30-49	1156	653	4.2	1 (reference)	3.4	0.8	0.30 (0.13-0.66)	3.4	1 (reference)	3.1	0.3	0.12(0.03-0.57)
50-59	602	271	4.0	0.96 (0.58-1.58)	3.2	0.8	0.32 (0.12-0.86)	3.3	0.98 (0.45-2.17)	2.2	1.1	0.44 (0.12-1.66)
60-69	740	366	4.4	1.08 (0.68-1.70)	1.9	2.5	1 (reference)	5.5	1.66 (0.89-3.08)	3.0	2.5	1 (reference)
70-89	363	141	3.3	0.79 (0.42-1.50)	1.7	1.7	0.64 (0.25-1.61)	1.4	0.41 (0.10-1.78)	0.0	1.4	0.57 (0.12-2.68)
Total	2861	1431	4.0	1.11(0.80-1.54)*	2.7	1.3	1.22(0.68-2.20)**	3.7	1 (ref. sex)*	2.6	1.1	1 (ref. sex)**

# 3.5 Reasons for using different OTC analgesics

Table 5. Reasons for use of different OTC analgesics, with numbers in each group. The Tromsø study: Tromsø 6

	All OT	C anal	gesic		Parac	Paracetamol			Ibupr	Ibuprofen			Naproxen			ASA			Phenazone					
	Women Men n=2861 n=1431		Women		Men		Women		N	1en	Women		Men		Wo	men	M	len	Wo	men	N	1en		
			431	n=2	475	n=1227		n=1638		n=809		n=187		n=66		n=182		n=174		n=117		n=53		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Headache	1967	68.8	982	68.6	1718	69.4	859	70.0	1176	71.8	572	70.7	124	66.3	40	60.6	126	69.1	128	736	98	83.8	42	79.2
Muscle/joint pain	1544	54.0	560	39.1	1355	54.7	482	39.3	941	57.4	358	44.3	131	70.1	43	65.2	104	57.1	71	408	63	53.8	20	37.7
Bach ache	626	21.9	279	19.5	553	22.3	247	20.1	361	22.0	181	22.4	69	36.9	24	36.4	49	26.9	25	14.4	25	21.4	7	13.2
Migraine	274	9.6	75	5.2	238	9.6	64	5.2	179	10.9	46	5.7	23	12.3	7	10.6	17	9.3	16	9.2	24	20.5	7	13.2
Menstrual pain	344	12.0	-	-	297	12.0	-	-	260	15.9	-	-	41	21.9	-	-	18	9.9	-	-	16	13.7	-	-
Tooth pain	159	5.6	96	6.7	141	5.2	82	6.7	114	7.0	64	7.9	12	6.4	3	4.5	11	6.0	9	5.2	9	7.7	4	7.5
Other	239	8.4	135	9.4	213	8.6	116	9.5	116	7.1	61	7.5	11	5.9	6	9.1	32	17.6	13	7.5	10	8.5	3	5.7

**Table 5** shows the reasons for using different OTC analgesics. A person may have given several reasons for using of OTC analgesics. For all OTC analgesics, headache is the main reason for use, and muscle and joint pain was the second reason, and backache was reason number three. The table shows that OTC analgesics were used more due to muscle or joint pain among women (54.0%) than among men (39.1%), OR=1.83(CI 95% 1.60-2.08). It shows also that OTC analgesics were used more due to migraine among women (9.6%) than among men (5.2%), OR=1.92(CI 95% 1.47-2.50). Twelve percent of women used OTC analgesics related to menstrual pain. When studying the female naproxen users, 21.9 % of the users reported menstrual pain as reason for use.

### 3.6 Amount of tablets used daily of different OTC analgesics

Table 6. Amount of tablets used daily of different OTC analgesics, mean, median, minimum and maximum compared with Defined Daily dose and use above DDD. The Tromsø Study: Tromsø 6

Amount of tablets used daily of different OTC analgesics	Valid number	mean	median	mini- mum	maxi- mum	DDD tabs (gram)	total above DDD n	total above DDD %
Paracetamol 500 mg/tab	2865	2.23	2	1	12	6 (3.0)	15	0.5
ASA 500 mg/tab	266	1.98	2	1	12	6 (3.0)	4	1.5
Ibuprofen 200 mg/tab	1815	2.09	2	1	10	6 (1.2)	9	0.6
Naproxen 250 mg/tab	222	2.20	2	1	6	2 (0.5)	65	29.7
Phenazone-caffeine 500 mg/tab	130	1.95	2	1	6	6 (3.0)	0	0.0

**Table 6** shows the amount of tablets used daily of different OTC analgesics and compare this with DDD. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults [25].

Fifteen persons (0.5%) used paracetamol above DDD and three of them used 12 tabs per day, which corresponds to the double of the defined daily dose. One of the twelve used paracetamol daily. It was 77.6 percent of the OTC paracetamol users who reported taking 1-2 tabs per day.

For ibuprofen, the maximum amount was 10 tablets daily. In addition, nine persons used OTC ibuprofen above one DDD per day. It was 86.6 percent who reported use of ordinarily 1-2 tablets daily of ibuprofen.

The DDD for OTC naproxen is two tabs (= 500 mg) and naproxen is used by more persons above DDD compared to the other OTC analgesics, where 29.7 % used OTC naproxen above one DDD per day. However, recommendations on the OTC package are up to three tabs per day. Thirty-one participants took three tablets, 27 took four tablets and seven persons took six tablets of OTC naproxen per day.

Acetylsalicylic acid was used by four persons (1.5%) above DDD. The maximum amount of ASA tablets that anyone used daily was 12 tablets. Two subjects reported a dosage of 12 tablets a day, i.e. the double amount of the defined daily dose.

It is not for sure that 500 mg tablets have been taken, 300 mg tablets was also available at the time. ASA 500 mg is the most common strength of ASA analgesic tablets in Norway at the time for the survey. In addition, one of them who reported 12 tablets/day has noted in the form that it is according to recommended dose from the physician.

Those four persons who used ASA above DDD did not use ASA daily.

Phenazone-caffeine was not used above the defined daily dose and 79.2 percent of the users reported use of 1-2 tabs per day.

#### 3.7 Side effect of OTC analgesics

Table 7. Side effect of OTC analgesics The Tromsø Study: Tromsø 6

n=4292	n	%
Paracetamol	102	2.4
Ibuprofen	147	3.4
Naproxen	118	2.7
Acetyl salicylic acid	147	3.4
Phenazone-caffeine	62	1.4

Users of OTC analgesic report that they have experienced side effects.

More people complain about side effects from ibuprofen and ASA than from other drugs.

### 3.8 Use of OTC analgesics above Defined Daily Dose

**Table 8** shows the characteristics of the subjects that use OTC analgesic above the defined daily dose compared to those who reported use of one defined daily dose per day or less. This table is not analysed gender specific because the number of participants in each group is too low to get statistical significance. The percentage of users above one DDD per day is the same in the group of men and women. There is differences within age groups. Within the younger age group there are more who use OTC analgesics above DDD than in the older age group, OR=2.06 (CI 95% 1.04-4.10). Those with bad health report more doses above DDD, than those with good health, OR 2.42 (CI 95% 1.19-4.91).

There are more persons in the group of low physical activity that use more OTC analgesics than those who are more active. Anyhow, there is no statistical evidence on that (CI 95%), probably because the material we analyse is too small.

It seems like the people that drink little or no alcohol and those with high consumption of alcohol use less OTC above DDD than those who drink alcohol 2-4 times/month.

Those who smoked daily reported dosage of OTC analgesic above the DDD more often than the non-smokers did, OR=1.77 (CI 95% 1.12-2-79). Within the group of people with a higher BMI than 30(obese) there is also reported dosage of OTC analgesic above the DDD more often than among those with BMI between 25-30(over-weighted), OR=2.04 (CI 95% 1.19-3.50).

The participants that had bought OTC analgesic both in the pharmacies and in the non-pharmacy outlets reported more often use of OTC analgesic above the DDD than those who only bought in pharmacy, OR=1.98 (CI 95% 1.25-3.13).

There is a bigger share of participants in the group of frequent users (weekly/daily use), who use more OTC above one DDD per day. Even if it has not 95% CI, it give us an indication that it might be more common with more use above DDD among the frequent users. In addition, it is small groups of users that we compare, too small to get statistical significance.

Table 8. Use of OTC analgesics above one DDD according to different characteristics. The Tromsø study: Tromsø 6

		OTC analgesic	Use ab	ove 1 DDD
		use number	%	OR (CI 95%)
Sex	n=3322			
Women		2249	2.6	1 (reference)
Men		1073	2.6	(0.96 (0.64-1.60))
Age	n=3322			
30-44		1035	3.3	2.06 (1.04-4.10)
45-64		1608	2.5	1.59 (0.81-3.11)
65-89		679	1.6	1 (reference)
Self-reported health	n=3301			
Bad		220	4.5	2.42 (1.19-4.91)
Neither bad or good		1083	3.4	1.80 (1.14-2.83)
Good		1998	2.0	1 (reference)
Level of education	n=3294			
Up to 9 years		827	2.1	0.60 (0.34-1.06)
10-12 years		1177	3.4	1 (reference)
More than 13 years		1290	2.2	0.63 (0.39-1.02)
Activity in leisure time	n=3140			
Low activity		655	3.1	1.25 (0.74-2.12)
Walking /cycling >4 hours/w		1941	2.4	1 (reference)
Sport activity / Hard training		544	2.6	1.05 (0.58-1.91)
Use of alcohol	n=3291			
Never or seldom		1229	2.2	0.66 (0.41-1.07)
2-4 times/month		1364	3.2	1 (reference)
several times/week		698	1.9	0.56 (0.30-1.04)
Smoking	n=3289			
Non-smoking		2534	2.2	1 (reference)
smoking		755	3.8	1.77 (1.12-2.79)
Body Mass Index	n=3313			
BMI <25		1207	2.7	1.40 (0.83-2.34)
BMI 25-30		1401	1.9	1 (reference)
BM I >30		705	3.8	2.04 (1.19-3.50)
Place of Purchase	n=3278			
The pharmacies		2173	2.0	1 (reference)
Non-pharmacy outlets		292	3.1	1.54 (0.74-3.17)
Both the pharmacies and non-pharmacy	outlets	813	3.9	1.98 (1.25-3.13)
Frequency of OTC analgesic use	n=3322			
OTC analgesic use <every td="" week<=""><td></td><td>2318</td><td>2.2</td><td>1 (reference)</td></every>		2318	2.2	1 (reference)
OTC analgesic use weekly/daily		1004	3.4	1.53 (0.98-2.37)

## 3.9 Where do people buy OTC analgesics

**Table 9** describes the purchase habits of the OTC analgesic users according to sex, age, health, level of education, physical activity, alcohol consumption, smoking and BMI. There was totally 6.3 percent women and 15.8 percent men who bought OTC analgesics from non-pharmacy outlets only, while 70.0 percent women and 60.5 percent men bought OTC analgesics from the pharmacies only. We found that 23.7 percent women and 23.8 percent men purchased OTC analgesics both places.

Men purchased more OTC analgesics outside pharmacy compared to women OR=2.81 (CI 95% 2.28-3.46), and younger people (30-44 years), buy more OTC analgesic from the non-pharmacy outlets compared to elderly (65-89 years), women OR=3.59 (CI 95% 2.07-6.22), men OR=3.99(CI 95% 2.36-6.73). Older people (65-89 years), men and women, buy more OTC analgesics compared to younger people (30-44 years) from the pharmacies only, OR=5.32 (CI 95% 4.28-6.60).

Persons with bad self-reported health, report buying in pharmacy only, more than persons with good health, women OR=1.48(CI 95% 1.05-2.10), men OR=1.86(CI 95% 1.13-3.06). Women with low education (up to 9 years), purchase more OTC analgesics from the pharmacies only compared to women with high education (more than 13 year), OR=1.73 (CI 95% 1.40-2.13). totally men and women OR=1.45 (CI 95% 1.23-1.72). We can see this trend among women but not among men. Higher educated women buy more OTC analgesics from non-pharmacy outlets compared to women with low education, OR=1.67(CI 95% 1.12-2.50).

Women who smokes reported to purchase OTC analgesics from non-pharmacy outlets more often than the non-smokers OR=1.58 (CI 95% 1.31-1.90), also men seems to do that but it is not significant in this survey.

There are no statistically significant (95%) differences in purchase habits when we compared the different levels of physical activity. Use of alcohol does not either give any significant differences compared to those who do not use alcohol except that, those who use alcohol 2-4 times/months bought less OTC analgesic in pharmacy only than those who drinks alcohol several times a week among women OR= 0.76 (CI 95% 0.61-0.95). There are neither any significant differences when we see those with higher BMI compared to those with BMI in the normal range.

There were 3826 out of 4224 persons (89.1 %) that reported to purchase OTC analysis from the pharmacies, either from the pharmacies only, or in combination with purchases in the non-pharmacy outlet (23.7%).

There were 398 persons, (9.4%) who reported to buy OTC analgesics from non-pharmacy outlets. Out of these persons 389 (97.7%) reported grocery stores as place of purchase, three persons at petrol station and seven persons abroad. None purchased via the internet.

Out of all OTC analgesic users, there was 1360 persons (31.7 %) that reported that they usually bought there analgesics in grocery shops. Most of the people (71.4 %) in this group have also usually bought OTC analgesics in other places.

There were only 53 persons that report that they usually had bought OTC analgesics at petrol station only 1.2 % and only 55 persons 1.3 % reported that they usually bought OTC analgesic abroad. To purchase at internet seemed to be almost unknown in 2007-2008, only two persons (0.05 %) has reported this, as the place where they usually bought OTC analgesics.

One usual purchase place were reported by 75% of all OTC analgesic users, while 25 % of participants answered with two or more alternatives.

Table 9. Characteristics of users according to place of purchase for OTC analgesics. The Tromsø Study: Tromsø 6

	Women	Men	Women					Men					
			outside pharmacy only		both in & outsi de	in p	oharmacy only	outsid	e pharmacy only	both in & outsi de			
	n	n	%	OR (CI 95%)	%	%	OR (CI 95%)	%	OR (CI 95%)	%	%	OR (CI 95%)	
Age												n=4224	
30-44	833	481	9.0	3.59 (2.07-6.22)	36.9	54.1	1 (reference)	22.9	3.99 (2.36-6.73)	30.4	46.8	1 (reference)	
45-64	1386	668	6.1	2.37 (1.38-4.08)	21.6	72.3	2.21(1.85-2.65)	14.1	2.20 (1.30-3.73)	23.4	62.6	1.90 (1.50-2.41)	
65-89	596	260	2.7	1 (reference)	10.4	86.9	5.62 (4.28-7.40)	6.9	1 (reference)	12.7	80.4	4.66 (3.27-6.65)	
Total	2815	1409	6.3	1 (reference)*	23.7	70.0	1.53 (1.34-1.75)**	15.8	2.81 (2.28-3.46)*	23.8	60.5	1 (reference)**	
Self-reported health												n=4196	
Bad	187	84	3.7	1 (reference)	20.9	75.4	1.48 (1.05-2.10)	9.5	1 (reference)	17.9	72.6	1.86 (1.13-3.06)	
Neither bad or good	895	461	4.1	1.09 (0.50-2.39)	21.9	74.0	1.37 (1.15-1.64)	12.1	1.21 (0,58-2.55)	26.5	61.4	1.14 (0.88-1.40)	
Good	1709	860	7.7	2.11 (1.02-4.37)	25.2	67.2	1 (reference)	18.3	1.96 (0.96-3.99)	22.9	58.8	1 (reference)	
Level of education												n=4185	
Up to 9 years	737	301	4.9	1 (reference)	17.9	77.2	1.73 (1.40-2.13)	14.3	1 (reference)	25.6	60.1	1.00 (0.75-1.32)	
10-12 years	958	517	5.9	1.28 (0.84-1.97)	25.2	68.9	1.13 (0.94-1.36)	14.7	1.05 (0.70-1.56)	24.4	60.9	1.03 (0.81-1.31)	
More than 13 years	1091	581	7.6	1.67 (1.12-2.50)	26.5	65.9	1 (reference)	17.6	1.29 (0.88-1.90)	22.5	59.9	1 (reference)	
Activity in leisure time												n=3983	
Low activity	514	318	6.6	1.22 (0.73-2.04)	24.9	68.5	0.88 (0.67-1.15)	14.5	0.86 (0.58-1.29)	28.3	57.2	0.88 (0.65-1.18)	
Walking /cycling >4 hours/w	1791	664	6.4	1.17 (0.76-1.79)	23.5	70.1	0.65 (0.76-1.18)	16.0	0.97 (0.70-1.35)	22.0	62.0	1.07 (0.84-1.37)	
Sport activity / Hard training	332	364	5.7	1 (reference)	29.2	65.1	1 (reference)	16.5	1 (reference)	23.4	60.1	1 (reference)	

<sup>\*</sup>this reference compares total men to women purchase outside pharmacy only \*\*this reference compares total men to women purchase in pharmacy only

Table 9. Characteristics of users according to place of purchase for OTC analgesics. The Tromsø Study: Tromsø 6 Continuous from last page

W	/omen	Men	Women					Men				
			outside pharmacy only		both in & outsi de	in p	harmacy only	outside	e pharmacy only	both in & outsi de	in pl	harmacy only
Use of alcohol n=4193	n	n	%	OR (CI 95%)	%	%	OR (CI 95%)	%	OR (CI 95%)	%	%	OR (CI 95%)
Never or seldom	1158	423	5.1	0.87 (0.56-1.34)	23.1	71.8	0.96 (0.77-1.20)	12.3	0.68 (0.45-1.01)	24.1	63.6	1.20 (0-90-1.60)
2-4 times/month	1091	637	7.7	1.35 (0.89-2.04)	25.5	66.8	0.76 (0.61-0.95)	17.3	1.01 (0.71-1.42)	23.7	59.0	0.99(0.76-1.29)
several times/week	539	345	6.1	1 (reference)	21.9	72.0	1 (reference)	17.4	1 (reference)	23.5	59.1	1 (reference)
Smoking												n4179
Non-smoking	2124	1101	5.8	1 (reference)	21.7	72.5	1.40 (1.00-1.96)	15.0	1 (reference)	23.6	61.4	1.34 (0.96-1.86)
smoking	655	299	7.9	1.58 (1.31-1.90)	29.5	62.6	1 (reference)	19.1	1.22 (0.94-1.58)	24.4	56.5	1 (reference)
ВМІ												n=4210
(normal range) BMI<25	1145	379	7.0	1 (reference)	24.0	69.0	1 (reference)	15.3	1 (reference)	23.7	60.9	1 (reference)
over weight BMI 25-30	1079	722	5.8	0.82 (0.58-1.15)	24.3	69.9	1.04 (0.87-1.25)	16.1	1.08 (0.77-1.52)	22.9	61.1	1.00 (0.78-1.29)
Obese BMI > 30	583	302	5.5	0.77 (0.50-1.17)	22.3	72.2	1.17 (0.94-1.45)	15.9	1.06 (0.70-1.62)	25.8	58.3	0.89 (0.66-1.21)

# 4. Discussion

- 4.1 Main findings from Tromsø 6 concerning use of OTC analgesics.
- 1. There was a 45.3 % use of OTC analgesics among the population within last 4 weeks (54.9 % women and 33.6 % men). Most of the OTC analgesics were used seldom (less than every week) by 73.5 % of users, and was mostly used in a small daily dose, 1-2 tabs by 78.4 %.
- **2.** Paracetamol was the most used OTC analgesic, 86.3 %, and it was used more frequently among the elderly OR=1.60 (95% CI 1.40-1.84). Ibuprofen was used by 57 %, used more frequently by women OR= 1.54 (95% CI 1.27-1.87) and mostly used among young people.
- **3.** The main reasons for use of OTC analgesics was headache/migraine, 76.8 %, followed by muscle and joint pain 54 % and for backache by 21.9 % of the OTC users.
- **4.** Side effects from OTC analgesics were reported by users of paracetamol 2.4 %, ibuprofen 3.4 %, naproxen 2.7 %, ASA 3.4 % and phenazone-caffeine 1.4 %.
- **5.** There was 2.6 percent that used OTC analgesics above defined daily dose. The people that bought OTC analgesic both in the pharmacies and in non-pharmacy outlet reported dosage above the DDD more often than those who only bought OTC analgesic in pharmacy OR=1.98 (CI 95% 1.25-3.13). Forty percent of OTC users, who used more than a Defined Daily Dose, used also OTC analgesic more frequently (daily/weekly use) than those who used a DDD or less per day.
- **6.** There was 70.0 percent women and 60.5 percent men who bought OTC analgesics from the pharmacies only, while 6.3 percent women and 15.8 percent men bought OTC analgesics from non-pharmacy outlets only. Younger people (30-44 years), buy more OTC analgesic from the non-pharmacy outlets compared to elderly (65-89 years), women OR=3.59 (CI 95% 2.07-6.22), men OR=3.99(CI 95% 2.36-6.73).

## 4.2 Main findings from wholesaler-based drug statistics NIPH: (Table 1).

The total sales (OTC+Rx) of paracetamol, ibuprofen, naproxen, diclofenac, ASA and phenazone-caffeine increased by 40 %, from the year 2003 to 2016. The OTC sales of analgesics decreased by 4.5 % in the same period. The sales of OTC analgesics outside pharmacy increased 2003 to 2009. Since then the sales of OTC analgesics outside pharmacy has been reduced by 6 %. The sales of Rx analgesics has doubled from 2003 to 2016. It is Paracetamol and Ibuprofen that are dominating the sale of OTC analgesic drugs and has increased mostly during the period. Phenazone-caffeine and ASA has decreased its share of the sale.

## 4.3 Comparison with other population studies

1. From the study in Nord-Trønderlag (HUNT3, 2006-08) they got many results similar to the present study [10]. In their study use of OTC analgesics are 47% within last month compared with this study of 45%, and among women 53%, in this study 54.9% use, men 40%, in this study 33.6%. It is a bigger difference between sexes in the present study than what they have in The HUNT3 study. In the HUNT3 study as well as in present study the use of OTC paracetamol where not influenced by age. NSAIDs decreased while ASA increased in relation to age in HUNT3 as well as in Tromsø 6. In both studies, there are higher risk for using OTC analgesics if you have low or little physical activity especially among those with frequent use of OTC analgesic. Smoking increased the risk of using OTC analgesic in both studies. Use of alcohol, several times a week, reduce also the risk of using OTC analgesics frequently, in both studies. It might be that alcohol is a substitute for OTC analgesic or a self-medication related to pain as they also speculate in their report. Similar results, about alcohol used as self-medication related to pain, has been found and are discussed in other studies, [46,47,48].

- **2.** In a German study in 2008-2011 [5] OTC analgesic use was significant higher among women OR 1.71 and smokers OR 1,55, but lower among those aged 45 years and older, similar to present study. Those with more physical activity used significant less Rx analgesics OR 0.71. Ibuprofen was the most commonly used analgesic, followed by ASA, paracetamol, diclofenac and naproxen.
- 3. In a Swedish study (1988-1989) the authors concluded that analgesics was used 50% higher among women than men [2]. This confirms the result of the present study that women use analgesics considerably more than men do. Overweight women used more analgesic then other women in Antonov's study. In present study, both women and men with overweight use more OTC analgesic. Self-reported poor health explain also much the use of analgesic in the Swedish study. In that study from 1988-89 there are also a higher consumption of analgesic among smokers.
- 4. In the Tromsø study 1986-87, (Tromsø 3), there was also twice as many users of analgesic among women compared to men [3]. People with low physical activity and daily smokers had also a high analgesic use. There was no age difference in analgesic use among people above 20 years. One fifth of the population used analgesics, women 28 % and men 13 %. It was headache, infection, backache, neck/shoulder ache that had the strongest association with analgesic use. Depression, sleeplessness and menstrual pain are also associated with higher use of analgesic.
- **5.** We compared this with the analgesic use in the same population study [9] 15 years later 2001-2002, (Women 53.7 % and men 29.1%). In 2007-2008, (Tromsø 6) the total analgesic drug use for women 59.6 % and men 36,7 %, all figures are age adjusted [9]. Also here more use among women then among men. (*In this report the percentage of only*

- OTC users are presented, excluding those who also use Rx, this makes the figures different from ours even though we have the same material to study.)
- 6. In Finland, the bestselling substance for pain management in 2002 was ibuprofen and paracetamol [49]. Fifty-four percent of ibuprofen was sold over the counter and that correspond very well to the present Norwegian figures. There was no significant difference in use of OTC analgesics in this study compared to sexes or age. Frequent analgesic use was more common in older age groups as well as in present study. OTC analgesic use were used mostly a few times a week rather than daily.
- 7. A study from Scotland who was published 2005 showed a prevalence of 37 % of OTC analgesics use [4] within the last two weeks. This correspond with some of our findings. Being young, female and drinking alcohol where associated with OTC analgesics users in both studies. Headache, back pain and joint pain are the most common reasons for use of OTC analgesics in Scotland as well as in Norway. No significant association between smoking and OTC analgesic use in Scotland as it was in Norway. The most frequent used OTC analgesic in the Scottish survey is Paracetamol that is used almost twice as much as ibuprofen, which relates well to findings in Norway.
- **8.** In an Australian survey [11] conducted 2001 and 2009, 85 % in both surveys reported use of OTC analgesics at least once a year. Regular use (at least once a month) declined from 67.5 % in 2001 to 55 % in 2009. There was more female regular users 57 % in both surveys. OTC NSAIDS increased from 11-26 % from 2001-2009. In 2001, NSAIDs were not available outside the pharmacy setting but in 2009, 42.0 % of regular OTC NSAID users purchased this product in a general sales environment. More use of OTC analgesic among participants under 54 years and more use of NSAIDs than paracetamol among younger participants than those aged 55 years or more.

#### 4.4 Characteristics of the users

The characteristics associated with an OTC analgesics user were being young, female, bad health, drink alcohol moderately, daily smoker and have a high BMI.

One reason that elderly people do not use as much OTC analgesics as younger does, are probably because they have those medicines on receipt from their physician [12]. We found that OTC ibuprofen was used almost twice as much in the youngest age group (30-49 years) compared to those above 70 years old. The reasons is probably that ibuprofen is not recommended for the elderly without close follow up by a physician [23], [35,p1071], [33,p253], because of serious adverse effects (gastric ulcer, kidney damage, heart failure etc.).

OTC naproxen is mostly used by young women. The only OTC indication is for menstrual pain, but we found that OTC naproxen were also used due to other reasons, i.e. middle aged men also reported use of naproxen. The reason why naproxen was reported used for other reasons than menstrual pain is probably that people know that naproxen can be used for other diagnoses. They may have got naproxen from their physician earlier for other reasons like muscle and joint pain.

### 4.5 Purchase of OTC analgesic in pharmacies or in non-pharmacy outlets

The important factors were sex, age, self-reported health, lifestyle and level of education. It seems that it is younger men, those with good health, high education and those who are smoking that buy more OTC analgesics at non-pharmacy outlets. Older people, women with low education and people who report bad health, inform that they use pharmacy more. It is fine, if our conclusions are correct, that those who are young have better health and have a higher education buy OTC analgesics outside pharmacy, and that those who are older and sick and need to ask somebody can do that in a pharmacy.

In a study from Sweden (2016) there was 76 % who had been to a pharmacy and 24 % that had bought drugs at non-pharmacy outlets last time they bought a drug [12]. In our study the question is formulated different, anyhow their result are comparable and confirm our results because the proportions are similar. The Swedish study showed that women, older people and those with lower education saw the availability of trained staff in the pharmacy as important. "Geographic proximity was reported as the overarching factor in the choice of retailer for any OTC drug." Opening hours and available products were also seen as important.

In a study from Australia they report from 2009 that 42 % of regular OTC NSAID users purchased this product in a general sales environment [11]. This is considerably higher than our figures for purchase at non-pharmacy outlets.

## 4.6 Reasons for use of OTC analgesics

The reasons for using OTC analgesics seemed to follow the OTC indications for use of the different drugs. The only exception is OTC naproxen, which was used for other reasons than menstrual pain, who is the only OTC indication. One may think people know other indications for naproxen and how to use it. Maybe because they have got it prescribed from their GP earlier for minor health problems. It has gone a long time since the decision to have menstrual pain as the only indication for OTC naproxen. May be one should discuss whether OTC naproxen could be recommended for more indications.

#### 4.7 Use above DDD and over use.

Those who reported to use more than one defined daily dose OTC analgesic daily were associated with being young, consider own health as bad, has a medium long education, are not physical active, drink alcohol moderately, daily smoker and are obese. They were also associated with buying OTC analgesics at non-pharmacy outlets and taking OTC analgesics regularly.

There were 2.6 % of the OTC users, who had taken more than one defined daily dose of OTC analgesics daily. Among OTC paracetamol users there is 14 persons (0.5%) who takes above one DDD daily. We have nine persons (0.5%) in this material who takes more than one DDD daily of ibuprofen. For ASA there is four persons (1.5%), who report use above one DDD daily. Phenazone-caffeine has no one reporting above one DDD daily. We found most users of more than one defined daily dose, daily among the OTC naproxen users. The defined daily dose for OTC naproxen is not based on the indication acute dysmenorrhea, but is based on the maintenance dose for the diagnosis rheumatoid arthritis. This may explain why so many users of OTC naproxen had used more than one DDD daily (65/222 OTC naproxen users, 29.3%). The recommended dosage found on the OTC naproxen package was up to three tablets (750 mg) daily (DDD=two tablets= 500 mg). The Norwegian Pharmaceutical Product Compendium (Felleskatalogen) based on the approved SPC of the drugs, says that acute dysmenorrhea may be treated with as much as five tablets (1250 mg) daily.

However, someone may have misunderstood the question and written a much higher number of tabs than what they actually did take. There might also be persons that use too much OTC analgesics that is not included because they did not show up in the survey. A survey of this kind is voluntary and those who are not so interested in health issues may

not show up. Other literature argue that "the vast majority do not take analgesic in overdose and that small minority who do suffer little or no sequel" [33,p255].

The Swedish medical products agency drew a conclusion from a comprehensive study in 2015, that the majority of the public has a balanced view of OTC analgesic use and security, and that the OTC analgesics are mostly used as intended [50].

#### 4.8 Adverse effects

Side effects from OTC analgesics were reported by users of paracetamol 2.4 %, ibuprofen 3.4 %, naproxen 2.7 %, ASA 3.4 % and phenazone-caffeine 1.4 %. Users that experienced adverse effects may not necessarily have taken high doses of analgesics. Jones stated that "Some analgesics have adverse effects in therapeutic doses and all analgesics are toxic in overdose" [33,p 245]. Paracetamol gives adverse effects in overdose while most of adverse effects occur in therapeutic NSAID doses. NSAIDs have lower incidence of severe features or death in overdose [33,p245]. Those who reported experience of adverse effect from different OTC analgesics in this report may have used those medicines earlier. It might not been used on the time for the survey. Approximately 0.02-0.04% of each countries population take paracetamol in overdose each year. A total of 0,02% of the Australian population and 0.08% of the UK population require admission or assessment at a health care facility each year because of paracetamol poisoning [33,p247].

## 4.9 Overdose and intended poisoning with paracetamol

The availability of paracetamol increases the risk of self-poisoning." *National policy* decisions regarding restrictions on its availability need to weigh the inconvenience caused to the many who use the drug safely against those of the few in whom overdose may be fatal" [28,p313].

The problem with paracetamol is self-poisoning. If it is too easy to get the drug, it might be a choice for someone in a desperate situation. Many knows that it is dangerous with a lot of paracetamol and that it can be fatal, but not all knows the consequences [43]. Many resources are used to rescue mostly young people that have tried to take their lives with a very bad poison for suicide. Most of patients are saved, but some gets liver damage and a few is in need of liver-transplantation after being treated for overdose [51]. It is common to use as self-poisoning among young girls and we know that availability, quantity and increase in sale increase the cases of self-poisoning [28,29,41]. One way to reduce the possibilities of these desperate actions is to make the availability to get a big amount of this medicine more difficult. One way is to reduce the package size, sell it only in pharmacies where there is trained staff and limited opening hours. Prescription of large boxes with medicine that is common to use for self-poisoning should be reduced and instead be sold in smaller package with blisters [33,p 253-254]. To sell OTC paracetamol tabs only in pharmacies was introduced in Sweden in November 2015 after an extensive investigation from the Medical product agency, Sweden [50]. The background is an increase in the number of poisoning cases in recent years where one can see a connection with the increased availability[52].

### 4.10 Increased use of paracetamol and ibuprofen over time

The total paracetamol sale increased by 63.9 percent between 2003 and 2016. It is due to increased prescription of these drugs and specially Rx paracetamol that increased 2.7 times. Prescription of big packages caused the increase of total sale of paracetamol [30], The sales of OTC analgesics decreased with 4.5 percent in the period 2003-2016. One may speculate that this is caused by the huge difference in price between OTC and Rx paracetamol. It is a big difference in price, 5.5 times' higher price for OTC paracetamol

compared to prescribed medicine in large package sizes. The increase of paracetamol has also to do with the recommendations from authorities to use paracetamol rather than NSAID because of side effects like bleeding/ stomach ulcers [53]. It is common to prescribe a unit of 1g x100tabs, which makes many people to have a unit with several paracetamol tablets at home. This may be a potential danger related to poisoning [41,43]. The total sales of analgesics increased considerably in Norway over the last decades [9]. Since 1990 the sales, of ibuprofen has increased more than 6,5 times, and paracetamol 3 times in DDD/inhabitants/day [26,p73, table]. There is concern that people are using OTC analgesics incorrectly or improperly and cause danger to their health [7,33,40,54]. We can see that we use more paracetamol and ibuprofen totally but the sale of OTC analgesics are almost the same over time. However, the fact that many people/families have many medicines at home may worry more. Even if it is not correct to share prescribed medicine some will do it instead of buying other medicine to family members, you share it especially if the price difference between Rx and OTC analgesics is large [55,56,57].

### 4.11 Strengths and weaknesses of the study

The study has a big population with a relatively good participation. There might be a problem of selection bias even though there is an open invitation and a big population. It may be that those with more concern about their health and those who are more informed about health issues are more represented in the study. Those who are not so concerned or informed about the risks of overuse are probably less likely to participate in a voluntary population study. There may be an underrepresentation of people who use more OTC analgesics than they should do, because of a lack of interest to participate. It is also possible that people with more pain have been more willing to participate because of their concern in improvement of their health. That might be another confounder of the

result in the other direction. More women were participating in the study and women are using more OTC analgesics than men are, but most of the analysis was done with men and women separately. There may be an underestimation of the use of OTC analgesics within this study because of recall bias, but this is probably minimal, because we are asking about the last four weeks, which is a relatively short recall period. Anyhow, this is probably the best way to get accurate figures because it is impossible to get direct registration from OTC analgesics. The statistics from NIPH and wholesalers data shows that use of OTC analgesics is almost the same today as it was in 2008. It is the Rx share that has increased of these analgesic drugs. This shows that the statistics can be representative for today even though the data from Tromsø 6 are 10 years old. The Tromsø population may be regarded as representative of a Northern European, urban population and it could be generalized to such a population [44]. Comparison with other studies in the Northern Europe shows similarities in the use of OTC analgesics. That shows that findings from this study can be applicable to similar populations in Northern Europe.

### 4.12 Proposals on further studies

The questions about adverse reactions in the specific Questionnaire about OTC analgesics (Q2:16) were not detailed enough to provide information about what kind of adverse reactions that might have occurred because of the use of a specific OTC analgesics. It would have been interesting to analyze what kind of ADR that might have occurred, not only that something occurred from a specific analgesic. There was a question, if people use to mix Rx and OTC drugs, but details are missing about what kind of analgesics they are mixing.

Studies should be done in the future on whether the use of OTC analgesics is increasing or not within the population. It would also be interesting to study if availability of paracetamol and ibuprofen in large Rx packages results in intentional poisoning among young adults. Material that has been gathered for more than 20 years, by social workers, at the University Hospital of Northern Norway, UNN about those who use drugs for self-poisoning, could be used to investigate from where young adults get there paracetamol for self-poisoning, and suggest how interventions against this problem should be tackled.

## 4.13 Suggestions and recommendations

From this study, we can see that there are very little overuse and abuse of OTC analgesics among the general adult population. These analgesics should continue to be available Over-The-Counter and as far as possible in non-pharmacy outlets for the adult population. It is important for adults in need of analgesics, to be able to purchase them nearby. Geographic proximity, generous opening hours and a wide product range are important for ordinary consumers [12]. It is also recommended to discuss if e.g. naproxen, which is a very well known analgesic to treat muscle and joint pain, headache, backache and migraine, should be available OTC in pharmacies also for these indications. As it is today, it is only allowed to be sold Over-The-Counter to treat menstrual pain in Norway, but this is not followed according to results of present study.

There is a problem with too easy access of paracetamol related to self-poisoning, specially within the younger population[29,58]. Therefore, it might also be advisable to sell paracetamol tablets only in pharmacies where staff is available to give advices. As it is in Norway today, it is easy to go into a shop at night and buy paracetamol and the limitation of 10 gram can easily be circumvented by going to several shops. It is an ethical dilemma if we allow this medicine to be available for the adult population even while at the same

time it cause huge health care costs, sufferings and death for youngsters with suicidal thoughts. The question is if it is the OTC sale at non-pharmacy-outlets or the Rx part of the sale that cause problems with self-poisoning. Initiatives to reduce the opportunities for people who are suicidal, to obtain mainly paracetamol in large quantities is advisable. This could be done with restrictive prescription of paracetamol in large quantities. It would also be better if paracetamol only were prescribed in blister packages and information given to users how to keep them safe at home.

#### 4.14 Conclusion

The present cross sectional population study found that the majority of the adult OTC analgesic users follow the guidelines for use of OTC analgesics. Most of the OTC analgesics were used seldom and in a small daily dose. A small number of the participants report adverse effect from OTC analgesics. It is headache, muscle and joint pain and backache that is the main reasons for using OTC analgesics. The majority of the OTC analgesic users buy there OTC analgesics at the pharmacy. Very few purchased OTC analgesics on internet or abroad. It seems that it is younger men, those with good health, high education and those who are smoking that buy more OTC analgesics at non-pharmacy outlets. Older people, women with low education and people who report bad health, inform that they use pharmacy more.

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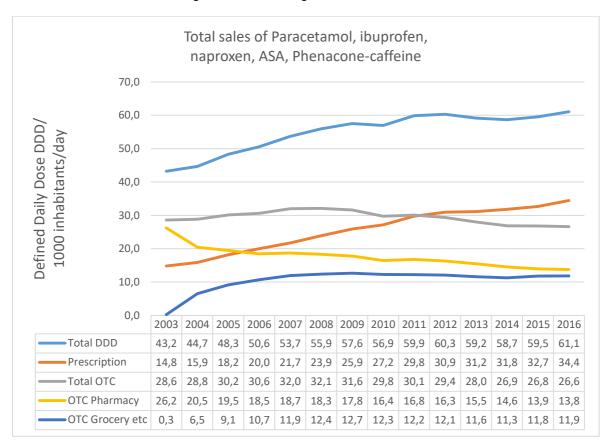
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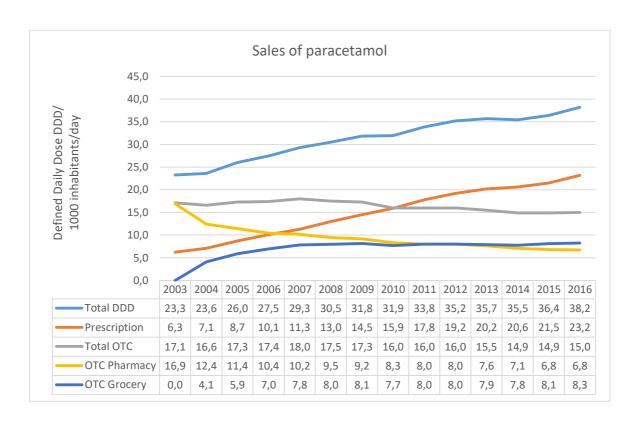
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The same Diagrams as shown on page 24, figure 5 and 6, with detailed figures. Those tables are summarised from the figures in Table 1, page 22. Source: Wholesaler-based drug statistics, Norwegian Institute of Public Health, NIPH







ulluci sekciscii					
The form will be read electronically. Please use a blue or black pen					
You can not use comas, use upper-case letters.					
2007 - 2008 Confidential					
2007 2000 CONTRACTICAL					
HEALTH AND DISEASES	Below you find a list of different situations.				
How do you in general consider your own	Have you experienced some of them in the last we				
health to be?	(including today)? (Tick once for each complaint)  No Little Pretty Very				
☐ Very good	complaint complaint much much				
☐ Good	Sudden fear without reason $\square$ $\square$ $\square$				
☐ Neither good nor bad	You felt afraid or				
□ Bad	WONTED				
□ Very bad +	Faintness or dizziness				
	upset				
How is your health compared to others in your age?	Easily blamed yourself				
☐ Much better	Sleeping problems				
☐ A little better	Depressed, sad				
About the same	You felt useless,				
☐ A little worse	worthless				
☐ Much worse	Feeling that life is a struggle \( \square\)				
Age first	Feeling of hopelessness with regard to the future				
Do you have, or have you had? Yes No time	regard to the ruttire				
Heart attack	USE OF HEALTH SERVICES				
Angina pectoris	Have you during the past year visited:				
Stroke/brain hemorrhage	If YES; how many times?  Yes No. No. of time				
Atrial fibrillation	General practitioner (GP)				
High blood pressure	Psychiatrist/psychologist				
Osteoporosis	Medical specialist outside hospital				
Asthma	(other than general practitioner/psychiatrist)				
Chronic bronchitis/Emphysyma/COPD 🗆 🗀 📗	Physiotherapist				
Diabetes mellitus	Chiropractor				
Psychological problems (for which you have sought help)	Alternative medical practitioner				
Low metabolism	(homeopath, acupuncturist, foot zone therapist, herbal medical practitioner, laying on hands				
Kidney disease, not including urinary	practitioner, healer, clairvoyant, etc.)  Dentist/dental service				
Migraine					
Do you have persistent or constantly recurring	Have you during the last 12 months been to a hospital?  Yes No No. of time				
pain that has lasted for 3 months or more?	Admitted to a hospital				
☐ Yes ☐ No	Had consultation in a hospital without admission;				
How often have you suffered from sleeplessness during	At psychiatric out-patient clinic				
the last 12 months?					
Nover or just a few times	At another out-patient clinic				
☐ Never, or just a few times ☐ 1-3 times a month	At another out-patient clinic				
<ul> <li>□ Never, or just a few times</li> <li>□ 1-3 times a month</li> <li>□ Approximately once a week</li> </ul>	Have you undergone any surgery during the last 3 years  Yes No				

USE OF MEDICINE  Do you take, or have you taken some of the			ne	Who do you live with? (Tick for each question
following medications?	(Tick onc	e for each		and give the number)  ———————————————————————————————————
L	Never	Now Earlier	Age first	Spouse/cohabitant
Drugs for high blood pre			time	Other persons older than 18 years
Lipid lowering drugs				Persons younger than 18 years
Drugs for heart disease			Tick for relatives who have or have had	
Diuretics		Parents Children Siblin		
Medications for				Myocardial infarction
osteoporosis				Myocardial infarction before 60 years
nsulin				Angina pectoris
Tablets for diabetes				Stroke/brain haemorrhage
Drugs for metabolism Thyroxine/levaxin				Osteoporosis
			lea waad	Stomach/duodenal ulcer
How often have you du the following medicati				Asthma
Not used	Less than	Every	en muser i marie estado de la Companya de la Compa	Diabetes mellitus
the last	every	week, but		Dementia
4 weeks Painkillers on	week	not daily	Daily	Psychological problems
prescription				Drugs/substance abuse
Painkillers non-		_	_	
prescription				Do you have enough friends who can give you help when you need it?
Sleeping pills 🗌				☐ Yes ☐ No
Tranquillizers				Do you have enough friends whom you can talk confidentially with?
Antidepressants				☐ Yes ☐ No
State the names of all				How often do you normally take part in
on prescription and no	n-prescri	est 4 wool	s you	organised gatherings, e.g. sports clubs, politica meetings, religious or other associations?
on prescription and no have used regularly du Do not include vitamins	ring the l	ast 4 weel , herbs, na	ks. Itural	organised gatherings, e.g. sports clubs, politica meetings, religious or other associations?   Never, or just a few times a year
on prescription and no have used regularly du Do not include vitamins	ring the l	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?
on prescription and no have used regularly du Do not include vitamins	ring the l	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month  Approximately once a week
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month  Approximately once a week  More than once a week
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week  WORK, SOCIAL SECURITY AND INCOME What is the highest level of education you have
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week  WORK, SOCIAL SECURITY AND INCOME What is the highest level of education you have completed? (Tick one)
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week  WORK, SOCIAL SECURITY AND INCOME What is the highest level of education you have completed? (Tick one) Primary, 1-2 years secondary school
on prescription and no have used regularly du Do not include vitamins	ring the l , minerals	ast 4 weel , herbs, na	ks. Itural	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week  WORK, SOCIAL SECURITY AND INCOME What is the highest level of education you have completed? (Tick one) Primary, 1-2 years secondary school Vocational school
on prescription and no have used regularly du Do not include vitamins	iring the l	ast 4 week, herbs, na	cs.	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week WORK, SOCIAL SECURITY AND INCOME What is the highest level of education you have completed? (Tick one) Primary, 1-2 years secondary school Vocational school High secondary school (A-level)
on prescription and no have used regularly du Do not include vitamins remedies, other nutrition of the space is not enough for paper of your own.	r all medicat	ions, use an a	additional	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week  WORK, SOCIAL SECURITY AND INCOME  What is the highest level of education you have completed? (Tick one) Primary, 1-2 years secondary school Vocational school High secondary school (A-level) College/university less than 4 years College/university 4 years or more  What is your main occupation/activity? (Tick one)
on prescription and no have used regularly du Do not include vitamins remedies, other nutrition of the space is not enough for paper of your own.  When attending the su asked whether you have	r all medicat	ions, use an a	additional	meetings, religious or other associations?  Never, or just a few times a year  1-2 times a month Approximately once a week More than once a week  WORK, SOCIAL SECURITY AND INCOME What is the highest level of education you have completed? (Tick one) Primary, 1-2 years secondary school Vocational school High secondary school (A-level) College/university less than 4 years College/university 4 years or more What is your main occupation/activity? (Tick one) Full time work Housekeeping
on prescription and no have used regularly du Do not include vitamins remedies, other nutrition of the space is not enough for	r all medicat rvey centre e used ant ours. If yo e the name	ions, use an a	additional be	<ul> <li>Never, or just a few times a year</li> <li>1-2 times a month</li> <li>Approximately once a week</li> <li>More than once a week</li> <li>WORK, SOCIAL SECURITY AND INCOME</li> <li>What is the highest level of education you have completed? (Tick one)</li> <li>Primary, 1-2 years secondary school</li> <li>Vocational school</li> <li>High secondary school (A-level)</li> <li>College/university less than 4 years</li> <li>College/university 4 years or more</li> <li>What is your main occupation/activity? (Tick one)</li> </ul>

Do you receive any of the following benefits?	How hard do you exercise on average?
☐ Old-age, early retirement or survivor pension	☐ Easy- do not become short-winded or sweaty
☐ Sickness benefit (are in a sick leave)	☐ You become short-winded and sweaty
☐ Rehabilitation benefit	☐ Hard- you become exhausted
☐ Full disability pension	5 b l bi d
☐ Partial disability pension	For how long time do you exercise every time on average?
☐ Unemployment benefits	Less than 15 minutes 30-60 minutes
☐ Transition benefit for single parents	☐ 15-29 minutes ☐ More than 1 hour
☐ Social welfare benefits	ALCOHOL AND TOBACCO
What was the households total taxable income last	
year? Include income from work, social benefits	How often do you drink alcohol?
and similar	Never
$\square$ Less than 125 000 NOK $\square$ 401 000-550 000 NOK	☐ Monthly or more infrequently
☐ 125 000-200 000 NOK ☐ 551 000-700 000 NOK	2-4 times a month
☐ 201 000-300 000 NOK ☐ 701 000 -850 000 NOK	2-3 times a week
☐ 301 000-400 000 NOK ☐ More than 850 000 NOK	☐ 4 or more times a week
Do you work outdoors at least 25% of the time, or	How many units of alcohol (a beer, a glass of wine or
in cold buildings (e.g. storehouse/industry buildings)?	a drink) do you usually drink when you drink alcohol?
Yes No	☐ 1-2 ☐ 5-6 ☐ 10 or more
2 163 2 160	□ 3-4 □ 7-9
PHYSICAL ACTIVITY	How often do you drink 6 units of alcohol or more in one occasion?
If you have paid or unpaid work, which statement describes your work best?	☐ Never
	Less frequently than monthly
	☐ Monthly
☐ Work that requires a lot of walking	☐ Weekly
(e.g. shop assistant, light industrial work, teaching)	☐ Daily or almost daily
☐ Work that requires a lot of walking and lifting	Daily of almost daily
(e.g. postman, nursing, construction)	Do you smoke sometimes, but not daily?
☐ Heavy manual labour	☐ Yes ☐ No
Describe your exercise and physical exertion in	D
leisure time. If you activity varies much, for example between summer and winter, then give	Do you/did you smoke daily?
an average. The question refers only to the last	☐ Yes, ☐ Yes, ☐ Never now previously
<u>year</u> . (Tick the one that fits best)	If you previously smoked daily, how long is it
$\square$ Reading, watching TV, or other sedentary	since you stopped?
activity.	Number of
<ul> <li>Walking, cycling, or other forms of exercise at least 4 hours a week (here including walking or</li> </ul>	years  If you currently smoke, or have smoked before:
cycling to place of work, Sunday-walking, etc.)	How many cigarettes do you or did you usually
$\ \square$ Participation in recreational sports, heavy gardening,	smoke per day?
etc. (note:duration of activity at least 4 hours a week)	Number of cigarettes
<ul> <li>Participation in hard training or sports competitions, regularly several times a week.</li> </ul>	Total Indian Indian
	How old were you when you began smoking daily?  Number of
How often do you exercise? (With exercise we mean for example walking, skiing, swimming or	years
training/sports)	How many years in all have you smoked daily?
☐ Never	Number of
Less than once a week	years
☐ Once a week	Do you use or have you used snuff or chewing tobacco?
2-3 times a week	☐ No, never ☐ Yes, sometimes
Approximately every day	☐ Yes, previously ☐ Yes, daily  十
•	

DIET	QUESTONS FOR WOMEN
Do you usually eat breakfast every day?	Are you currently pregnant?
☐ Yes ☐ No	☐ Yes ☐ No ☐ Uncertain
How many units of fruits or vegetables do you eat on average per day? (units means for example	How many children have you given birth to?
a fruit, a cup of juice, potatoes, vegetables)	If you have given high fill in for each childs
Number of units	If you have given birth, fill in for each child: birth year, birth weight and months of breastfeeding (Fill in the best you can)
How many times per week do you eat hot dinner?  Number	Child Birth year Birth weight in grams breastfeeding
How often do you usually eat these products? (Tick once for each line)	2
0-1 2-3 1-3 4-6 1-2 times/ times/ times/ times/ mth mth week week day	4
Potatoes	5
Meat (not processed)	Poster and the black
Processed meat (sausages/meatloaf/meatballs)	During pregnancy, have you had high blood pressure?
Fruits, vegetables, berries	☐ Yes ☐ No
Lean fish	If yes, which pregnancy?
Fat fish	☐ The first ☐ Second or later
How much do you normally drink the following? (Tick once for each line)	During pregnancy, have you had proteinuria?
1-6 1 2-3 4 or more Rarely/ glasses glasses glasses	Yes No
never /week /day /day /day	If yes, which pregnancy?
Milk, curdled milk, yoghurt	☐ The first ☐ Second or later
Juice	Were any of your children delivered prematurely
Soft drinks	(a month or more before the due date) because
with sugar	
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No
with sugar	(a month or more before the due date) because of preeclampsia?
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started
How many cups of coffee and tea do you drink daily? (Put 0 for the types you do not drink daily)  Number of cups  Filtered coffee	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?
With sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started
With sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?  Age  Do you currently use any prescribed drug influencing the menstruation?
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?  Age
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?  Age  Do you currently use any prescribed drug influencing the menstruation?
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?  Age
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?  Age How our currently use any prescribed drug influencing the menstruation?  Oral contraceptives, hormonal IUD or similar Hormone treatment for menopausal problems Yes No  When attending the survey centre you will get a questionnaire about menstruation and possible use
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child    How old were you when you started menstruating?  Age
with sugar	(a month or more before the due date) because of preeclampsia?  Yes No  If yes, which child?  1st child 2nd child 3rd child 4th child 5th child 6th child  How old were you when you started menstruating?  Age How our currently use any prescribed drug influencing the menstruation?  Oral contraceptives, hormonal IUD or similar Hormone treatment for menopausal problems Yes No  When attending the survey centre you will get a questionnaire about menstruation and possible use

In the first questionnaire you answered that yo	ou had used non-prescription painkillers (analgesic)
medications in the last 4 weeks. Here are so	me follow-up questions we hope you will answer.
What types of non-prescription painkiller medications have you used?	Phenazone with caffeine: (Antineuralgica, Fanalgin, Fenazon-koffein, Fenazon-koffein sterke)
	Not used
Paracetamol: (Pamol, Panodil, Paracet, Paracetamol, Pinex)	Less than every week
Not used	Every week, but not daily
	daily
Less than every week	How much you take usually daily
Every week, but not daily	when you use the medications?
☐ daily	(number of tablets)
How much you take usually daily when you use the medications? (number of tablets, suppositories)	For which complains do you use non- prescription painkiller drugs? (multiple ticks are possible)
	Headache
AcetylsalicylatesAspirin,Dispril, Globoid)	Menstrual pain
Not used	Migraine
Less than every week	Back pain
Every week, but not daily	Muscle/joint pain
Daily	Tooth pain
How much you take usually daily	Other
when you use the medications? (number of tablets)	□ Other
(number of tablets)	Do you think you have experienced side
Ibuprofen: (Ibumetin, Ibuprofen, Ibuprox, Ibux)	effects of some of the medications? (tick
Not used	once for each line) Yes No
Less than every week	Paracetamol
Every week, but not daily	Acetylsalicylates
	Ibuprofen
□ Daily     How much you take usually daily	Naproxen
when you use the medications? (number of tablets, suppositories)	Phenazone with caffeine
	Where do you use to buy such medications?
Naproxen: (Ledox, Naproxen)	Pharmacy
Not used	Grocery
Less than every week	Patrol stations
Every week, but not daily	Abroad
Daily	Internet
How much you take usually daily	_ meme
when you use the medications? (number of tablets)	Do you combine the treatment with the use of prescribed pain-relief medications?
L	_ 163 _ NO
24	+

3 out of 12984 excluded from your selection, did not consent to medical research.

### **GENERAL INFORMATION - GENERAL INFORMATION**

YEAR\_BORN\_T6 - Birth year

MONTH\_BORN\_T6 - Birth month

AGE\_T6 - Age per 31.12.2007

SEX\_T6 - Sex

1: Male

0: Female

MARITAL\_STATUS\_T6 - Marital status

1: Single

2: Married

3: Widow/Widower

4: Divorced

5: Separated

6: Registered partnership

7: Separeted partnership

8: Divorced partnership Q2\_IMPORTED\_T6 - Q2-imported

1: Yes

### PHYSICAL EXAMINATION - PHYSICAL EXAMINATION

HEIGHT\_T6 - Body height in cm measured at screening WEIGHT\_T6 - Body weight in kg measured at screening

# **HEALTH AND DISEASES** - **HEALTH AND DISEASES**

HEALTH\_T6 - How do you in general consider your own health to be?

5: Excellent

4: Good

3: Neither good nor bad

2: Bad

1: Very bad

HEALTH\_COMPARED\_T6 - How is your health now compared to others of your age?

5: Much better

4: A little better

3: About the same

2: A little worse

1: Much worse
MIGRAINE\_T6 - Have you ever had, or do you still have migraine?

1: Yes

0: No

CHRONIC\_PAIN\_T6 - Do you have persistent or constantly recurring pain that has lasted for 3 months or

more?

1: Yes 0: No

# **USE OF HEALTH SERVICES - USE OF HEALTH SERVICES**

CONSULTATION\_GP\_T6 - Have you during the past year visited a general practitioner (GP)?

1: Yes

0: No

CONSULTATION\_GP\_TIMES\_T6 - If you have visited a general practitioner (GP) the past year, how many visits have you made?

### **USE OF MEDICINE - USE OF MEDICINE**

PAINKILLERS\_PRESC\_4WEEKS\_T6 - How often have you used painkillers with prescription during the last 4 weeks?

1: Not used

2: Less frequently than every week

3: Every week, but not daily

4: Daily

PAINKILLERS\_NOPRÉSC\_4WEEKS\_T6 - How often have you used painkillers without prescription during the last 4 weeks?

1: Not used

2: Less frequently than every week

3: Every week, but not daily

4: Daily

### FAMILY AND FRIENDS - FAMILY AND FRIENDS

LIVE\_WITH\_SPOUSE\_T6 - Do you live with a spouse/partner?

1: Yes 0: No

# WORK, SOCIAL SECURITY PAYMENTS AND INCOME - WORK, SOCIAL SECURITY PAYMENTS AND INCOME

EDUCATION\_T6 - What is the highest levels of education you have completed?

1: Primary/secondary school, modern secondary school

2: Technical school, vocational school, 1-2 years senior high school

3: High school diploma

4: College/university less than 4 years

5: College/university 4 years or more

OCCUPATION\_FULLTIME\_T6 - Is your main occupation/activity - full time work?

1: Yes

OCCUPATION\_PARTTIME\_T6 - Is your main occupation/activity - part time work?

1: Yes

OCCUPATION\_UNEMPLOYED\_T6 - Is your main occupation/activity - unemployed

1: Yes

OCCUPATION\_HOUSEKEEPING\_T6 - Is your main occupation/activity - housekeeping

1: Yes

OCCUPATION\_RETIRED\_T6 - Is your main occupation/activity - retired/benefit recipient?

1: Yes

OCCUPATION\_STUDENT\_T6 - Is your main occupation/activity - student/military service?

1: Yes

HOUSEHOLD\_INCOME\_AVERAGE\_T6 - What was the households total taxable income last year? Include income from work, social benefits and similar.

1: 55 100 NOK 2: 165 100 NOK

3: 250 300 NOK

4: 349 800 NOK

5: 467 400 NOK

6: 626 400 NOK

7: 771 300 NOK

8: 1 183 200 NOK

#### PHYSICAL ACTIVITY - PHYSICAL ACTIVITY

PHYSICAL\_ACTIVITY\_WORK\_T6 - If you have paid or unpaid work, which statement describes your work best?

1: Mostly sedentary work? (e.g. office work, mounting)

2: Work that requires a lot of walking? (e.g. shop assistant, light industrial work, teaching)

3: Work that requires a lot of walking and lifting? (e.g. postman, nursing, construction)

4: Heavy manual labour? (e.g. forestry, heavy farmwork, heavy construction)

PHYS\_ACTIVITY\_LEISURE\_T6 - Exercise and physical exertion in leisure time. If your activity varies much, for example between summer and winter, then give an average. The question refer only to the last twelwe months.

1: Reading, watching TV, or other sedentary activity?

2: Walking, cycling, or other forms of exercise at least 4 hours a week? (including walking or cycling to place of work, Sunday-walking, etc.)

3: Participation in recreational sports, heavy gardening, etc.? (note: duration of activity at least 4 hours a week).

4: Participation in hard training or sports competitions, regularly several times a week?

EXERCISE\_T6 - How often do you exercise (i.e walking, skiing, swimming or training/sports)?

1: Never

2: Less than once a week

3: Once a week

4: 2-3 times a week

5: Approximately every day

EXERCISE\_LEVEL\_T6 - If you exercise - how hard do you exercise?

1: Easy - you do not become shortwinded or sweaty

2: You become shortwinded and sweaty

3: Hard - you become exhausted

EXERCISE\_DURATION\_T6 - For how long time do you exercise? (give an average)

1: Less than 15 minutes

2: 15-29 minutes

3: 30-60 minutes

4: More than 1 hour

### <u>ALCOHOL AND TOBACCO - ALCOHOL AND TOBACCO</u>

ALCOHOL\_FREQUENCY\_T6 - How often do you usually drink alcohol? 1: Never 2: Monthly or less frequently 3: 2-4 times a month 4: 2-3 times a week 5: 4 or more times a week ALCOHOL\_UNITS\_T6 - How many units of alcohol (a beer, a glass of wine or a drink) do you usually drink when you drink alcohol? 1: 1-2 2: 3-4 5-6 3: 4: 7-9 5: 10 or more ALCOHOL 6UNITS T6 - How often do you drink 6 units alcohol or more in one occasion? 1: Never 2: Less frequently than monthly 3: Monthly 4: Weekly 5: Daily or almost daily SMOKE\_DAILY\_T6 Do you/did you smoke daily? 1: Yes, now 2: Yes, previously 3 · Never

# **CONSUMPTION OF OTC ANALGESICS - Q2 - CONSUMPTION OF OTC**

# **ANALGESICS - Q2**

```
PARACETAMOL_T6
                                   - Which OTC analgesics have you used? - Paracetamol (Pamol, Panodil, Paracet,
Paracetamol, Pinex)?
                 1:
                         Not used
                 2:
                         Not every week
                         Every week, but not daily
                 3:
                 4:
                         Daily
        PARACETAMOL_DOSE_T6
                                           - What is your normal daily dose when taking paracetamol? (Number of
tablets, suppositories)?
        ACETYL_SALICYLIC_ACID_T6
                                           - Which OTC analgesics have you used? - Acetyl salicylic acid (Aspirin,
Dispril, Globoid)
                 1:
                         Not used
                 2:
                         Not every week
                 3:
                         Every week, but not daily
                 4:
                         Daily
        ACETYL_SALICYLIC_ACID_DOSE_T6
                                                    - What is your normal daily dose when taking acetyl salicylic
acid? (Number of tablets)
        IBUPROFEN_T6
                          - Which OTC analgesics have you used? - Ibuprofen (Ibumetin, Ibuprofen, Ibuprox, Ibux)
                 1:
                         Not used
                         Not every week
                 2:
                 3:
                         Every week, but not daily
                 4:
                         Daily
        IBUPROFEN_DOSE_T6
                                   - What is your normal daily dose when taking ibuprofen? (Number of tablets)
        NAPROXEN_T6
                          - Which OTC analgesics have you used? - Naproxen (Ledox, Naproxen)
                 1:
                         Not used
                 2:
                         Not every week
                 3:
                         Every week, but not daily
                         Daily
        NAPROXEN_DOSE_T6
                                  - What is your normal daily dose when taking naproxen? (Number of tablets)
        PHENAZON_CAFFEINE_T6
                                           - Which OTC analgesics have you used? - Phenazone-caffeine
(Antineuralgica, Fanalgin, Fenazon-koffein, Fenazon-koffein sterke)
                         Not used
                 1:
                 2:
                         Not every week
                 3:
                         Every week, but not daily
                         Daily
        PHENAZON_CAFFEINE_DOSE_T6 - What is your normal daily dose when taking phenazone-caffeine?
(Number of tablets)
                                                                                                              3.
```

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REASON_OTC_HEADACHE_T6
                                 - Reason for taking OTC analgesics - Headache
        REASON_OTC_MENS_PAINS_T6 - Reason for taking OTC analgesics - Menstrual pain
                1:
                        Yes
        REASON_OTC_MIGRAINE_T6
                                         - Reason for taking OTC analgesics - Migraine
                1:
                        Yes
        REASON_OTC_BACK_ACHE_T6
                                         - Reason for taking OTC analgesics - Back ache
                        Yes
        REASON_OTC_MUSCLE_JOINT_T6
                                                 - Reason for taking OTC analgesics - Muscle ache/joint pains
                        Yes
        REASON_OTC_TOOTH_PAIN_T6 - Reason for taking OTC analgesics - Tooth pain
                        Yes
        REASON_OTC_OTHER_T6
                                         - Reason for taking OTC analgesics - Others than Headache, Menstrual
pains, Migraine, Back ache, Muscle ache/joint pains, Tooth pain
                        Yes
        SIDE_EFFECTS_PARACETAMOL_T6
                                                 - Have you experienced side effects taking the OTC analgesics -
Paracetamol?
                1:
                        Yes
                0.
                        No
        SIDE EFFECTS ASPIRIN T6
                                         - Have you experienced side effects taking the OTC analgesics - Acetyl
salicylic acid?
                1:
                        Yes
                0:
        SIDE_EFFECTS_IBUPROFEN_T6
                                        - Have you experienced side effects taking the OTC analgesics -
Ibuprofen?
                1:
                        Yes
                0:
                        No
        SIDE_EFFECTS_NAPROXEN_T6
                                        - Have you experienced side effects taking the OTC analgesics -
Naproxen?
                1:
                        Yes
                0:
                        Nο
        SIDE_EFFECT_PHENAZONE_CAFF_T6
                                                 - Have you experienced side effects taking the OTC analgesics -
Phenazone-caffeine?
                        Yes
                0:
                        Nο
        BUY_OTC_PHARMACY_T6
                                         - Where do you normally buy OTC analgetics? Pharmacy
                        Yes
                                         - Where do you normally buy OTC analgetics? Supermarket
        BUY_OTC_SUPERMARKET_T6
                        Yes
        BUY_OTC_PETROL_STATION_T6 - Where do you normally buy OTC analgetics? Petrol station
                        Yes
                                 - Where do you normally buy OTC analgetics? Abroad
        BUY_OTC_ABROAD_T6
                        Yes
        BUY_OTC_INTERNET_T6 - Where do you normally buy OTC analgetics? Internet
                        Yes
        COMBINE_OTC
                       _RX_T6
                                 - Do you combine OTC analgetics with Rx analgetics?
                        Yes
                1:
                0:
                        No
```